Volume 24 Supplement 1 March 2015 ISSN 0960 9776

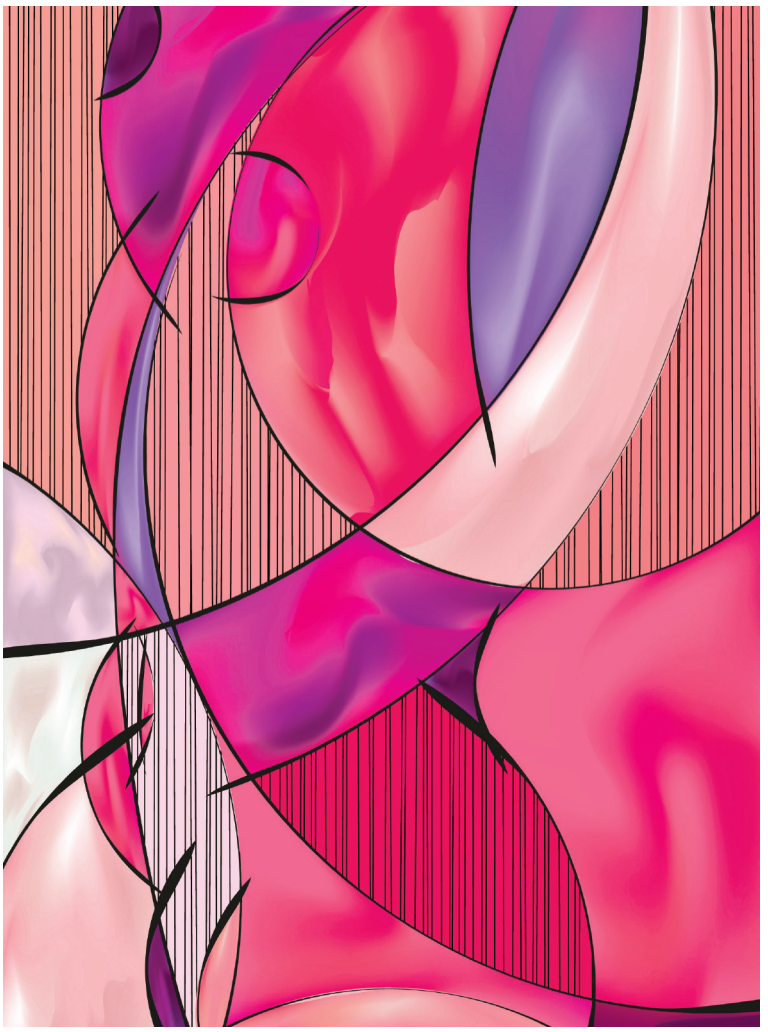
ELSEVIER

IN THIS SUPPLEMENT

PRIMARY THERAPY OF EARLY BREAST CANCER
14TH ST.GALLEN INTERNATIONAL BREAST CANCER CONFERENCE
VIENNA, AUSTRIA, 18–21 MARCH 2015

THE BREAST

An Associate Journal of the Australasian Society for Breast Disease
Affiliated with the European Society of Breast Cancer Specialists
Official Journal of the Breast Centres Network



For HR+, early-stage invasive breast cancer

Confidence begins with a highly accurate risk assessment

Introducing Prosigna®: Guide your decisions with the power of PAM50-based molecular subtypes[1]

- Prosigna translates a patient's underlying tumor biology into intrinsic subtypes and an individualized risk assessment
- Prosigna's PAM50-based genomic assay quickly and accurately provides prognostic information you need
- Prosigna is CE-marked and FDA 510(k) cleared for use in local qualified laboratories
- Obtain precise, reproducible results from formalin-fixed paraffin-embedded (FFPE) tissue in as few as 3 days

To find out more please visit the Prosigna Booth 16

or visit Prosigna.com

References: 1. Prosigna [Package Insert]. Seattle, WA: NanoString Technologies, Inc., 2014.

Prosigna is indicated for use in postmenopausal women with hormone receptor–positive, node-negative or node-positive early-stage (stages I and II) breast cancer to be treated with adjuvant endocrine therapy.

Special conditions for use:
Prosigna is not intended for diagnosis, to predict or detect response to therapy, or to help select the optimal therapy for patients.

nanoString TECHNOLOGIES

prosigna®
Breast cancer gene signature assay

Proceed with **CONFIDENCE**

THE BREAST

PRIMARY THERAPY OF EARLY BREAST CANCER

Evidence, Controversies, Consensus

14th St.Gallen International Breast Cancer Conference

Vienna, Austria, 18–21 March 2015

Conference Chairpersons
Alan S. Coates, Melbourne, Australia
Richard Gelber, Boston, USA
Michel Gnant, Vienna, Austria
Aron Goldhirsch, Lugano, Switzerland / Milan, Italy
Martine Piccart, Brussels, Belgium
Hans-Jörg Senn, St.Gallen, Switzerland
Beat Thürlimann, St.Gallen, Switzerland

THE BREAST

www.elsevier.com/brst
An Associate Journal of the Australasian Society for Breast Disease: www.asbd.org.au
Affiliated with the European Society of Breast Cancer Specialists: www.eusoma.org
Official Journal of Breast Centres Network: www.BreastCentresNetwork.org
Amsterdam . Boston . London . New York . Oxford . Paris . Philadelphia . San Diego . St Louis

ELSEVIER

Aims and Scope

The Breast is an international, multidisciplinary journal for clinicians, which focuses on translational and clinical research for the advancement of breast cancer prevention and therapy. The Editors welcome the submission of original research articles, systematic reviews, viewpoint and debate articles and correspondence on all areas of pre-malignant and malignant breast disease, including:

- Surgery
- Medical oncology and translational medicine
- Radiation oncology
- Breast endocrinology
- Epidemiology and prevention
- Gynecology
- Imaging, screening and early diagnosis
- Pathology
- Psycho-oncology and quality of life
- Advocacy
- Supportive and palliative care
- Nursing
- Research and management in countries with limited resources

The Breast is a valuable source of information for surgeons, medical oncologists, gynecologists, radiation oncologists, endocrinologists, epidemiologists, radiologists, pathologists, breast care nurses, breast cancer advocates, psychologists and all those with a special interest in breast cancer.

Author enquiries
You can track your submitted article at http://help.elsevier.com/app/answers/detail/a_id/89/p/8045/. You can track your accepted article at http://www.elsevier.com/trackarticle. You are also welcome to contact Customer Support via http://support.elsevier.com.

Publication information. *The Breast* (ISSN 0960-9776). For 2015, volume 24 (6 issues) is scheduled for publication. Subscription prices are available upon request from the Publisher or from the Elsevier Customer Service Department nearest you or from this journal's website (http://www.elsevier.com/brst). Further information is available on this journal and other Elsevier products through Elsevier's website: (http://www.elsevier.com). Subscriptions are accepted on a prepaid basis only and are entered on a calendar year basis. Issues are sent by standard mail (surface within Europe, air delivery outside Europe). Priority rates are available upon request. Claims for missing issues should be made within six months of the date of dispatch.
Orders, claims, and journal enquiries: Please contact the Elsevier Customer Service Department nearest you:
St. Louis: Elsevier Customer Service Department, 3251 Riverport Lane, Maryland Heights, MO 63043, USA; phone: (800) 6542452 [toll free within the USA]; (+1) (314) 4478871 [outside the USA]; fax: (+1) (314) 4478029; e-mail: JournalsCustomerService-usa@elsevier.com
Oxford: Elsevier Customer Service Department, The Boulevard, Langford Lane, Kidlington, Oxford OX5 1GB, UK; phone: (+44) (1865) 843434; fax: (+44) (1865) 843970; e-mail: JournalsCustomerServiceEMEA@elsevier.com
Tokyo: Elsevier Customer Service Department, 4F Higashi-Azabu, 1-Chome Bldg, 1-9-15 Higashi-Azabu, Minato-ku, Tokyo 106-0044, Japan; phone: (+81) (3) 5561 5037; fax: (+81) (3) 5561 5047; e-mail: JournalsCustomerServiceJapan@elsevier.com
Singapore: Elsevier Customer Service Department, 3 Killiney Road, #08-01 Winsland House I, Singapore 239519; phone: (+65) 63490222; fax: (+65) 67331510; e-mail: JournalsCustomerServiceAPAC@elsevier.com

USA mailing notice: *The Breast* (ISSN 0960-9776) is published bimonthly by Elsevier Ltd. (P.O. Box 211, 1000 AE Amsterdam, The Netherlands). Periodicals postage paid at Jamaica, NY 11431 and additional mailing offices.
USA POSTMASTER: Send address changes to *The Breast*, Elsevier Customer Service Department, 3251 Riverport Lane, Maryland Heights, MO 63043, USA.

AIRFREIGHT AND MAILING in USA by Air Business Ltd., c/o Worldnet Shipping Inc., 156-15, 146th Avenue, 2nd Floor, Jamaica, NY 11434, USA.

The Breast has no page charges.

The paper used in this publication meets the requirements of ANSI/NISO Z39.48-1992 (Permanence of Paper).

Printed in the United Kingdom by Henry Ling Limited, at the Dorset Press, Dorchester, DT1 1HD.

Next St.Gallen International Breast Cancer Conferences

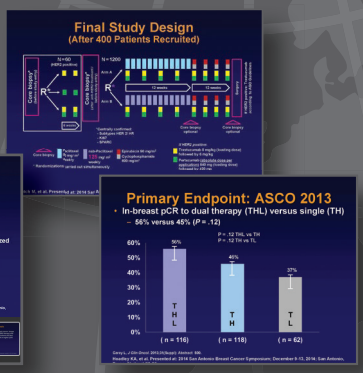
2017 15th St.Gallen International Breast Cancer Conference
Primary Therapy of Early Breast Cancer
15–18 March 2017

2019 16th St.Gallen International Breast Cancer Conference
Primary Therapy of Early Breast Cancer
13–16 March 2019

YOUR GLOBAL ONLINE EDUCATION RESOURCE IN ONCOLOGY

ABOUT prIME ONCOLOGY

*prIME Oncology is a global **pr**ofessional **I**ndependent **M**edical **E**ducation organization specializing in educational activities for physicians who treat patients with cancer. With the ultimate goal of improving patient outcomes, prIME Oncology provides evidence-based, state-of-the-art educational activities that assist oncology clinicians in making up-to-date and appropriate treatment decisions.*



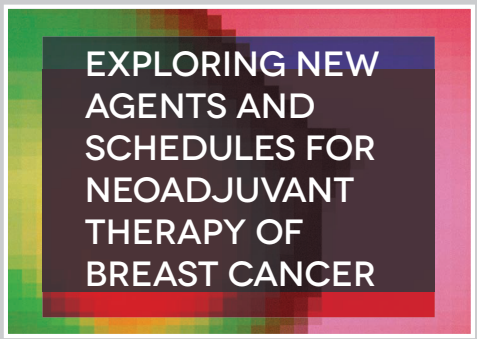
- *Interactive presentations*
- *Clinical cases*
- *Expert interviews*
- *Newsletters*
- *Downloadable slides*
- *Podcasts*

www.prIMEoncology.org

prIME oncology

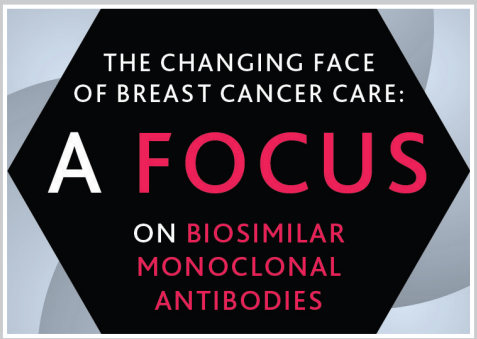
professional • independent • medical • education

Join prIME Oncology at the 14th St Gallen International Breast Cancer Conference



Thursday, 19 March 2015, 12.45-13.45

Downloadable slides will be available online in April 2015 at:
www.prIMEoncology.org/Neoadjuvant_Vienna2015_PDS



Thursday, 19 March 2015, 18.15-19.45

Downloadable slides and Webcast will be available online in April 2015 at:
www.prIMEoncology.org/Biosimilars_Vienna2015_Webcast

Friday, 20 March 2015, 17.30-19.10

Downloadable slides will be available online in April 2015 at:
www.prIMEoncology.org/Breast_Vienna2015_PDS

Contents

CONFERENCE PROGRAMME WEDNESDAY (overview)

Wednesday, 18 March 2015

07.30 Conference venue opens

08.00

09.00 — 08.30 – 10.00
International Society of Cancer Prevention (ISCaP) workshop
(recommended related pre-conference session)

10.00

11.00 — 10.30 – 12.00
Industry sponsored satellite symposium

12.00

13.00 — 12.30 – 14.00
Industry sponsored satellite symposium

14.00

15.00 — 14.30 – 15.30 Opening ceremony
15.00 Opening address
by the St. Gallen 2015 Award Winner

16.00 — 15.30 – 17.00
Session 1: News since St. Gallen 2013
Chairs: Alan S. Coates (Australia),
Hans-Jörg Senn (Switzerland)

17.00 — 17.00 – 17.30 Coffee break, exhibition

18.00 — 17.30 – 18.45
Session 2: Biology of breast cancer I:
Bridging the gap between high throughput technologies and breast cancer treatment in real life
Chairs: C. Kent Osborne (USA), Beat Thürlimann (CH)

19.00

19.00 – 21.00
Grand welcome reception
on the premises of the
Austria Center Vienna

20.00

CONFERENCE PROGRAMME THURSDAY (overview)

Thursday, 19 March 2015

07.30 Conference venue opens

08.00

09.00 — 08.30 – 09.45
Session 3: Biology of breast cancer II: Tumor heterogeneity and disease segmentation in breast cancer
Chairs: Fraser W. Symmans (USA), Jonas Bergh (Sweden)

10.00 — 09.45 – 10.45 Session 4: Biology of breast cancer III:
Genome remodeling and tumor microenvironment
Chairs: Mitch Dowsett (UK),
Daniel F. Hayes (USA)

11.00 — 10.45 – 11.20 Coffee break, poster exhibition I, exhibition

12.00 — 11.20 – 12.30
Session 5: Bridging clinic with biology: Emerging drugable pathways on the horizon
Chairs: Giuseppe Curigliano (Italy), Clifford A. Hudis (USA)

12.30 – 14.00 Lunch break, poster exhibition I, exhibition

13.00 — 12.45 – 13.45 Industry sponsored satellite symposium

14.00

15.00 — 14.00 – 15.00
Session 6: Primary prevention, metabolism and genetics
Chairs: John F. Forbes (Australia), Marco Colleoni (Italy)

16.00 — 15.00 – 16.15
Session 7: Beyond pathology of breast cancer in 2015
Chairs: Giuseppe Viale (Italy), Hervé Bonnefoi (France)

16.15 – 16.45 Coffee break, poster exhibition I, exhibition

17.00 — 16.45 – 18.00
Session 8: Primary systemic therapy of early breast cancer
Chairs: Eric Winer (USA), Giuseppe Curigliano (Italy)

18.00

19.00 — 18.15 – 19.45
Industry sponsored satellite symposium

20.00

CONFERENCE PROGRAMME FRIDAY (overview)

Friday, 20 March 2015

07.30 Conference venue opens

08.00

09.00 — 08.30 – 10.00
Session 9: Areas of controversy in surgery of early breast cancer, in special populations
Chairs: Michael Gnant (Austria), Masakazu Toi (Japan)

10.00 — 10.00 – 11.00 Session 10: Radiotherapy: Innovation and long term effects in early breast cancer
Chairs: Roberto Orecchia (Italy), Felix Sedlmayer (AT)

11.00

11.00 – 11.30 Coffee break, poster exhibition II, exhibition

12.00 — 11.30 – 12.30 Session 11: Adjuvant systemic treatment for individual patients I Endocrine therapies
Chairs: James N. Ingle (USA), Kathleen I. Pritchard (Canada)

12.30 – 14.00 Lunch break, poster exhibition II, exhibition

13.00 — 12.45 – 13.45
Industry sponsored satellite symposium

14.00 — 14.00 – 15.30 Session 12: Adjuvant systemic treatment for the individual patient II: Cytotoxic chemotherapy and targeted agents
Chairs: Ian Smith (UK), Sibylle Loibl (Germany)

15.00

15.30 – 16.00 Coffee break, poster exhibition II, exhibition

16.00 — 16.00 – 17.15 Session 13: Adjuvant systemic treatment for the individual patient III: Special patient populations and patient needs
Chairs: Martine Piccart-Gebhart (Belgium), Bent Ejlertsen (Denmark)

17.00

18.00 — 17.30 – 19.00
Industry sponsored satellite symposium

19.00

20.00

CONFERENCE PROGRAMME SATURDAY (overview)

Saturday, 21 March 2015

07.30 Conference venue opens

08.00

09.00 — 08.30 – 12.30
Session 14: St. Gallen International Consensus Session: Seeking consensus on evidence and opinions about the optimal treatment of early breast cancer
Chairs: Aron Goldhirsch (Switzerland/Italy) and Eric Winer (USA)
Secretary: Giuseppe Curigliano (Italy)

Coffee break in between

10.00

11.00

12.00

13.00 — 13.00
Annual meeting 2015 of the International Breast Cancer Study Group (IBCSG)
For members and registered IBCSG guests only

14.00

15.00

16.00

17.00

18.00

19.00

20.00

The Breast 24S1 (2015) S1–S25

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Speakers' Abstracts

Wednesday, 18 March 2015 **15.00–15.30**

Opening address by the St.Gallen 2015 Award Winner (Prof. Alan Coates, AUS)

PG 0.1
Evolution of the St. Gallen Consensus process for the optimal treatment of women with breast cancer

A.S. Coates*. *International Breast Cancer Study Group, IBCSG, Centennial Park, Australia*

Research over the last half century or so has created vast volumes of information on the treatment of early breast cancer. Several quite different methods have evolved in an attempt to distil this enormous resource into something useful to the patient and her doctor seeking best current management of the disease.

Statistically, the individual patient meta-analyses conducted by the Early Breast Trialists Collaborative Group (EBCTCG) under the leadership of Sir Richard Peto, provide methodologically solid syntheses of the results of almost all randomised clinical trials. This information is of obvious and enormous value. The weakness of the EBCTCG system is that it gives particular weight to older trials (which have accumulated more event endpoints) and is frequently unable to collect sufficient detail on the patients and tumours in the trials to allow assessment of whether the treatments which are better on average offer equal value to all currently definable patient subgroups. Although not updated recently, the United States National Institutes of Health consensus statements used a process in which experts presented data to a panel chosen not to be breast cancer experts for adjudication, avoiding potential conflicts of interest but also risking less than optimal interpretation.

Guidelines prepared by bodies such as the American Society of Clinical Oncology, the US National Comprehensive Cancer Network and similar bodies in other countries involve assessment and grading of evidence for treatment recommendations, but are inevitably focussed on the patterns of practice and ability to pay relevant to the respective host countries.

The biennial St. Gallen Consensus process differs from all of these. It uses an international panel to identify current issues across all aspects of the biology, pathology and treatment of early breast cancer. Selected speakers present the state of the art in all these fields. The multidisciplinary and international membership of the Panel ensures that the resulting guidelines will take due cognisance of the variable resource limitations in different countries. The Panel formulates and then votes on a series of questions designed to guide the general principles of management for the next two years. These summarised highlights are promptly published [1–6], and are widely influential, with a high level of academic citation. More importantly, they seem to be influential in improving clinical management. As Professor Hans-Joerg Senn summarised it recently, this provides a "clinically useful updated breast cancer treatment consensus for the majority of patients treated outside of clinical trials (>90%) in most countries."

Reference(s)

[1] Goldhirsch A, Glick JH, Gelber RD, et al.: Meeting highlights: International Consensus Panel on the Treatment of Primary Breast Cancer. Seventh International Conference on Adjuvant Therapy of Primary Breast Cancer. J Clin Oncol 19: 3817–3827, 2001.
[2] Goldhirsch A, Glick JH, Gelber RD, et al.: Meeting highlights: international expert consensus on the primary therapy of early breast cancer 2005. Ann Oncol 16: 1569–1583, 2005.
[3] Goldhirsch A, Wood WC, Gelber RD, et al.: Progress and promise: highlights of the international expert consensus on the primary therapy of early breast cancer 2007. Ann Oncol 18: 1133–1144, 2007.
[4] Goldhirsch A, Ingle JN, Gelber RD, et al.: Thresholds for therapies: highlights of the St. Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2009. Ann Oncol 20: 1319–1329, 2009.
[5] Goldhirsch A, Wood WC, Coates AS, et al.: Strategies for subtypes – dealing with the diversity of breast cancer: highlights of the St. Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2011. Ann Oncol 22: 1736–1747, 2011.
[6] Goldhirsch A, Winer EP, Coates AS, et al.: Personalizing the treatment of women with early breast cancer: highlights of the St. Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2013. Ann Oncol 24: 2206–2223, 2013.

Disclosure of Interest: No significant relationships.

Wednesday, 18 March 2015 **15.30–17.00**

Session 1: News since St.Gallen 2013

PG 1.01
Surgical management of early breast cancer 2015

M. Morrow*. *Breast Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, United States of America*

Traditionally, local control has been equated with disease burden, and the role of surgery has been to remove all carcinoma evident on clinical exam or imaging. It is increasingly clear that local control is a function of disease burden, tumor biology, and use of effective systemic therapy, offering the opportunity to decrease the extent of surgery and reduce the burden of treatment in some patients. Changes in practice reflecting this understanding have already occurred and include new guidelines on margin width in breast-conserving therapy (BCT) and alternatives to axillary dissection (ALND). The ACOSOG Z0011 study was a landmark trial demonstrating that ALND is not necessary in cN0 women undergoing BCT with metastases to 1–2 sentinel nodes (SNs) [1]. Major criticisms of the study included randomization of only a favorable patient subset and irradiation of the axilla. We have now shown that approximately 80% of a consecutive series of unselected women undergoing BCT and found to have SN metastases

avoided ALND [2]. Others have confirmed that the majority of "high-risk patients" (ER− PR− HER2−, HER2+, <40 yrs) are eligible for this approach, while a retrospective review of approximately 30% of the RT plans in the ACOSOG Z0011 study showed no differences in the radiation therapy (RT) fields used between study arms [3]. The AMAROS [4] and the OTOSAR [5] trials studied axillary nodal RT as an alternative to ALND in patients with positive SNs and observed no differences in axillary recurrence or survival compared to ALND. All 3 of these studies sought to leverage the limited axillary disease in most clinically cN0 patients and the benefits of systemic therapy to minimize surgical morbidity. The fact that microscopic disease in the axilla is controlled with systemic therapy and less than full dose RT, coupled with the observation that locoregional recurrence (LRR) as a proportion of all recurrences decreased from 30% to 15% between 1985 and 2010 [6], prompted the Society of Surgical Oncology (SSO) and the American Society for Therapeutic Radiation Oncology (ASTRO) to develop a multidisciplinary consensus on the optimal margin width in BCT. Based on a metaanalysis [7] and other literature, it was concluded that margins more widely clear than no ink on tumor do not reduce local recurrence, and the routine use of re-excision to obtain larger margins is not indicated [8]. Further evidence of the ability to decrease locoregional therapy was provided in the ACOSOG Z1071 [9] and SENTINA [10] trials. These studies found that in cN+ patients, the false-negative rate of SN biopsy after NAC was <10% when ≥3 SNs were found, allowing avoidance of ALND in those having nodal pCR. There is no follow-up data on regional recurrence rates since all patients had ALND. In contrast, 2 large unpublished studies (MA 20, EORTC 22922/10925) suggest that all pN+ patients benefit from nodal RT after ALND. A major issue for the future is how to resolve these divergent viewpoints. Studies using NAC will offer important information. The NRG 9353 trial addresses whether N+ patients at presentation who become cN0 after NAC require nodal RT. The Alliance A11202 trial randomizes to ALND or node field RT in N+ women who do not achieve nodal pCR after NAC. Just as LRR varies by ER, PR, and HER2 status, and Oncotype Dx score, it is likely that appropriate local therapy will vary, particularly since ER+ and HER2+ patients who do not achieve pCR receive additional effective systemic therapy. If ongoing trials demonstrate the ability to further individualize local therapy based on the response to NAC, they will provide a compelling rationale for adopting NAC as a standard, even in early-stage breast cancer.

Reference(s)

[1] Giuliano AE JAMA 2011; 305: 589.
[2] Dengel L, Ann Surg Oncol; 21: 22.
[3] Jagsi R, J Clin Oncol 2014; 32: 3600.
[4] Rutgers EJ, ASCO 2013.
[5] Savolt A, Orv. Hetil 2013; 154: 1934.
[6] Bouganim N, Breast Cancer Res Treat 2013; 139: 603.
[7] Houssami N, Ann Surg Oncol 2014; 21: 717.
[8] Moran MS, Ann Surg Oncol 2014; epub.
[9] Boughey JC, JAMA 2013; 310: 1455.
[10] Kuehn T, Lancet Oncol 2013; 14: 609.

Disclosure of Interest: No significant relationships.

PG 1.02
Clinical utility of genetic signatures in selecting adjuvant treatment: risk stratification in early versus late recurrences

D.F. Hayes*. *Comprehensive Cancer Center, University of Michigan, Ann Arbor, MI, United States of America*

Adjuvant endocrine therapy (ET) reduces the odds of distant recurrence and mortalityin women with hormone receptor (HR) positive early stage breast cancer [1]. These patients have ongoing recurrences over many years [2]. Extended adjuvant ET reduces recurrence during this late follow-up [3]. ET induces side effects (hot flashes, sexual dysfunction, mood changes, and weight gain), and occasional major toxicities (thrombosis and endometrial cancer with tamoxifen; bone mineral loss and possibly heart disease with AIs) [1,4]. Accurate estimates of the risk of late recurrence would permit appropriate extended ET decisions. Several multiparameter assays [IHC4, 21-gene OncotypeDX, 12-gene Endopredict, PAM50, 2-gene Breast Cancer Index (BCI)] have been investigated. The clinical validity of IHC4, OncotypeDX, and the BCI assays have been compared in the ATAC trial [5]. All three assays had significant prognostic ability for early distant recurrence, but BCI-L was the only assay that predicted recurrence beyond 5 years. The risk of distant relapse for patients with intermediate or high risk BCI-L scores exceed 10% during years 5–10, while that for patients with low risk score was approximately 3%. Likewise Endopredict identified patients who participated in ABCSG 6 and 8 had a <5% risk of recurrence in years 5–10 after discontinuing ET, especially [6], and results from the ABCSG 8 combined with ATAC have suggested that the PAM50 identifies a group of women with a <5% risk of recurrence during years 5–10 after discontinuing ET [7,8]. These data suggest that these assays have "clinical validity" for identifying women with ER positive breast cancer who might be spared extended ET. However, the stakes are high, and although each of these represents a "prospective retrospective" study, they require further validation in subsequent datasets before they should be considered to have "clinical utility" and are used to withhold potentially life-saving treatment [9].

Reference(s)

[1] Davies C, Godwin J, Gray R, et al: Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. Lancet 378: 771–84, 2011.
[2] Saphner T, Tormey DC, Gray R: Annual hazard rates of recurrence for breast cancer after primary therapy. Journal of Clinical Oncology 14: 2738–46, 1996.
[3] Burstein HJ, Temin S, Anderson H, et al.: Adjuvant endocrine therapy for women with hormone receptor-positive breast cancer: American Society of Clinical Oncology clinical practice guideline focused update. J Clin Oncol 32: 2255–69, 2014.
[4] Goss PE, Ingle JN, Pater JL, et al.: Late extended adjuvant treatment with letrozole improves outcome in women with early-stage breast cancer who complete 5 years of tamoxifen. J Clin Oncol 26: 1948–55, 2008.
[5] Sgroi DC, Sestak I, Cuzick J, et al.: Prediction of late distant recurrence in patients with oestrogen-receptor-positive breast cancer: a prospective comparison of the breast-cancer index (BCI) assay, 21-gene recurrence score, and IHC4 in the TransATAC study population. Lancet Oncol 14: 1067–1076, 2013.
[6] Dubsky P, Brase JC, Jakesz R, et al.: The EndoPredict score provides prognostic information on late distant metastases in ER+/HER2− breast cancer patients. Br J Cancer 109: 2959–64, 2013.
[7] Filipits M, Nielsen TO, Rudas M, et al.: The PAM50 risk-of-recurrence score predicts risk for late distant recurrence after endocrine therapy in postmenopausal women with endocrine-responsive early breast cancer. Clin Cancer Res 20: 1298–305, 2014.
[8] Sestak I, Cuzick J, Dowsett M, et al.: Prediction of Late Distant Recurrence After 5 Years of Endocrine Treatment: A Combined Analysis of Patients From the Austrian Breast and Colorectal Cancer Study Group 8 and Arimidex, Tamoxifen Alone or in Combination Randomized Trials Using the PAM50 Risk of Recurrence Score. J Clin Oncol, 2014.
[9] Simon RM, Paik S, Hayes DF: Use of archived specimens in evaluation of prognostic and predictive biomarkers. J Natl Cancer Inst 101: 1446–52, 2009.

Disclosure of Interest: I have no conflicts that relate to this talk. I have the following conflicts in general: Category Company Personal Financial Interest (Stock ownership, membership on advisory board, board of directors, or other substantive relationships) 7/20/09 Oncimm.

PG 1.03
Picking the optimal endocrine adjuvant treatment for pre-menopausal women

M. Colleoni*, E. Munzone. *Medical Senology, Istituto Europeo di Oncologia, Milano, Italy*

Endocrine treatments continue to represent a crucial component of adjuvant therapies for pre-menopausal patients with tumors that express steroid hormone receptors (HR). Endocrine agents are commonly well tolerated. Nevertheless selected side effects should be considered when evaluating treatment options, based upon risk of relapse, degree of endocrine responsiveness, expectations of the patient and co-morbidities. Tamoxifen (T) should still be regarded as a proper endocrine therapy in a large number of pre-menopausal patients. However, according to the results of the SOFT [1] and TEXT [2] trials, the use of T alone in selected higher risk patient may be questioned. The SOFT and TEXT trials, dedicated to pre-menopausal women with HR+ breast cancer, were developed to determine the role of ovarian function suppression (OFS) in women who remain pre-menopausal and are treated with T alone (OFS question) and also to test whether adjuvant aromatase inhibitor (AI) improves outcomes in patients treated with OFS (AI question). Overall, in the SOFT study patients did not benefit from the addition of OFS. Nevertheless, for women at higher risk of recurrence who received adjuvant chemotherapy and maintained pre-menopausal levels of estradiol, addition of OFS to tamoxifen reduced the risk of recurrence. The magnitude of the effect was larger in younger patients. In the TEXT trial, adjuvant treatment with exemestane plus OFS, as compared with T plus OFS, significantly improved disease-free survival, breast cancer-free interval and distant disease-free survival, therefore representing a new treatment option. Tailored endocrine treatments should be considered in pre-menopausal patients with endocrine responsive tumors. In fact, breast cancer in pre-menopausal patients includes heterogeneous groups of tumors and patients where issues of safety, quality of life and subjective side-effects should be properly weighted with the benefit of adjuvant endocrine therapy. Patient preferences should be regularly taken into consideration in the definition of the threshold of expected benefit at which therapies should be attempted. Picking the best tolerated agent that can enhance adherence and reduces the impact on health status is key to make progress on how to treat individual pre-menopausal breast cancer patients.

Reference(s)

[1] Francis PA, Regan MM, Fleming GF, et al. Adjuvant Ovarian Suppression in Premenopausal Breast Cancer. N Engl J Med. 2014 Dec 11 [Epub ahead of print].
[2] Pagani O, Regan MM, Francis PA et al. Exemestane with ovarian suppression in premenopausal breast cancer. N Engl J Med. 2014; 371: 1358–9.

Disclosure of Interest: No significant relationships.

PG 1.04
Big data: are large prospective randomized trials obsolete in the future?

C. Hudis*. , *Memorial Sloan-Kettering Cancer Center, New York, United States of America*

A distinguishing feature of medical oncology in general, and breast cancer treatment in particular, has been a longstanding reliance on, and trust in, prospective randomized clinical trials as the basis of recommendations for standard therapy. In the early days of systemic therapy, the poor prognosis and limited benefits of palliative therapies mandated this approach to allow us to reliably detect small differences that could be obscured by biased observations – both in terms of efficacy and toxicity. In the early stage setting, large randomized trials with long follow-up were needed for similar reasons: to reliably detect modest differences in the risks of relapse and death over many years. This culminated in the performance of a series of meta-analyses by the Early Breast Cancer Trialists' Collaborative Group that led to broadly accepted standards of care such as tamoxifen for hormone-receptor positive disease and chemotherapy for higher risk subsets [1]. One of the consequences of the meta-analyses was the recognition that small trials could mislead our community when treatment impact is modest (but real). This led, in the past two decades, to a number of large trials that stand alone and are able to define practice without resorting to a meta-analysis. Studies of the adjuvant use of taxanes and more recently trastuzumab are examples [2–8].

Changes in our understanding of the molecular biology of cancer will challenge our historical approach. To the degree that subgroups of patients with superficially similar cancers (ie, HER2 positive) can be identified where the underlying biology is actually distinct (PTEN loss as a possible example in the setting of HER2 positivity) it may be that for some drugs the conventional large randomized trial will neither be feasible nor informative. A fundamental question going forward then is how we will establish adequate levels of evidence to inform standards of care that responsibly change (improve) global outcomes.

The relatively rapid uptake of electronic medical records (EMRs) in many communities and especially in oncology may provide an alternative path to the development of useful and reliable evidence. Indeed, we have begun to build an unprecedented warehouse of medical information that will be a rich resource. It should be able to link special circumstances, such as tumor genotypes, patient phenotypes, and routine treatment choices with outcomes. This may illuminate trends that can guide prospective research while also perhaps informing routine care.

To make the most of this global investment in electronic records ASCO is developing the Cancer Learning Intelligence Network for Quality (CancerLinQ) with the assistance of a large enterprise software company [9]. This "big data" project will rely on both clinical insights (from disease experts) and technical support (from technology experts) to report back to practices. For some purposes, the system will extract data, anonymize it, perform analyses, and then report cancer treatment outcomes in an aggregated fashion. While this is a secondary goal, it is potentially supportive of the global goal of a more efficient system for developing and comparing treatment options. The pilot project demonstrated feasibility in more than 170,000 patients with breast cancer (although the initial plan only called for about 35,000!) drawn from private and academically affiliated practices in the US [10]. CancerLinQ and other similar programs and projects offer the possibility of supporting a transformation in how we do cancer care research, not through the elimination of prospective clinical trials but instead as an additional source of reliable information that can guide the planning of clinical trials and identify unanticipated areas of concern. This may allow us to conduct more efficient drug development in larger numbers of patients despite the rapid growth in our perception of the complexity of breast and other cancers.

Reference(s)

[1] Early Breast Cancer Trialists' Collaborative Group. Lancet 2005; 365: 1687–1717.
[2] Henderson IC, Berry D, Demetri C, et al. J Clin Oncol 21: 976–983, 2003.
[3] Mamounas EP, Bryant J, Lembersky BC, et al. J Clin Oncol, 23: 3686–3696, 2005.
[4] Citron ML, Berry DA, Cirrincione C, et al. J Clin Oncol 2003; 21: 1431–1439.
[5] Sparano JA, Wang M, Martini S, et al. N Engl J Med 2008; 358: 1663–1671.
[6] Romond EH, Perez EA, Bryant J, et al. N Engl J Med 353(16): 1673–1684, 2005.

[7] Piccart-Gebhart MJ, Procter M, Leyland-Jones B, et al. N Engl J Med 353(16): 1659–1672, 2005.
[8] Slamon D, Eiermann W, Robert N, et al. N Engl J Med 2011; 365: 1273–1283.
[9] Schilsky R, Michaels DL, Kearbey AH, et al. J Clin Oncol 2014 32(22): 2373–2379.
[10] http://cancerlinq.org/

Disclosure of Interest: No significant relationships.

Wednesday, 18 March 2015 **17.30–18.45**

Session 2: Biology of breast cancer I: Bridging the gap between high throughput technologies and breast cancer treatment in real life

PG 2.01
Interpreting genomics data at a functional level: What are we learning from large molecular screening projects?

P. Campbell*. *Wellcome Trust Sanger Institute, Cancer Genetics and Genomics, Cambridgeshire, United Kingdom*

No abstract submitted.

PG 2.02
Deep genomic analysis and treatment decisions based on genomic-driven and pathway-matched therapies

F. André*. *Department of Medical Oncology, Institut de Cancérologie Gustave Roussy, Villejuif, France*

Advances in biotechnologies and computer sciences have allowed to apply high throughput genomics to cancer samples. These analyses have shown that each cancer sample presents a specific genomic portrait. These findings have generated the concept that each patient could be treated individually based on the molecular analysis of her cancer sample.

Several studies have shown that high throughput genomics is feasible and robust in the context of daily practice. This approach is now being evaluated in two different trial designs. The first concept is to use this approach to screen for genomic alterations and further enrich therapeutic trials in patients presenting a candidate targetable alteration. This concept is being used in several trials including SAFIR01, AURORA, etc. The second concept consists in evaluating the medical usefulness of performing genomic analyses for BC patients. This concept is currently being evaluated in the SAFIR02 trial.

There are several applications for genomics to personalize therapies. First, genomics could be used to identify drivers. At least 20 genomic alterations are candidate targets in breast cancers. Nevertheless, only a few of them are validated as drivers. Until now, only PIK3CA, AKT1 and ERBB2 mutations constitute robust drivers. The second application of genomic could be the detection of genomic alterations involved in resistance to therapies. As illustration, ESR1 mutations have been shown to emerge after resistance to endocrine therapy, and could be targetable. Finally, high throughput genomics could be used to identify DNA repair defects and tumor immunogenicity.

There is some debate about which technologies should be used in clinical trials, and further in daily practice. The current approach consists in finding drivers using targeted sequencings in few genes. Several prospective programs add CGH arrays to this approach. The next two technological steps include the use of circulating DNA and whole exome sequencing. Circulating DNA could avoid biopsies. Whole exome sequencing could allow better assessment of immunogenicity, intratumor heterogeneity and DNA repair defects.

Disclosure of Interest: Grant/Research Support: Novartis, AstraZeneca. Honoraria/Consultation Fee: Novartis, AstraZeneca.

PG 2.03
Discrepancies between genetic tools and immunohistochemistry: bad pathology and good signature, and vice-versa

J.S. Reis-Filho*, B. Weigelt. *Pathology, Memorial Sloan-Kettering Cancer Center, New York, United States of America*

The advent of high-throughput technologies, in particular of gene expression profiling by microarray analysis, has resulted in the development of numerous gene signatures to predict the outcome of breast cancer patients [1]. These signatures have largely been perceived as a means to overcome the challenges stemming from the intra- and inter-observer variability in the assessment of pathologic variables for the prognostication of breast cancer patients, prediction of response to specific therapeutic regimens, and a means to provide essential information for the delivery of precision medicine for patients with breast cancer. The first type of signatures developed focused on predicting the outcome of all breast cancer patients [1]. Although these first-generation signatures have been shown to provide prognostic information that is independent from that offered by the clinico-pathologic parameters used to define prognosis of breast cancer patients, independent re-analyses and meta-analyses of microarray data have demonstrated that these gene signatures derive their prognostic information from the expression levels of proliferation-related genes, that they offer potentially useful prognostic information for patients with estrogen receptor-positive disease, but that their utility is negligible in patients with estrogen receptor-negative breast cancers [1,2]. Detailed pathologic analyses have also demonstrated that the tissue composition of the samples from which RNA is extracted has a profound impact on the results of the signatures, with variations in tumor:stroma content resulting in different classifications by gene expression profiling [3]. Furthermore, given that the signatures were developed by the analysis of the commonest form of breast cancer, the so-called invasive ductal carcinomas of no special type, there is evidence to suggest that these signatures may not perform as well when special histologic types are analyzed. For instance, adenoid cystic carcinomas of the breast, an indolent special histologic type of triple-negative breast cancer, are often classified as of poor prognosis by first-generation prognostic signatures [4]. Microarray-based gene expression profiling has also resulted in the development of an 'intrinsic' gene classification of breast cancers into luminal A, luminal B, HER2-enriched, basal-like and claudin-low tumors [5,6]. PAM50, a commercially available robust test based on a derivative transcriptomic technology, has been developed and can be applied to pathology samples [5]. The PAM50 classification system has undoubtedly changed the way breast cancers are perceived and how clinical trials and translational research endeavors are carried out. The clinical utility of this classification system, however, has yet to be fully established. Furthermore, discrepancies between the molecular subtypes and validated pathology-based biomarkers (e.g. estrogen receptor, progesterone receptor and HER2) are not uncommon. For instance, only 61% of HER2-positive breast cancers as defined by validated immunohistochemical and in situ hybridization assays are classified as HER2-enriched; on the other hand, 40% of HER2-enriched cases are HER2-positive by optimized pathology methods [7]. Importantly discrepancies between different prognostic signatures and the molecular classification have also been documented in a substantial number of cases [8]. At present, it is unclear as to how these discrepancies should be reconciled. Finally, one of the greatest promises of gene expression profiling was in the development of signatures predictive of response to therapeutic agents. Independent studies have demonstrated, however, that if multiple mechanisms of resistance to therapeutic agents exist, current approaches for the development of gene expression profiling-based signatures may not yield robust predictors [9,10].

Reference(s)
[1] Reis-Filho JS, Pusztai L. Gene expression profiling in breast cancer: classification, prognostication, and prediction. Lancet 2011; **378**: 1812–1823.
[2] Wirapati P, Sotiriou C, Kunkel S, et al. Meta-analysis of gene expression profiles in breast cancer: toward a unified understanding of breast cancer subtyping and prognosis signatures. Breast Cancer Res 2008; **10**: R65.
[3] Elloumi F, Hu Z, Li Y, et al. Systematic bias in genomic classification due to contaminating non-neoplastic tissue in breast tumor samples. BMC Med Genomics 2011; **4**: 54.
[4] Weigelt B, Horlings HM, Kreike B, et al. Refinement of breast cancer classification by molecular characterization of histological special types. J Pathol 2008; **216**: 141–150.
[5] Parker JS, Mullins M, Cheang MC, et al. Supervised risk predictor of breast cancer based on intrinsic subtypes. J Clin Oncol 2009; **27**: 1160–1167.
[6] Prat A, Parker JS, Karginova O, et al. Phenotypic and molecular characterization of the claudin-low intrinsic subtype of breast cancer. Breast Cancer Res 2010; **12**: R68.
[7] Bastien RR, Rodriguez-Lescure A, Ebbert MT, et al. PAM50 breast cancer subtyping by RT-qPCR and concordance with standard clinical molecular markers. BMC Med Genomics 2012; **5**: 44.
[8] Kelly CM, Bernard PS, Krishnamurthy S, et al. Agreement in risk prediction between the 21-gene recurrence score assay (Oncotype DX®) and the PAM50 breast cancer intrinsic Classifier in early-stage estrogen receptor-positive breast cancer. Oncologist 2012; **17**: 492–498.
[9] Borst P, Wessels L. Do predictive signatures really predict response to cancer chemotherapy? Cell Cycle 2010; **9**: 4836–4840.
[10] Ng CK, Weigelt B, A'Hern R, et al. Predictive performance of microarray gene signatures: impact of tumor heterogeneity and multiple mechanisms of drug resistance. Cancer Res 2014; **74**: 2946–2961.

Disclosure of Interest: No significant relationships.

PG 2.04
A bad tumor biomarker is as bad as a bad drug: the gap between genomics data and phenotype to predict response

G. Viale*. *Pathology, Istituto Europeo di Oncologia, University of Milan, Milano, Italy*

The recent technological advances and the extraordinary team efforts of consortia like the Cancer Genome Atlas (TCGA) [1] and the Molecular Taxonomy of Breast cancer International Consortium (METABRIC) [2] have dramatically increased our understanding of the molecular pathways and their derangements in human solid tumours. The combined evaluation of recurrent genomic abnormalities (gene mutations and gene copy number variations) and transcriptomic profiles has led to a continuous refinement of the molecular classification of breast cancer with prognostic implications. The original molecular classes (Luminal, HER2-enriched and Basal-like) have been further dissected in more and more SUBGROUPS, like the 10 integrative subgroups from the METABRIC consortium, or the complex arm-wise aberration index (CAAI)-positive and negative tumours [3]. Even within Luminal A breast cancers, commonly considered a relatively homogeneous subgroup of tumours with a good clinical outcome, a remarkable molecular diversity can be detected according to distinct gene copy number variations and mutation profiles. The molecular stratification of Luminal A tumours allows to identify new subgroups with a significantly worse prognosis, and possibly to predict resistance to endocrine therapy [4]. It remains to be assessed when and how much this more comprehensive understanding of the molecular heterogeneity of breast cancer will affect the process of clinical decision making in the daily practice. We are still awaiting results of ongoing clinical trials with gene expression-based prognostic classifiers to eventually implement them in the clinical practice. For now, available predictive models to inform the systemic treatment of individual patients are still limited to a few established biomarkers (hormone receptor and HER2 status, and markers of cell proliferation). As new therapeutic strategies are being evaluated in clinical studies, new predictive biomarkers are being sought. This is the case for example of the aberrations of the BRCA genes, or of the modulation of immune checkpoints.

Reference(s)
[1] TCGA. Comprehensive molecular portraits of human breast tumors. Nature 490: 61–70, 2012.
[2] Curtis C, Shah S, Chin S-F, et al. The genomic and transcriptomic architecture of 2,000 breast tumours reveals novel subgroups. Nature 486: 346–352, 2012.
[3] Vollan HK, Rueda OM, Chin S-F, et al. A tumor DNA complex aberration index is an independent predictor of survival in breast and ovarian cancer. Mol Oncol 9: 115–127, 2015.
[4] Ciriello G, Sinha R, Hoadley KA, et al. The molecular diversity of Luminal A breast tumors. Breast Cancer Res Treat 141: 409–420, 2013.

Disclosure of Interest: No significant relationships.

Thursday, 19 March 2015 **17.30–18.45**

Session 3: Biology of breast cancer II: Tumor heterogeneity and disease segmentation in breast cancer

PG 3.01
Clinical implications of the intrinsic molecular subtypes

A. Prat*. *Medical Oncology Hospital Clinic, Vall d'Hebron Institute of Oncology, Barcelona, Spain*

Gene-expression profiling has had a considerable impact on our understanding of breast cancer biology. During the last 15 years (yrs), 5 intrinsic molecular subtypes of breast cancer (Luminal A, Luminal B, HER2-enriched, Basal-like and Claudin-low) and a normal breast-like group have been identified and intensively studied [1–3]. In this presentation, I will focus on recent data regarding the potential clinical implications of the intrinsic molecular subtypes beyond the current pathological-based classification endorsed by the 2013 St. Gallen Consensus Recommendations [4]. Within hormone receptor (HR)-positive and HER2-negative breast cancer, the Luminal A and B subtypes represent the vast majority of cases. Compared to Luminal A tumours, Luminal B tumours are characterized by higher expression of proliferation/cell cycle-related genes and lower expression of several luminal-related genes such as the progesterone receptor (PR) [5]. Clinically, Luminal B tumours show higher pathological complete response rates following neoadjuvant multi-agent chemotherapy [6] but worse distant recurrence-free survival at 5- and 10-yrs regardless of adjuvant systemic therapy compared to Luminal A tumours. This Luminal A vs B classification, together with tumour size and nodal status, also predicts distant recurrence within the 5- to 10-yrs of follow-up and thus may inform decisions concerning the length of endocrine therapy treatments (i.e. 5 vs 10 yrs). Interestingly, although we and others have proposed pathology-based surrogate definitions of the Luminal A and B subtypes using semi-quantitative IHC scoring of Ki-67 and PR, the discordance rate versus multi-gene expression assays is still high (~30–40%) [5,7].
Within clinically HER2+ disease, all the 4 main intrinsic subtypes can be identified beyond HR status, albeit with different proportions [8]. Among them, the HER2-enriched subtype represents the majority of HER2+ tumours and shows higher expression of HER2 and lower expression of luminal genes compared to both luminal subtypes [8]. In addition, retrospective data suggests that patients with HER2-enriched disease benefit the most from neoadjuvant trastuzumab,

or dual HER2 blockade with trastuzumab/lapatinib, in combination with chemotherapy. Of note, once intrinsic subtype is taken into account, the biological impact and the prognostic ability of clinical HER2 disappears [8]. For example, patients with Luminal A/HER2+ early breast cancer have similar survival outcomes as patients with Luminal A/HER2-negative tumours in the absence of adjuvant trastuzumab.

Finally, within triple-negative breast cancer (TNBC), the Basal-like disease predominates (70–80%), but again, all the intrinsic subtypes can also be identified. Interestingly, luminal/TNBC or HER2-enriched/TNBC show similar gene expression patterns as Luminal/HR+ or HER2-enriched/HER2+, except for ERBB2 and the rest of genes in the 17q amplicon which are not found overexpressed in HER2-enriched/TNBC [9]. Importantly, the distinction between Basal-like versus non-Basal-like within TNBC seems to be important for predicting survival following (neo)adjvuvant multi-agent chemotherapy [10], bevacizumab benefit in the neoadjuvant setting (CALGB40603) [11], and docetaxel vs. carboplatin benefit in first-line metastatic disease (TNT study) [12]. Overall, this data suggests that intrinsic molecular profiling provides clinically relevant information beyond current pathology-based classifications.

Reference(s)

[1] Perou CM, Sorlie T, Eisen MB, et al: Molecular portraits of human breast tumours. Nature 406: 747–752, 2000.

[2] Prat A, Parker J, Karginova O, et al: Phenotypic and Molecular Characterization of the Claudin-low Intrinsic Subtype of Breast Cancer. Breast Cancer Research 12: R68, 2010.

[3] Prat A, Perou CM: Deconstructing the molecular portraits of breast cancer. Molecular Oncology 5: 5–23, 2011.

[4] Goldhirsch A, Winer EP, Coates AS, et al: Personalizing the treatment of women with early breast cancer: highlights of the St. Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2013. Annals of Oncology 24: 2206–2223, 2013.

[5] Prat A, Cheang MCU, Martín M, et al: Prognostic Significance of Progesterone Receptor-Positive Tumor Cells Within Immunohistochemically Defined Luminal A Breast Cancer. Journal of Clinical Oncology 31: 203–209, 2013.

[6] Usary J, Zhao W, Darr D, et al: Predicting Drug Responsiveness in Human Cancers Using Genetically Engineered Mice. Clinical Cancer Research 19: 4889–4899, 2013.

[7] Martín M, González-Rivera M, Morales S, et al: Prospective study of the impact of the Prosigna™ assay on adjuvant clinical decision-making in an unselected population of women with estrogen receptor-positive, HER2-negative, node-negative breast cancer: A GEICAM study. San Antonio Breast Cancer Symposium 2014 abstract #P6-08-10.

[8] Prat A, Carey LA, Adamo B, et al: Molecular Features and Survival Outcomes of the Intrinsic Subtypes Within HER2-Positive Breast Cancer. JNCI 106, 2014.

[9] Prat A, Adamo B, Cheang MCU, et al: Molecular Characterization of Basal-Like and Non-Basal-Like Triple-Negative Breast Cancer. The Oncologist 18: 123–133, 2013.

[10] Prat A, Lluch A, Albanell J, et al: Predicting response and survival in chemotherapy-treated triple-negative breast cancer. Br J Cancer 111: 1532–1541, 2014.

[11] Sikov W, Barry W, Hoadley K, et al: Impact of intrinsic subtype by PAM50 and other gene signatures on pathologic complete response (pCR) rates in triple-negative breast cancer (TNBC) after neoadjuvant chemotherapy (NACT) +/− carboplatin (Cb) or bevacizumab (Bev): CALGB 40603/150709 (Alliance). San Antonio Breast Cancer Symposium 2014 abstract #S4-06.

[12] Tutt A, Ellis P, Kilburn L, et al: TNT: A randomized phase III trial of carboplatin (C) compared with docetaxel (D) for patients with metastatic or recurrent locally advanced triple negative or BRCA1/2 breast cancer (CRUK/07/012). San Antonio Breast Cancer Symposium 2014 abstract #S3-01.

Disclosure of Interest: Consultant/advisory board member: Nanostring Technology.

PG 3.02

Heterogeneity of triple negative subtype: gene expression profile and phenotype

B.D. Lehmann*. *Biochemistry, Vanderbilt University, Nashville, United States of America*

Triple negative breast cancer (TNBC) represents 10–20% of all breast cancers that lack estrogen receptor (ER) and progesterone receptor expression as well as amplification of the human epidermal growth factor receptor 2 (HER2). TNBCs more frequently affect younger and African-American women and are more aggressive with an increased likelihood of distant recurrence and death compared with women with other types of breast cancer. While, targeted therapies exist for ER-positive and HER2-amplified breast cancers, treatment options for TNBC are limited by a lack of molecular understanding of this disease. We recently have classified TNBC into six molecular subtypes using molecular profiling and identified representative cell lines for each TNBC subgroup. We identified two basal-like subgroups enriched in basal cytokeratins. The first, basal-like 1 (BL1), is characterized by cell cycle and DNA damage response genes and cell lines that preferentially responded to cisplatin. The second, basal-like 2 (BL2), is enriched in growth factor receptors and expresses myoepithelial markers. Two mesenchymal-like subgroups (M and MSL) were enriched in differentiation, epithelial–mesenchymal transition and growth factor pathways, in which cell lines were more sensitive to PI3K inhibitors and dasatinib. We described an immunomodulatory (IM) subgroup, defined by immune cell markers and signaling genes. Finally, we identified a luminal androgen receptor (LAR) subgroup, driven by androgen receptor (AR) signaling and PIK3CA mutations, rendering cell lines sensitive to AR antagonists and PI3K inhibitors. PIK3CA kinase mutations were highly clonal, more frequent in AR+ vs. AR− TNBC clinical samples and often associated with concurrent amplification of the PIK3CA locus. PI3K/mTOR inhibitors had an additive growth inhibitory effect when combined with genetic or pharmacological AR targeting in AR+ TNBC cells. Comparison to intrinsic molecular subtyping showed majority of BL1, BL2, IM and M to be basal-like, MSL to be enriched in normal-like subtype and LAR to be mostly consist of the luminal A subtype.

Through a collaborative retrospective analysis of TNBC patients treated with sequential anthracycline + cyclophosphamide followed by taxane chemotherapy, we demonstrate TNBC subtyping of pretreatment biopsies to be an independent predictor of pathological complete response (pCR). These data show patients with tumors displaying the BL1 subtype achieve the highest pCR, while BL2 and LAR had very little response. Together with the statistically significant increased age upon diagnosis for LAR and BL2 patients, suggest that these older patients could potentially be spared the toxic side effects of anthracycline and cyclophosphamide chemotherapy. Altogether, these data provide significant insight into future clinical trial design and biomarker selection for alignment of TNBC patients to appropriate targeted therapies and chemotherapy.

Disclosure of Interest: Licensing of royalties for development of TNBctype from Insight Genetics.

PG 3.03

Molecular segmentation in luminal breast cancer: how to select the driver pathways

S. Loi*. *Division of Cancer Medicine, Division of Cancer Research, Peter MacCallum Cancer Center, Victoria Australia, Australia*

Next generation sequencing (NGS) has allowed us to investigate the genomic landscape of breast cancer with regards to copy number alterations and recurrent somatic mutations. To date, studies involving nearly 1000 primary breast cancer exomes/genomes have been published. These studies have confirmed the presence of

PIK3CA, TP53, GATA3, MAP3K1, MLL3 and CDH1 as the most commonly mutated in breast cancers. Apart from the 3 highly mutated genes (TP53, PIK3CA and GATA3), that is, occurring at >10% frequency, other known oncogenic mutations appears uncommonly. The critical issue at present is trying to determine if any of these mutations may act as clinically useful prognostic or predictive markers to specific therapies. This problem is becoming more and more pertinent as NGS verges on the edge of clinical implementation as the technologies advance rapidly with decreasing cost.

For example, PIK3CA mutations are the most frequent activating mutation in breast cancer, yet their clinical relevance in patient management is far from clear. It is likely that PIK3CA mutations may be a good prognostic marker in early-stage luminal breast cancers treated with endocrine therapy. Thus far data in the metastatic setting does not imply increased responsiveness to pan-Class I PI3K inhibitors or everolimus with endocrine therapy. We await definitive data from the newer PI3K alpha-specific inhibitors. Given the difficulties encountered with a highly frequent aberration, the rare mutations will require considerable global cooperation in order to bring potentially effective therapies to patients with a high level of evidence.

In this talk, I will discuss how we may move forward with regards to understanding the clinically relevant driver mutations.

Disclosure of Interest: Receipt of grants/research supports: Genentech and Pfizer.

PG 3.04
Insights in biology of luminal HER2 vs enriched HER2 subtypes: therapeutic implications

N. Harbeck*. *Frauenkliniken Maistrasse-Innenstadt und Großhadern, Brustzentrum der Universität München, München, Germany*

Until recently, due to its aggressive clinical behavior, HER2-positive disease has been considered as a single breast cancer subtype and treated accordingly, in particular in the early breast cancer setting (eBC). Based on the pivotal trial data from the metastatic breast cancer setting, anti-HER2 therapy in eBC has been developed as a one size fits all approach with a chemotherapy backbone independently of tumor endocrine sensitivity. The concept of intrinsic subtypes has now provide insights into heterogeneity of HER2-positive disease, yet in the absence of anti-HER2 therapy, this does not seem to affect patient outcome (Prat et al., 2014).

Recent data demonstrated different response rates after neoadjuvant chemotherapy + HER2-targeted therapy in HER2-positive disease for hormone-receptor (HR) negative vs. HR-positive tumors (Cortazar et al., 2014). Pathological complete response seems to have a different impact on patient outcome according to HER2-subtype with the strongest correlation found in HR-negative disease. Moreover, substantial preclinical and emerging clinical data in breast cancer suggest that there is a crosstalk between endocrine and HER2 pathways conferring resistance to agents targeting either pathway and suggesting co-targeted approaches (Osborne et al., 2005).

Early clinical results indicate meaningful pathological response rates by co-targeted approaches against ER and HER2. New clinical trial concepts such as WSG-ADAPT (Hofmann et al., 2013) have started to consider luminal (ER/PR-positive) vs. HER2-enriched HER2-positive tumors separately. In luminal HER2-positive disease, 12 weeks of trastuzumab + endocrine therapy is being compared to T-DM1 + endocrine therapy before surgery. In non-luminal HER2-positive disease, efficacy of dual blockade + taxane chemotherapy is being evaluated. After surgery, standard chemotherapy and one year of trastuzumab will be given. First data will be available by mid-2015.

The big challenge for HER2-positive eBC in the upcoming years will be to individualize anti-HER2 therapy according to endocrine responsiveness as well as relapse risk in order to avoid overtreatment, minimize therapy resistance, and optimally utilize the available treatment options. Taking molecular subtype into account as well as applying early response monitoring by early re-biopsy in the pre-operative setting, dynamic biomarkers, or molecular imaging may help to achieve this goal. Further innovative trial concepts addressing these issues and aiming to optimize co-targeted approaches are therefore urgently needed in HER2-positive early breast cancer.

Reference(s)

Cortazar P, Zhang L, Untch M, Mehta K, Costantino JP, Wolmark N, Bonnefoi H, Cameron D, Gianni L, Valagussa P, Swain SM, Prowell T, Loibl S, Wickerham DL, Bogaerts J, Baselga J, Perou C, Blumenthal G, Blohmer J, Mamounas EP, Bergh J, Semiglazov V, Justice R, Eidtmann H, Paik S, Piccart M, Sridhara R, Fasching PA, Slaets L, Tang S, Gerber B, Geyer CE Jr, Pazdur R, Ditsch N, Rastogi P, Eiermann W, von Minckwitz G. Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis. Lancet. 2014 Jul 12; 384(9938): 164–72.

Hofmann D, Nitz U, Gluz O, Kates RE, Schinkoethe T, Staib P, Harbeck N. WSG ADAPT – adjuvant dynamic marker-adjusted personalized therapy trial optimizing risk assessment and therapy response prediction in early breast cancer: study protocol for a prospective, multi-center, controlled, non-blinded, randomized, investigator initiated phase II/III trial. Trials 14(1): 261 (2013).

Osborne CK, Shou J, Massarweh S, Schiff R. Crosstalk between estrogen receptor and growth factor receptor pathways as a cause for endocrine therapy resistance in breast cancer. Clin Cancer Res 11(2Pt2): 865s–870s (2005).

Prat A, Carey LA, Adamo B, Vidal M, Tabernero J, Cortés J, Parker JS, Perou CM, Baselga J. Molecular features and survival outcomes of the intrinsic subtypes within HER2-positive breast cancer. J Natl Cancer Inst 106(8) (2014).

Disclosure of Interest: Grant/Research Support: Amgen, Celgene, Genomic Health, Nanostring Technologies, Roche, Teva. Honoraria/Consultation Fee: Celgene, Novartis, Roche, Pierre Fabre, Teva. Participation in Company Sponsored Speakers' Bureau: Amgen, AstraZeneca, Celgene, Nanostring Technologies, Novartis, Roche, Pfizer.

Thursday, 19 March 2015 **9.45–10.45**

Session 4: Biology of breast cancer III: Genome remodeling and tumor microenvironment

PG 4.01
Tumor–stroma crosstalk: targeting stroma and inflammation

F. Balkwill*. *Centre for Cancer and Inflammation, Barts Cancer Institute, Queen Mary University of London, London, United Kingdom*

Tumour promoting inflammation is considered one of the enabling characteristics of cancer development. Chronic inflammatory disease increases the risk of some cancers and there is strong epidemiological evidence that NSAIDs, particularly aspirin, are powerful chemopreventive agents. Tumour microenvironments contain many inflammatory cells and complex networks of inflammatory mediators such as cytokines and chemokines. Pre-clinical experiments in mouse models have shown that targeting these inflammatory networks with therapeutic antibodies or small molecule inhibitors can decrease tumor growth and spread.

While there is exciting potential for targeting inflammatory pathways in cancer prevention, targeting cancer-related inflammation and innate immunity in patients with advanced cancer has not yet proven as promising an approach as recent immunotherapies that modulate the adaptive immune system. There are many possible reasons for this and most trials at too early a stage to draw firm conclusions. This talk will focus on the potential of targeting

inflammatory cytokines such as IL-6 in combination or in sequence with other agents.
Clinical, pre-clinical and in silico experiments show that IL-6 can have multiple systemic and local actions within the tumor microenvironment including contributing to tumor angiogenesis and the leukocyte infiltrate, as well as stimulating paraneoplastic thrombocytosis. Data will be presented on the rationale for combining anti-IL-6 antibodies with other treatments including neoadjuvant chemotherapy, growth factor receptor inhibitors and inhibitors of angiogenesis.
Disclosure of Interest: No significant relationships.

PG 4.02
Immune pathways and immunome as a target

G. Curigliano*. *Division of Experimental Therapeutics, Breast Cancer Program, Istituto Europeo di Oncologia, Milano, Italy*

A fundamental "dogma" of tumor immunology and of cancer immunosurveillance in particular is that cancer cells express antigens that differentiate them from their non-transformed counterparts. Tumor antigens are overexpressed normal proteins and therefore are subject to immunological tolerance. Immune system controls not only tumor "burden" (quantity) but also tumor "quality" (immunogenicity). As a consequence of constant immune selection pressure placed on genetically unstable tumor cells held in equilibrium, tumor cell variants will be selected. They are no longer recognized by adaptive immunity (antigen loss variants or tumors cells that develop defects in antigen processing or presentation). They become insensitive to immune effector mechanisms, or induce an immunosuppressive state within the tumor microenvironment (tolerance). These tumor cells may then enter the escape phase, in which their outgrowth is no longer blocked by immunity. Is breast cancer immunogenic? Many observations demonstrated the prognostic role of TILs in TNBC and HER2 positive breast cancer. TNBC are poorly differentiated tumor with high genetic instability and very high heterogeneity. This heterogeneity enhances the "danger signals" and select clone variants that could be more antigenic or, in other words, that could more strongly stimulate a host immune antitumor response. Better prognosis in patients with TN/HER2 positive BC and higher TILs is also the result of an "immunoediting" process induced by chemotherapy. Chemotherapy can stimulate the immune system to recognize and destroy malignant cells is commonly known as immunogenic cell death (ICD). Cancer cells succumbing to ICD are de facto converted into an anticancer vaccine and as such elicit an adaptive immune response. Which are the clinical implications of all "immunome" data produced in the last years? First, validation of whether TILs are prognostic or predictive in HER2+ and TN breast cancer is needed, preferably in a large population set with appropriate follow up time. Second, validate immune genomic signatures that may be predictive and prognostic in patients with triple negative and HER2 positive disease. Third, it will be essential to incorporate an 'immunoscore' into traditional classification of breast cancer, thus providing an essential prognostic and potentially predictive tool in the pathology report. Fourth, implement clinical trials for TN and HER2 positive breast cancer in the metastatic setting with drugs that target immune-cell-intrinsic checkpoints. Blockade of one of these checkpoints, cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) or the programmed death 1 (PD-1) receptor may provide proof of concepts for the activity of an immune-modulation approach in the treatment of a breast cancer. We need also to better assess the role of TILs in DCIS and to better explore the relationship between autoimmune disease and cancer. The immune system remembers what it targets, so once the system is correctly activated, it may mediate a durable tumor response.

Reference(s)

[1] V. Shankaranet al., IFNγ and lymphocytes prevent primary tumour development and shape tumour immunogenicity. Nature 2001, 410, 1107.
[2] G. P. Dunn, A. T. Bruce, H. Ikeda, L. J. Old, R. D. Schreiber, Cancer immunoediting: From immunosurveillance to tumor escape. Nat. Immunol. 2002; 3, 991.
[3] Loi S, Sirtaine N, Piette F, et al. Prognostic and predictive value of tumor-infiltrating lymphocytes in a phase III randomized adjuvant breast cancer trial in node-positive breast cancer comparing the addition of docetaxel to doxorubicin with doxorubicin-based chemotherapy: BIG 02-98. J Clin Oncol 2013; 31: 860–867.
[4] Dieci MV, Criscitiello C, Goubar A, et al. Prognostic value of tumor-infiltrating lymphocytes on residual disease after primary chemotherapy for triple-negative breast cancer: a retrospective multicenter study. Ann Oncol. 2014 Mar; 25(3): 611–8.
[5] Zitvogel L, Kepp O, Kroemer G: Immune parameters affecting the efficacy of chemotherapeutic regimens. Nat Rev Clin Oncol 2011; 8: 151–160.

Disclosure of Interest: No significant relationships.

PG 4.03
Targeting bone microenvironment: clinical implications

M. Gnant*. *Comprehensive Cancer Center Vienna, Medical University of Vienna, Vienna, Austria*

Bone-targeting agents such as bisphosphonates are well established for the prevention and treatment of osteoporosis and the prevention of skeletal related events associated with bone metastases from solid tumors including breast cancer [1]. Recently, bisphosphonates have also been studied in randomized trials in the adjuvant setting of early breast cancer to investigate their ability to either prevent cancer treatment induced bone loss and/or their potential to prevent disease recurrence and metastases [2]. Metastasis of breast cancer involves a number of complex mechanisms – it is believed that the bone marrow microenvironment plays an important role [3]: Following dissemination, circulating tumour cells are attracted to bone surfaces within the bone marrow, where they are thought to displace haematopoietic stem cells and bind to the osteoblastic niche. Targeting bone cell function using bisphosphonates to manipulate this microenvironment provides a potential additional approach to current standard adjuvant treatments [4]. With respect of cancer-therapy induced bone loss (CTIBL), several trials have demonstrated the usefulness of adjuvant bisphosphonates for the prevention and treatment of CTIBL both in premenopausal [5] and postmenopausal women [6,7]. As a result, anti-resorptive therapy is part of current guidelines for the treatment of breast cancer patients [8]. With respect to anti-cancer effects of adjuvant anti-resorptive treatments, clinical studies have yielded conflicting results, both in the early trials assessing oral clodronate [9–11] as well as in recent Zoledronic Acid trials [12,13]. Remarkably, the effect of adjuvant bisphosphonates appear to be different in women after (natural or induced) menopause [14], and a number of scientific explanations have been offered to explain this [15,16]. A recent patient-level meta-analysis by the Early Breast Cancer Trials Collaborative Group (EBCTCG) has confirmed this observation based on data of 18,766 women from randomized clinical trials, with 3,459 breast cancer recurrences and 2,112 breast cancer deaths reported, respectively [17]. For the entire population, bisphosphonates reduced first distant recurrence in bone. For postmenopausal (natural or induced) women, bisphosphonates also improved overall breast cancer recurrence, distant recurrence, and breast cancer mortality. In summary, adjuvant anti-resorptive treatments provide persistent benefits to breast cancer patients in low-oestrogen situations, and should be considered an important part of the treatment algorithm.

Reference(s)

[1] Coleman, R, Body JJ, Aapro M, et al. Annals of Oncology 2014; 25(S3): iii124–iii137.
[2] Coleman R, Gnant M, Morgan G, Clezardin P. Journal of National Cancer Institute 2012; 104: 1059–1067.
[3] Weilbaecher KN, Guise TA, McCauley LK. Nature Rev Cancer 2011; 11: 411–425.
[4] Mundy GR. Nat Rev Cancer 2003; 2: 584–593.
[5] Gnant, M, Mlineritsch B, Luschin-Ebengreuth G, et al. Lancet Oncology 2008; 9: 840–849.
[6] Coleman RE, de Boer R, Eidtmann H et al. Annals of Oncology 2013; 24: 398–405.
[7] Paterson AHG, Anderson SJ, Lembersky BC et al. Lancet Oncology 2012; 13: 734–742.
[8] Hadji, P, Aapro MS, Body JJ, et al. Annals of Oncology 2011; 22: 2546–2555.
[9] Powles TJ, Paterson AE, McCloskey E, et al. Breast Cancer Res Treat 2006; 8R13: 1–7.
[10] Diel IJ, Jaschke A, Solomayer EF, et al. Annals of Oncology 2008; 19: 2007–2011.
[11] Saarto, T, Vehmanen L, Elomaa I, et al. Acta Oncologica 2004; 43: 650–656.
[12] Gnant M, Mlineritsch B, Schippinger W, et al. N Engl J Med 2009; 360: 679–691.
[13] Coleman RE, Cameron D, Dodwell D, et al. Lancet Oncol 2014; 15: 997–1006.
[14] Hadji P, Coleman R, Gnant M, Green J. Annals of Oncology 2012; 23: 2782–2790.
[15] Coleman RE, Gnant M, Morgan G, Clezardin P. J Nat Cancer Inst 2012; 104: 1059–1067.
[16] Ottewell, PD, Wang N, Brown HK, et al. Clinical Cancer Res 2014; 20: 2922–2932.
[17] Coleman RE, Gnant M, Gray R, et al. SABCS 2013.

Disclosure of Interest: Research Support: sanofi-aventis, Novartis, Roche, GlaxoSmithKline, Pfizer, Smith Medical. Consultancy: AstraZeneca, Novartis, Accelsiors. Honoraria (Speaking, Advisory Boards, etc.) and Travel Support: Amgen, Novartis, GlaxoSmithKline.

Thursday, 19 March 2015 **11.20–12.30**

Session 5: Bridging clinic with biology: Emerging drugable pathways on the horizon

PG 5.01
Targeting CDK 4–6 pathway

R.S. Finn*, D.J. Slamon. *Division of Hematology/Oncology, Geffen School of Medicine, UCLA Medical Center, Santa Monica, Santa Monica, United States of America*

Cell cycle dysregulation has long been recognized as a "hallmark" of cancer [1]. In normal cells, this complex process is tightly regulated by the interactions of several proteins throughout the various checkpoints and phases (i.e. G1, S, G2, etc). The cyclins and their associated signaling partners, the cyclin-dependent kinases (CDKs), are expressed and function throughout the cell cycle, with specific cyclin–CDK pairs functioning in various phases of the cycle [2]. In G1, CDK 4/6 and cyclin D play a key role in regulating phosphorylation of the RB gene product (pRb). Once hyperphosphorylated, pRB allows for cell cycle progression from G1 to S. For over a decade, there have been efforts to target CDK biology in cancer. First generation CDK inhibitors did not progress far in clinical development given toxicity and the lack of significant clinical activity. These drugs were generally pan-CDK inhibitors. More recently, highly specific CDK inhibitors have come into development. These include palbociclib (PD-0332991), abemaciclib (LY2835219), and LEE011 all of which have preferential activity against CDK 4/6. Critical to the development of this class of agents in cancer medicine is the identification of biomarkers of response. Using molecular characterized pre-clinical cell lines of breast cancer, we identified preferential activity of the CDK 4/6 inhibitor palbociclib in both ER+ breast cancer models as well as in HER2 amplified models [3]. Additional studies confirmed that his effect was the result of an intact and robust Rb pathway in these models, as compared to those models representing non-luminal/"triple-negative" subtypes. To support a clinical development plan, pre-clinical work also identified significant synergy between palbociclib and tamoxifen in ER+ models. These studies led to the rational design of a Phase I/II study to evaluate the safety and efficacy of palbociclib in combination with letrozole in the treatment of advanced ER+ breast cancer. The PALOMA-1/TRIO 18 study represents a global randomized phase II study that evaluated the combination in two cohorts of women with ER+/HER2− breast cancer: (1) selected for being ER+/HER2− (n = 66) and (2) selected for being ER+/HER2− as well as having the additional biomarkers of cyclin D1 amplification and/or loss of p16 (n = 99) [4]. The results of this study revealed a significant improvement in progression-free survival (PFS) in each of these cohorts. When the entire intent to treat population from both cohorts was analyzed together, PFS increased from 10.2 month to 20.2 months (HR 0.488, 95% CI 0.319–0.748; one-sided p = 0.0004) confirming the preclinical observations that addition of palbociclib to letrozole would improve efficacy in ER+/HER2− breast cancers. This PFS improvement was associated with a manageable side effect profile with the most common adverse events being neutropenia and fatigue. Based on these data, palbociclib was designated a "Breakthrough Therapy" by the US FDA in April of 2013. Confirmation that the preclinical data demonstrating CDK 4/6 inhibition in combination with anti-estrogens translates into markedly improved clinical efficacy supports further development of CDK 4/6 inhibitors such as palbociclib as well as abemaciclib and LEE011 in ER+/HER2− breast cancers.

Reference(s)

[1] Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. Cell 2011; 144: 646–674.
[2] Stone A, Sutherland RL, Musgrove EA. Inhibitors of cell cycle kinases: recent advances and future prospects as cancer therapeutics. Crit Rev Oncog 2012; 17: 175–198.
[3] Finn RS, Dering J, Conklin D, Kalous O, Cohen DJ, Desai AJ, Ginther C, Atefi M, Chen I, Fowst C, Los G, Slamon DJ. PD 0332991, a selective cyclin D kinase 4/6 inhibitor, preferentially inhibits proliferation of luminal estrogen receptor-positive human breast cancer cell lines in vitro. Breast Cancer Res 2009; 11: R77.
[4] Finn RS, Crown JP, Lang I, Boer K, Bondarenko IM, Kulyk SO, Ettl J, Patel R, Pinter T, Schmidt M, Shparyk Y, Thummala AR, Voytko NL, Fowst C, Huang X, Kim ST, Randolph S, Slamon DJ. The cyclin-dependent kinase 4/6 inhibitor palbociclib in combination with letrozole versus letrozole alone as first-line treatment of oestrogen receptor-positive, HER2-negative, advanced breast cancer (PALOMA-1/TRIO-18): a randomised phase 2 study. Lancet Oncol. 2014 Dec 15. S1470–2045(14)71159–3 [Epub ahead of print].

Disclosure of Interest: Grant/Research Support: Pfizer. Honoraria/Consultation Fee: Pfizer.

PG 5.02
Targeting DNA repair pathways

A. Tutt*. *Breakthrough Research Unit. Research Oncology, King's Health Partners AHSC, London, United Kingdom*

A high proportion of breast cancers demonstrate high degrees of genome instability. This genome instability leads to a very large number of copy number aberrations and mutations many of which have low frequency or recurrency across the disease. This genome instability is itself heterogeneous in form resulting from likely variations in DNA repair competency between and within the reported biological groups of breast cancer.

It has long been recognised that there is an association between familial predisposition to breast cancer and the Triple Negative Breast Cancer (TNBC). This is driven by the specific enrichment for TNBC in the breast cancers arising in BRCA1 mutation carriers. Loss of function of BRCA1 or BRCA2 leads to impairment of an accurate DNA repair process called Homologous Recombination (HR) used by proliferating cells to repair DNA replication forks that encounter spontaneous or therapeutic damage in DNA. Failure of HR causes a high degree of genome instability that can have distinctive features driven by the cell's need to use other DNA repair processes. HR is used to repair damage caused by certain forms of chemotherapy including that caused by platinum salts. This leads to high levels of platinum cell kill in preclinical studies of BRCA1 and BRCA2 mutation. Recently the use of PARP inhibitors has been shown to kill malignant cells with deficient HR, such as those with BRCA1 and BRCA2 mutation, through "synthetic lethality". A wider group of genes is known to have function in the homologous recombination and the DNA replication stress response pathways and many of these are also known to be breast cancer predisposition alleles.

Recent studies and some clinical trials have begun to address whether the specific defects in DNA repair that underlie BRCA1/2 associated breast cancer and sub-populations within sporadic breast cancer may lead to sensitivity to platinum salts and PARP inhibitors. Other kinases such as ATR, CHK1 and PI3-kinase may also form therapeutic targets that modify the DNA damage response and of which could be combined with PARP inhibition or platinum salts. I will review the biological mechanisms relevant to these approaches within specific breast cancer types. I will also review relevant clinical trials that have recently reported, and highlight others that are on going and discuss some emerging companion diagnostic approaches that seek to identify breast cancers that have deficiencies in HR and might benefit from platinum or DNA repair inhibitor therapies.

Disclosure of Interest: Grants/research support: Vertex, AstraZeneca, Myriad Genetics, Roche. Honoraria/consultation fees: Vertex, Eisai. Other: Named on Patent (KCL) Genome Instability Scars as biomarkers of DNA damage defects. ICR Rewards to inventors scheme – PARP inhibitors.

PG 5.03
Targeting PIK3CA pathway

J. Baselga*. *Memorial Sloan Kettering Cancer Center, Memorial Sloan-Kettering Cancer Center, New York, United States of America*

Pharmacologic and genetic evidences point to the PI3K/AKT/mTOR pathway as a key mediator of oncogenic signaling in breast cancer. PIK3CA, the gene encoding for p110α, is frequently mutated in human cancers. In particular, hot spot mutations of this gene reside in the helical (E542K and E545K) or catalytic (H1047R) domains are found in over a third of estrogen receptor (ER)-positive breast cancer, representing the most common genomic alteration in this group of tumors.

Direct pharmacologic inhibition of the PI3K/AKT/mTOR signaling is, therefore, an attractive clinical strategy for breast cancer. In addition to mTOR inhibitors already approved for the therapy of patients with advanced ER+ breast cancer, there are now a number of additional experimental agents that are in clinical development including pan-PI3K inhibitors. Among them, Buparlisib is a pan-PI3K inhibitor that is being studied in two large phase III studies in combination with fulvestrant in patients with advanced disease. More recently, PI3Kα specific inhibitors have shown remarkable clinical activity in the phase I setting in patients with breast tumors that harbor PI3Kα mutations and these agents are also entering now phase III studies in combination with hormonal therapies.

The underlying reason to study these agents in combination with hormonal therapies is compelling. Given that the vast majority of PIK3CA-mutant tumors are ER-positive, it is plausible to hypothesize that both pathways can drive proliferation and survival in these cells. A tangible evidence that the PI3K and ER pathways can cooperate in tumor progression came from the Bolero 2 study that showed an impressive improvement in progression-free survival (PFS) in ER-positive breast cancer patients treated with the mTOR inhibitor everolimus in combination with the anti-estrogen aromatase inhibitor exemestane. These patients had failed prior endocrine therapy and taking in consideration that activity of single agent mTOR inhibitors is minimal, these results suggest an interaction between mTOR and ER. In addition, it is known that anti-estrogen therapy induces the activation of the PI3K pathway in vitro and we have also observed that PI3K inhibition results in a powerful activation of ER signaling.

In summary, there is ample evidence that PI3K inhibition will be a fruitful approach in the treatment of patients with advanced breast cancer and it is likely that determining the presence of PI3Kα mutations in breast cancer will become useful in the daily clinical practice. The results of the ongoing phase III studies will further delineate the role of these agents in the therapy of breast cancer.

Disclosure of Interest: Consultant/Advisor: Novartis, Verastem, Roche, Juno, Infinity.

PG 5.04
Targeting FGFR pathway

N. Turner*. *Breast Unit, Royal Cancer Hospital, London, United Kingdom*

The Fibroblast Growth Factor Receptors can be activated by diverse mechanisms in breast cancer, including amplification of FGFR1 and FGFR2, rare activating mutations and translocations, as well as potentially through aberrant ligand dependent signaling. Amplification of FGFR1 occurs in 10% of ER positive cancer, enriched in luminal B type breast cancer, with FGFR1 amplification associating with increased risk of relapse. A number of early phase clinical trials have selected breast cancers with FGFR1 amplification, providing preliminary evidence of activity for small molecule FGFR inhibitors in FGFR1 amplified breast cancer. The preclinical and clinical data will be reviewed, and prospects for later stage clinical development of FGFR inhibitors discussed.

Disclosure of Interest: Grants/research support: AstraZeneca, Pfizer. Honoraria or consultation fees: Novartis, Roche, AstraZeneca, Servier, Clovis, Astellas, Tesaro, Genomic Health.

Thursday, 19 March 2015 **14.00–15.00**

Session 6: Primary prevention, metabolism and genetics

PG 6.01
Using germline genetics in the management of breast cancer patients and their families

J. Garber*. *Center for Cancer Genetics and Prevention, Dana-Farber Cancer Institute, Boston, United States of America*

A subset of women with breast cancer carry a heritable predisposing mutation in a breast cancer susceptibility gene that may underlie the development of their breast cancer. There are a number of circumstances in which a woman's BRCA mutation status may now affect decisions about her care, over and above the implications for the management of breast, ovarian and other cancer risk in family members, for whom data continues to show an advantage for intensified breast cancer surveillance and risk reducing preventive surgeries. These include:

1. The higher risk of second primary cancer may affect decisions in BRCA carriers about primary surgical option: breast conservation vs. bilateral mastectomies.
2. The SOFT data show the advantage of ovarian suppression plus hormonal therapy in premenopausal women requiring chemotherapy in treatment of their hormone receptor positive tumors. BRCA carriers would more likely undergo risk-reducing bilateral salpingo-oophorectomies rather than LHRH-agonist therapy.
3. Data from two neoadjuvant trials in triple negative breast cancer (GeparSEXTO and Alliance 4003) show an advantage for the use of platinum in BRCA carriers: The TNT trial shows a similar advantage in metastatic disease. Additional tumor biomarkers may predict response better than BRCA1/2 mutation status.
4. BRCA1/2 mutation carriers are eligible for the BIG/NRG adjuvant parp inhibitor trial, OlympiA, and other neoadjuvant trials.
5. BRCA mutation status may affect interventions to reduce the risk of additional primary cancers of the ovary (RRSO) and melanoma. Family members may use the information to reduce their risks of breast cancer, ovarian cancer, prostate cancer and possibly pancreatic cancer.

Mechanisms of acquired resistance against therapies targeting the DNA repair pathways are emerging. In addition, genetic testing now frequently includes evaluation of additional genes that have been associated with increased breast cancer risk, including TP53, PTEN, STK11, and CDH1, as well as an expanding group of moderate penetrance genes. Many women are now offered panels of genes for assessment of their risk either as a comprehensive germline test or following a negative BRCA1/2 examination. These genes do not yet affect treatment options, but may be used to assess risk of additional primary tumors and options for reducing those risks.

These data suggest that women with early onset breast cancer, triple negative breast cancers and other features suggesting hereditary predisposition underlying the diagnosis should consider genetic evaluation. The results may affect their own breast cancer care, and the cancer risk assessment among their family members.

Disclosure of Interest: Grants/research support: Myriad Genetics, Novartis (self); Novartis, Pfizer (spouse). Honoraria or consultation fees: Novartis, Pfizer (spouse); Pfizer (self).

PG 6.02
Preventing invasive breast cancer in women at high risk based on benign/in situ pathology

J. Cuzick*, M. Thorat. *Centre for Cancer Prevention, Queen Mary University of London, London, United Kingdom*

There are three main ways in which women can be identified as being at high risk of breast cancer: (i) family history of breast and/or ovarian cancer, which includes genetic factors, (ii) mammographically identified high breast density, and (iii) certain types of benign breast disease. The last category is the least common, but in some ways the easiest one for which treatment can be offered, because these women have already entered into the treatment system. Not all types of benign breast disease are associated with increased risk. The highest risk is seen in women with lobular carcinoma in situ, but this is very rare. More common is atypical hyperplasia, which comprises about 5–10% biopsied lesions and carries a 4–5 relative risk of subsequent breast cancer. It is most often an incidental finding when micro calcifications are seen on a mammogram. More common is hyperplasia of the usual type which is typically defined as breast duct epithelium thickness four or more cells deep and displaying admixture of two or more cell types; epithelial, myoepithelial and/or metaplastic apocrine cells. It carries a roughly twofold increase risk. Other types of benign lesions, notably about 50% of fibroadenomas and biopsied breast cysts which do not display hyperplasia, do not carry an increased risk of breast cancer. However women with aspirated cysts (and no histology) are also at increased risk of subsequent breast cancer. Tamoxifen has been shown to be particularly effective in preventing subsequent breast cancer in women with atypical hyperplasia – with a more than 70% reduction in the P1 trial and a 60% reduction in IBIS I. No data specific to atypical hyperplasia are available for the other two tamoxifen prevention trials. The aromatase inhibitors also are highly effective for atypical hyperplasia, with somewhat larger risk reductions than for other high risk women. There are no published data on the effectiveness of tamoxifen or the aromatase inhibitors for breast cancer prevention in women with hyperplasia of the usual type, or for women with aspirated cysts. A full review of breast cancer risk for different types of benign breast disease and the impact of preventive therapy in women with atypical hyperplasia and hyperplasia of the usual type will be presented.

Disclosure of Interest: Prof. Cuzick has received research funding from Astra Zeneca and is their advisory board member.

PG 6.03
Obesity and insulin resistance: clinical relevance and research priorities

P.J. Goodwin*. *University of Toronto, Mount Sinai Hospital, Toronto, Canada*

There is growing recognition that obesity is associated with adverse breast cancer outcomes. Research since St. Gallen 2013 has focused on four key areas, discussed below.

1. Is obesity associated with poor outcomes in all biologic subtypes of breast cancer? A recent meta-analysis provides evidence for an adverse association in estrogen receptor (ER) positive and negative BC. Some, but not all, subsequent analyses (many embedded in RCTs, including one by the Oxford Overview) suggest associations may be restricted to ER positive BC. Patient selection (e.g. exclusion of women with cardiac risk factors associated with insulin resistance/obesity) leading to exclusion of metabolically unhealthy women from RCTs, and other factors, may have contributed to these inconsistencies.
2. Does obesity impact AI efficacy or estrogen suppression in the adjuvant setting? Obesity is an adverse prognostic factor in women receiving letrozole or anastrozole; the relative benefit of anastrozole (but not letrozole) vs tamoxifen may be lowered in obese women. Emerging data suggest that endogenous estrogen suppression by AIs may be somewhat less complete in obese women; data are inconsistent and the clinical significance of these observations is unclear; for instance, one report suggests benefits of extended adjuvant anastrozole may be limited to normal weight women.
3. What are the potential biologic underpinnings of the obesity–breast cancer association? Components of the insulin resistance syndrome (hyperinsulinemia, dysglycemia, inflammation, altered adipokine profile) as well as obesity associated elevations in endogenous estrogen levels have been proposed as potential biologic mediators. The biology is likely complex, with the relative importance of different mediators varying across BC subtypes and over time (e.g. we found insulin to be important in the first 5 years after diagnosis while obesity and leptin associations persisted beyond 5 years).
4. Are interventions studies warranted? If so, which interventions in which populations? In the 45 years since the obesity-breast cancer prognosis association was first reported, dozens of observational studies have confirmed an adverse association, without identifying consistent subgroup patterns. It is not clear whether this association is causal, nor is it clear that reducing weight/improving metabolism will improve prognosis (ie: obesity effects may be "built into" BC biology and not be responsive to changes in weight or metabolism). The WINS RCT suggested

a beneficial effect of dietary fat reduction (associated with weight loss) on relapse, potentially greatest in ER negative BC. Additional intervention trials (weight loss, targeted metabolic agents such as metformin) are needed to investigate these issues. A metformin trial is nearing completion and weight loss trials are underway/proposed. Weight loss interventions should target overweight/obese but there is little support for targeting BC subtypes.

Reference(s)
[1] Chan DS et al. Ann Oncol 2014; 10: 1901–14.
[2] Niraula S et al. Breast Cancer Res Treat 2012; 134: 769–81.
[3] Sparano JA et al. Cancer 2012; 118: 5937–46.
[4] Goodwin PJ. Breast 2013; 22(Suppl 2): S44–7.
[5] Lonning PE et al. Eur J Cancer 2014; 50: 1055–1064.
[6] Gnant M et al. Br J Cancer 2013; 109: 589–596.
[7] Goodwin PJ, Stambolic V. Ann Rev Med 2015 [epub Nov 2014].
[8] Goodwin PJ et al. J Clin Oncol 2012; 30: 164–71.
[9] Chlebowski RT et al JNCI 2006; 98: 1767–76.
[10] Ligibel JA, Strickler HD. Am Soc Oncol Educ Book 2013: 52–9.
Disclosure of Interest: No significant relationships.

Thursday, 19 March 2015 **15.00–16.15**

Session 7: Beyond pathology of breast cancer in 2015

PG 7.01
The special case of "equivocal" pathological biomarkers (ER, PgR and HER2): Implications for breast cancer treatment

F.W. Symmans*. *UT MD Anderson Cancer Center, Dept. of Pathology, Houston, United States of America*

No abstract received.
Disclosure of Interest: No significant relationships.

PG 7.02
BCL-2: a new therapeutic target in estrogen receptor-positive breast cancer?

G.J. Lindeman*, D. Merino, F. Vaillant, S.W. Lok, K. Shackleton, J.E. Visvader. *Stem Cells and Cancer Division, The Walter and Eliza Hall Institute, Parkville, Australia*

Despite their relentless growth, cancer cells are poised in a life or death predicament. Faced with multiple genetic aberrations, tumors recalibrate key survival pathways to support their growth, measures that can reduce their vulnerability to cytotoxic or endocrine therapy. The steps taken to evade cell death are a recognized hallmark of cancer. Intense efforts over the last three decades have provided important insights into the molecular mechanisms that govern programmed cell death.

The pro-survival protein BCL-2 is overexpressed in approximately 75% of breast cancer, where it is has emerged as an important prognostic marker. Indeed, BCL-2 expression is a key component of the Oncotype DX assay. BCL-2 overexpression is even more prominent in luminal tumors (~85%), reflecting its estrogen-responsiveness. Other key pro-survival family members, MCL-1 and BCL-XL, are also commonly expressed across breast cancer subtypes. This group of pro-survival 'guardian' proteins play a critical role in keeping pro-apoptotic 'effector' proteins (such as BAX and BAK) in check. The effector proteins are essential for commitment to apoptosis, which occurs following mitochondrial cytochrome c release and caspase activation, resulting in cell death. BCL-2 guardian proteins also neutralize a group of 'sensor' proteins (such as BIM). The sensor proteins are triggered by distinct cytotoxic stimuli (such as chemotherapy) to activate the effectors BAX and BAK. The sensor proteins are termed 'BH3 only' proteins, as they lack the BCL-2 Homology (BH) domains BH1, BH2 and BH4 found in the two other subgroups.

While BCL-2 is an important prognostic marker in breast cancer, its precise role as a predictive marker of tumor response has yet to be clarified, with disparate findings reported across several studies. Nevertheless, there is increasing evidence that augmented levels of pro-survival BCL-2 proteins can prime tumors for death induced by conventional chemotherapy or endocrine therapy. This is due to the high occupation of pro-survival BCL-2 proteins by pro-apoptotic BH3 proteins, which can be activated by therapy, thereby committing tumor cells to apoptosis.

Small molecule inhibitors termed 'BH3 mimetics' that bind and neutralize BCL-2 pro-survival proteins have recently been described. These are showing considerable promise in early phase studies of lymphoid malignancies. We recently explored the feasibility of targeting luminal B tumors in combination therapy comprising endocrine therapy (tamoxifen) and a BH3 mimetic (ABT-737 or ABT-199) using patient derived xenograft (PDX) models of primary breast cancer. Tumor response and overall survival were significantly improved by combination therapy, when compared to tamoxifen alone. Moreover, synergy between BH3 mimetics and PI3K/mTOR inhibitors could be exploited by concomitant targeting of both survival pathways, a strategy that appeared both safe and effective. Since the potent and selective BCL-2 inhibitor ABT-199 was effective in these models (despite abundant BCL-XL expression), BCL-2 may be a crucial target for some luminal tumors, where we speculate it could provide a suitable 'companion' biomarker for patient selection.

The potential for testing this new class of drug in breast cancer will be reviewed (including early phase clinical trials), as well as prospects for the development of BCL-XL and MCL-1 inhibitors.

Disclosure of Interest: Grant/research support: Amgen, Servier. Honoraria or consultation fees: Amgen. The Walter and Eliza Hall Insitute has a commercial agreement with Abbvie (formerly Abbott) and Genentech, and receives commercial income related to ABT-199.

PG 7.03
The changing role of ER in endocrine resistance

C.K. Osborne*, R. Schiff. *Dan L. Duncan Cancer Center, Baylor College of Medicine, Houston, United States of America*

Despite the success of endocrine therapy targeting estrogen receptor-α (ER) in ER-positive breast cancer, more than half of metastatic patients do not respond to first line therapy, and almost all responders eventually progress. Nonetheless, many patients who progress on one endocrine treatment still respond to other types of endocrine therapies given in sequence. Similarly, in preclinical models of acquired endocrine resistance, downregulation of ER by genetic or pharmacological approaches inhibit tumor cell growth. Together, these observations highlight a continued role for ER signaling, albeit altered, in the resistant tumors. Recent advances in understanding the nature and biology of ER in recurrent metastatic disease in patients and in preclinical endocrine-resistant models have revealed new key mechanisms that explain how altered ER activity might mediate resistance. Importantly, these mechanisms may arise as a result of clonal selection under the pressure of chronic endocrine therapy. Over the past year, a few studies utilizing next-generation sequencing have identified gain-of-function recurrent mutations in the ligand-binding domain of ER gene (ESR1) in ~15–20% of patients with resistant metastatic breast cancers that emerge after endocrine therapy. Most of these mutations confer constitutive ligand-independent activity to ER, causing resistance to estrogen-deprivation (i.e., aromatase inhibitors) and reduced sensitivity to the ER antagonist tamoxifen and the selective ER downregulator (SERD) fulvestrant. Additional

and more rare ESR1-related genomic alterations including gene amplification, rearrangements, and gain-of-function fusions have also been identified mostly in patients with recurrent metastatic disease. These ESR1 mutations represent a novel mechanism for acquired endocrine resistance. Alterations in ER activity and its transcriptional program in endocrine resistance can also result from deregulated growth factor receptor signaling and changes in ER coregulatory proteins such as the ER coactivator SRC3 and the pioneering factor FOXA1. Our new studies in acquired endocrine-resistant preclinical models suggest that FOXA1 gene amplification, which involves activation of a cytokine loop, can mediate endocrine resistance. Specifically, the resulting FOXA1 hyperactivity induces, in an ER-dependent manner, high levels of IL-8, which supports the growth of the resistant cells. Further, exogenous overexpression of FOXA1 in endocrine-sensitive cells increases IL-8 levels and also activates multiple signaling pathways, resulting in endocrine resistance. Collectively, these recent findings highlight the importance of routine biopsy of recurrent lesions to assess the changes in epi/genomics and signaling landscape for tailoring therapies to effectively overcome endocrine resistance. In addition, more completely abolishing the levels and activity of ER together with its coactivators may provide a better therapeutic strategy in combating endocrine resistance. These strategies include novel epigenomic approaches to inhibit gene expression of ER and its coactivators, high-dose or more potent SERDs, recently identified inhibitors of SRC3, signal transduction inhibitors that modulate levels and activity of ER and its coactivators, and inhibitors of key mediators of the altered ER pathway such as IL-8 in endocrine resistance.

Disclosure of Interest: Honoraria/consultation fees: Pfizer, GSK, Nanostring, AstraZeneca, Novartis.

PG 7.04
Developing Ki67 as a useful marker

C. Denkert*. *Institute of Pathology, Charité Universtitätsmedizin Berlin, Berlin, Germany*

Increased proliferation is a hallmark of malignant tumors and an important parameter for prediction of therapy response. The proliferation marker Ki67 has been suggested as a promising breast cancer biomarker, but the best cutpoints and the best methods for determination are still under debate. The standardisation of Ki67 is still relevant for diagnostic pathology, because this marker can be viewed as the prototype of a quantitative immunohistochemical biomarker, and the experience gained with Ki67 is relevant for other upcoming immunohistochemistry-based prognostic and predictive biomarkers, as well.

This presentation gives an overview on the efforts to standardize Ki67 and on the methodological parameters that are relevant for optimal performance of this marker. As for other diagnostic markers, the main parameters for evaluation of Ki67 include (a) clinical validity, (b) analytical validity and (c) clinical utility.

In particular the analytical standardisation of Ki67 is still a challenge, and an international standardisation approach is currently in progress. This presentation gives an overview on the relevant parameters for standardisation of Ki67, with a focus on different approaches to cutpoints as well as the role of Ki67 in different tumor types. Different options for evaluation including automated image analysis will be discussed.

The clinical validity of Ki67 as a prognostic marker as well as a predictive marker in the neoadjuvant setting has been shown in several metaanalyses. Depending on the tumor type and the clinical setting, Ki67 is a mixture of a prognostic and a predictive marker. On the one hand, a low Ki67 level is linked to a low proliferation rate and an improved outcome, in particular in luminal tumors. On the other hand, an increased Ki67 level suggests an improved response to chemotherapy. The combination of both, prognostic and predictive effects will determine the performance of Ki67 as a biomarker in different clinical cohorts. Several different cutpoints for Ki67 have been reported to be significant and it is very difficult to determine an evidence-based "optimal" cutpoint. This supports the view that Ki67 should be regarded as a continuous marker, reflecting the continuous variation of the proliferation rate in different types of tumors.

Reference(s)

[1] Polley MY, Leung SC, McShane LM, Gao D, Hugh JC, Mastropasqua MG, Viale G, Zabaglo LA, Penault-Llorca F, Bartlett JM, Gown AM, Symmans WF, Piper T, Mehl E, Enos RA, Hayes DF, Dowsett M, Nielsen TO; International Ki67 in Breast Cancer Working Group of the Breast International Group and North American Breast Cancer Group. An international Ki67 reproducibility study. J Natl Cancer Inst. 2013 Dec 18; 105(24): 1897–906.

[2] Klauschen F, Wienert S, Schmitt W, Loibl S, Gerber B, Blohmer JU, Huober J, Ruediger T, Erbstoesser E, Mehta K, Lederer B, Dietel M, Denkert C, von Minckwitz G. Standardized Ki67 diagnostics using automated scoring – clinical validation in the GeparTrio breast cancer study. Clin Cancer Res. 2014 Dec 11. pii: clincanres.1283.2014. [Epub ahead of print]. PubMed PMID: 25501130.

[3] Denkert C, Loibl S, Müller BM, Eidtmann H, Schmitt WD, Eiermann W, Gerber B, Tesch H, Hilfrich J, Huober J, Fehm T, Barinoff J, Jackisch C, Prinzler J, Rüdiger T, Erbstösser E, Blohmer JU, Budczies J, Mehta KM, von Minckwitz G. Ki67 levels as predictive and prognostic parameters in pretherapeutic breast cancer core biopsies: a translational investigation in the neoadjuvant GeparTrio trial. Ann Oncol. 2013 Nov; 24(11): 2786–93. doi: 10.1093/annonc/mdt350. Epub 2013 Aug 22. PubMed PMID: 23970015.

[4] Dowsett M, Nielsen TO, A'Hern R, Bartlett J, Coombes RC, Cuzick J, Ellis M, Henry NL, Hugh JC, Lively T, McShane L, Paik S, Penault-Llorca F, Prudkin L, Regan M, Salter J, Sotiriou C, Smith IE, Viale G, Zujewski JA, Hayes DF; International Ki-67 in Breast Cancer Working Group. Assessment of Ki67 in breast cancer: recommendations from the International Ki67 in Breast Cancer working group. J Natl Cancer Inst. 2011 Nov 16; 103(22): 1656–64. doi: 10.1093/jnci/djr393. Epub 2011 Sep 29. PubMed PMID: 21960707; PubMed Central PMCID: PMC3216967.

Disclosure of Interest: CD is cofounder and shareholder of Sividon Diagnostics, Cologne.

Thursday, 19 March 2015 **16.45–18.00**

Session 8: Primary systemic therapy of early breast cancer

PG 8.01
Primary systemic therapy for clinicians: medical and research perspectives

S. Loibl*. *Medicine & Research, GBG Forschungs GmbH, Neu-Isenburg, Germany*

The primary systemic or neoadjuvant therapy has become one standard option for treating patients with early stage breast cancer irrespective of the extend of the disease. It could be shown that patients who achieve a pathological complete response (pCR) have a better disease-free and overall survival. The hazard between pCR and no pCR is largest in TNBC and HER2+ patients. Based on the data of the GeparTrio trial one could argue that in patients with TNBC it is important to achieve a pCR, irrespective of the given therapy. Changing the treatmend midway according to clinical response does not influence the longe-term outcome, whereas in patients with hormone-receptor positive tumours pCR is important, but the long-term outcome can be improved by adapting the therapy based on clinical response.

In recent years the rat of pathological complete response increased in TNBC as well as in HER2 breast cancer. In TNBC the rate increased from around 45% to 60% by adding Carboplatin and using dose-dense or weekly regimen, e.g. Paclitaxel weekly plus Carboplatin followed by AC every 2 weeks. New studies are currently investigating the role of PARP-inhibitors irrespective of the gBRCA status. Whereas in HER2+ breast cancer the pCR could be increased to over 70% by using the double HER2 blockade either with trastuzumab plus lapatinib or trastuzumab plus pertuzumab in addition to an 18–24 weeks anthracycline/taxane based chemotherapy. In all trials patients with a HER2+/HR+ tumour had a significantly lower pCR rate than those with a HER2+/HR− tumour. Trastuzumab plus lapatinib with or without endocrine treatment was investigated in two smaller phase II studies. The chemofree approach with the double blockade plus an endocrine therapy is an option worth investigating further in the HR+ subgroup.

Besides the HR-status, several other biomarkers have been investigated to select patients with the highest chance for a pCR. The PI3Kinase pathway has been investigated by several groups. It could be demonstrated that tumours harbouring a mutation of the PIK3CA have a significantly lower pCR rate with trastuzumab and lapatinib than those with wild-type PIK3CA. However, it is not yet prime time for selecting patients according to the PIK3CA status.

Tumour infiltrating lymphocytes and immune markers significantly independently predict a higher pCR rate.

Neoadjuvant studies, especially window of opportunity studies either as stand alone studies or as an integrated part of a trial, are an excellent research tool, because tumour material can be investigated before and after treatment.

Reference(s)

Cortazar P, Zhang L, Untch M, etal. Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis. Lancet. 2014 Jul 12; 384(9938): 164–72.

von Minckwitz G, Blohmer JU, Costa SD, et al. Response-guided neoadjuvant chemotherapy for breast cancer. J Clin Oncol. 2013 Oct 10; 31(29): 3623–30.

Sikov WM, Berry DA, Perou CM, et al. Impact of the Addition of Carboplatin and/or Bevacizumab to Neoadjuvant Once-per-Week Paclitaxel Followed by Dose-Dense Doxorubicin and Cyclophosphamide on Pathologic Complete Response Rates in Stage II to III Triple-Negative Breast Cancer: CALGB 40603 (Alliance). J Clin Oncol 2015; 33: 13–21.

Loibl S. Neoadjuvant treatment of breast cancer: maximizing pathologic complete response rates to improve prognosis. Curr Opin Obstet Gynecol 2015; 27: 85–91.

Loibl S, von Minckwitz G, Schneeweiss A, et al. PIK3CA mutations are associated with lower rates of pathologic complete response to anti-human epidermal growth factor receptor 2 (her2) therapy in primary HER2-overexpressing breast cancer. J Clin Oncol 2014; 32: 3212–20.

Denkert C, von Minckwitz G, Brase JC, et al. Tumor-Infiltrating Lymphocytes and Response to Neoadjuvant Chemotherapy With or Without Carboplatin in Human Epidermal Growth Factor Receptor 2-Positive and Triple-Negative Primary Breast Cancers. J Clin Oncol 2014 Dec 22 [Epub ahead of print].

Disclosure of Interest: Honoraria or consultation fees from Novartis, Roche, Celgene, Amgen, Pfizer.

PG 8.02
Neoadjuvant endocrine therapy: patient selection, treatment duration and surrogate endpoints

M. Dowsett*. *Institute of Cancer Research, Royal Marsden Hospital, London, United Kingdom*

Neoadjuvant endocrine treatment has become of increasing interest for downstaging primary ER+ breast cancers as it has become clear that the pathologic complete response rate of luminal tumours to chemotherapy is much lower than that of non-luminal and differs little from that from endocrine therapy.

There is much more experience in postmenopausal than premenopausal women. Aromatase inhibitors are generally the agent of choice. Responses are lower in those with the low levels of ER.

While duration of endocrine treatment in clinical trials has usually been standardized at around three to four months it is clear that volume reductions continue to occur beyond that time in a large proportion of cases and routine clinical practice is often to treat to maximum response.

This relatively slow emergence of downstaging relates to the absence of any increase in apoptosis with endocrine therapy and dependence of responses on the antiproliferative effects of oestrogen withdrawal: apoptosis occurs but a slightly lower rate such that cell loss is attritional. The dependence of responses on the reduced proliferation underpins the value of Ki67 as an intermediate end-point for treatment benefit with multiple studies having found that relative effects on proliferation by different drugs in neoadjuvant trials match their relative impact on recurrence. While change in Ki67 is now accepted as a validated endpoint for comparing endocrine agents in the neoadjuvant scenario, on-treatment levels of Ki67 are related to long-term prognosis more closely than pretreatment Ki67.

The Preoperative Endocrine Prognostic Index (PEPI) that combines residual Ki67 score with measures of on-treatment ER and other clinicopathologic factors has also found application in clinical trials.

The potential to make longitudinal assessments of both clinical and biomarker responses has encouraged the development of novel clinical trial designs for assessing the impact of agents that aim to enhance response beyond that of endocrine agents alone. Such strategies include the early measurement of residual Ki67 levels after challenge with an endocrine agent alone and evaluation of the impact of the added agent on Ki67 or other agent-specific end-points.

Disclosure of Interest: Grants/Research support: Pfizer, Roche, AstraZeneca. Honoraria/Consultation fees: Roche, Pfizer, Nanostring, Novartis, Ventana, Janssen. Other: Institute of Cancer Research Rewards for Inventors Scheme related to Abiraterone.

PG 8.03
Clinical usefulness and relevance of intermediate endpoints for cytotoxic primary systemic therapy

G. Von Minckwitz*. *Germanbreastgroup, Univ. Frankfurt, Neu-Isenburg, Germany*

Intermediate endpoints in oncology are surrogate markers of treatment efficacy assessed earlier than the true outcome of interest (usually survival) and they are determined in the middle of the causal sequence relating treatment to survival [1]. Intermediate endpoints in the context of neoadjuvant systemic treatment can be assessed as early after 1 cycle of treatment or more robustly after end of chemotherapy at surgery by histomorphologic examination of all surgically removed tissues from the breast and regional nodes. Several meta-analyses indicated that the risk of death among patients who attain a pathological complete response (pCR) is lower than the risk of patients with residual tumor at the time of surgery; patients who achieved a pCR have a more favorable long-term outcome, such as DFS and OS [2–5]. Even the largest of these metaanalyses [5] could not find a linkage of improvements of pCR rates by a randomized treatment and improvement of survival by the same treatment and therefore did not establish the surrogacy of pCR. Nevertheless, the Food and Drug Administration (FDA) recently allowed using pCR as a surrogate endpoint for accelerated approval process [6]. FDA will be accepting two definitions for pCR: no invasive or non-invasive residual cancer in breast and nodes (ypT0 ypN0); or no invasive residual in breast and nodes irrespective of residual non-invasive disease (ypT0/is ypN0). A recent

pooled analysis of 6,377 subjects [3] demonstrated that patients who attained ypT0 ypN0 experienced better DFS and a trend in better OS compared with patients who attained ypTis ypN0. Several meta-analysis highlighted that the association of pCR and survival was stronger in patients with HER2-positive and triple-negative tumors, compared to less aggressive tumor subtypes (such as low-grade HR-positive) [2,3,5]. Usefulness of an earlier intermediate endpoints, i.e. clinical response determined after two cycles of docetaxel, doxorubicin, and cyclophosphamide (TAC) was prospectively demonstrated in the GeparTrio trial; patients showing an early response achieved 4 times more frequently a pCR than those without early response [7,8]. Experimental arms (8 TAC cycles in responding patients or switch to another chemotherapy in non-responding patients) did not lead to different pCR rates compared to 6 TAC cycles, but achieved a better outcome only in patients with HR-positive tumors where pCR showed no surrogacy with outcome [9].

Reference(s)

[1] Prentice RL. Surrogate endpoints in clinical trials: definition and operational criteria. Stat Med. 1989, 8: 431–440.

[2] Houssami N, Macaskill P, von Minckwitz G, Marinovich ML, Mamounas E. Meta-analysis of the association of breast cancer subtype and pathologic complete response to neoadjuvant chemotherapy. Eur J Cancer. 2012, 48: 3342–54.

[3] von Minckwitz G, Untch M, Blohmer JU, et al. Definition and impact of pathologic complete response on prognosis after neoadjuvant chemotherapy in various intrinsic breast cancer subtypes. J Clin Oncol. 2012, 30: 1796–804.

[4] Mieog JS, van der Hage JA, van de Velde CJ. Preoperative chemotherapy for women with operable breast cancer. Cochrane Database Syst Rev. 2007 (2): CD005002.

[5] Cortazar P, Zhang L, Untch M, et al.: Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis. Lancet 2014, 384: 164–72.

[6] http://www.fda.gov/downloads/drugs/guidancecomplianceregulatory information/guidances/ucm305501.pdf

[7] von Minckwitz G, Kümmel S, Vogel P et al. Intensified neoadjuvant chemotherapy in early-responding breast cancer: phase III randomized GeparTrio study. J Natl Cancer Inst. 2008, 100: 552–62.

[8] von Minckwitz G, Kümmel S, Vogel P, et al. Neoadjuvant vinorelbine-capecitabine versus docetaxel-doxorubicin-cyclophosphamide in early nonresponsive breast cancer: phase III randomized GeparTrio trial. J Natl Cancer Inst. 2008, 100: 542–51.

[9] von Minckwitz G, Blohmer JU, Costa SD, et al. Response-guided neoadjuvant chemotherapy for breast cancer. J Clin Oncol 2013, 31: 3623–30.

Disclosure of Interest: No significant relationships.

PG 8.04
Clinical trial designs in the neoadjuvant setting: challenges of the genomic era

L.A. Carey*. *UNC Breast Center, UNC-Lineberger Cancer Center, Chapel Hill, United States of America*

The advent of the genomic era has brought great promise for truly individualized therapy in breast cancer, as with other tumor types. However the fragmentation of breast cancer into multiple subtypes (and subtypes within subtypes) also brings enormous challenges for the clinical trials required to prove these therapeutic strategies. These challenges include establishing the validity of the genomic (or proteomic, or transcriptomic, or other assay type) approach being used to identify a subtype of clinical relevance, and the statistical and logistical issues of clinical trials in small subpopulations.

The neoadjuvant approach has become increasingly popular for clinical trials because it permits testing new drugs or new regimens in primary, untreated breast cancer in a way that facilitates both rapid study completion, since the study endpoint (usually pathologic complete response, or pCR) is achieved in months rather than years, and embedded biomarker exploration, since the breast cancer tissue is readily accessible. As "breast cancer" by necessity has been splintered into biologically relevant subsets, and drug development has exploded, neoadjuvant trials, which require substantially smaller sample sizes than adjuvant trials, become not just convenient, but necessary. These span the range from traditional single arm phase II trials, which are difficult to interpret since populations can vary substantially among trials, or randomized designs, which are blessedly becoming increasingly the norm. Many modern trials incorporate mandatory research tissue components, permitting near-simultaneous examination of drug and underlying biology on treatment effect.

Newer innovative designs include adaptive randomization ratio designs, like the ISPY2 trial, which has already contributed regimens being tested in more definitive designs [1]. These are the clinical trial equivalent of a drug modeling laboratory. They are comparatively fast, and are nimble – the design incorporates changes in drugs and regimens within the same trial – and for providing an early "green light" for regimens with a high degree of promise. However, they also carry a higher risk of inadvertently discarding promising regimens or drugs. Another popular twist on neoadjuvant trials are residual disease trials, in which eligibility is restricted to those tumors that were not eradicated by conventional therapy. These trials are attractive because they enrich for a population of interest (resistant to conventional drugs), with post-treatment tissue often available for interrogation of resistance markers, and a high event rate so they are often well powered with a smaller sample size. However these are still adjuvant trials. There is no access to additional tissue, and there are no intermediate endpoints.

Several recent clinical trials have demonstrated that even within an enriched population, multiple tumor and host factors impact on pCR beyond treatment arm, creating substantial noise and impacting on interpretability of individual trial results. For example, in two Cancer and Leukemia Group B (CALGB) neoadjuvant studies, one in HER2-positive breast cancer, the other in triple negative breast cancer, expression of immune cells significantly and independently influenced pCR rate, as did p53 mutation status and proliferation [2,3]. Moreover, clinical subtypes often include multiple molecular subtypes, which itself significantly affects pCR rate regardless of treatment [2,4–6].

The last challenge that must be acknowledged is that while the relationship of pCR to outcome is amply established, there is no formula correlating a quantitative pCR change to changes in outcomes of clinical importance, like disease-free or overall survival [7]. It is likely that we will need to learn better how to identify and integrate tumor and microenvironmental parameters before we will be able to use neoadjuvant trial results to change clinical practice.

Reference(s)

[1] Rugo H, Olopade O, DeMichele A, van't Veer L, Buxton M, et al. Veliparib/carboplatin plus standard neoadjuvant therapy for high-risk breast cancer: First efficacy results from the I-SPY 2 TRIAL; 2013. pp. 10–14.

[2] Carey LA, Barry WT, Pitcher B, Hoadley KA, Cheang MCU, et al. Gene expression signatures in pre-and post-therapy (Rx) specimens from CALGB 40601 (Alliance), a neoadjuvant phase III trial of weekly paclitaxel and trastuzumab with or without lapatinib for HER2-positive breast cancer (BrCa); 2014. pp. 506.

[3] Sikov W, Barry W, Hoadley KA, al e (2014) Impact of intrinsic subtype by PAM50 and other gene signatures on pathologic complete response (pCR) rates in triple-negative breast cancer (TNBC) after neoadjuvant chemotherapy (NACT) +/− carboplatin (Cb) or vevacizumab (Bev): CALGB 40603/150709 (Alliance). CTRC-AACR San Antonio Breast Cancer Symposium. San Antonio, TX. pp. S4–05.

[4] Ellis MJ, Suman VJ, Hoog J, Lin L, Snider J, et al. (2011) Randomized phase II neoadjuvant comparison between letrozole, anastrozole, and exemestane for postmenopausal women with estrogen receptor-rich

stage 2 to 3 breast cancer: clinical and biomarker outcomes and predictive value of the baseline PAM50-based intrinsic subtype – ACOSOG Z1031. J Clin Oncol 29: 2342–2349.
[5] Rouzier R, Perou C, Symmans W, Ibrahim N, Cristofanilli M, et al. (2005) Molecular subtypes of breast cancer respond differently to preoperative chemotherapy. Clin Cancer Res 11: 5678–5685.
[6] Sikov WM, Berry DA, Perou CM, Singh B, Cirrincione CT, et al. (2015) Impact of the Addition of Carboplatin and/or Bevacizumab to Neoadjuvant Once-per-Week Paclitaxel Followed by Dose-Dense Doxorubicin and Cyclophosphamide on Pathologic Complete Response Rates in Stage II to III Triple-Negative Breast Cancer: CALGB 40603 (Alliance). J Clin Oncol 33: 13–21.
[7] Cortazar P, Zhang L, Untch M, Mehta K, Costantino JP, et al. (2014) Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis. Lancet 384: 164–172.

Disclosure of Interest: Consultant/Speaker/Advisor (uncompensated): Sanofi-Oncology, Wyeth-Pfizer, Genentech/Roche, BMS, Novartis, GSK, Medigene AG. Research Support: GSK, Sanofi Oncology, Genentech. Dr. Carey does not receive any compensation, all monies are given to UNC.

Friday, 20 March 2015 **08.30–10.00**

Session 9: Areas of controversy in surgery of early breast cancer, in special populations

PG 9.01
Optimal surgical management for high risk populations

T. King*. *Breast Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, United States of America*

The recognition that breast cancer is a group of genetically distinct diseases with differing responses to treatment and varying patterns of both local and systemic failure has led to many questions regarding optimal therapy for those considered to be high risk. Young patients, patients with triple-negative breast cancer (TNBC), and those who harbor a deleterious mutation in BRCA1 or 2 are frequently considered to be at highest risk of local failure, leading to speculation that more aggressive surgical treatment is warranted in these patients. In addition, there is considerable overlap among these risk factors whereby up to 40% of women under the age of 40 with TNBC will be found to harbor a BRCA mutation, adding to the complexity of surgical decision making. It is clear that young breast cancer patients experience higher local recurrence (LR) rates, and they also frequently present with more aggressive clinicopathologic features, including hormone receptor negative and HER2/neu overexpressing disease, when compared to their older counterparts [1]. Yet, in the absence of a BRCA mutation, it is unclear what factors are truly responsible for the increase in LR and poorer survival. Although studies comparing LR rates in young women following breast-conserving therapy (BCT) versus mastectomy report conflicting results, there is no evidence that mastectomy or contralateral prophylactic mastectomy (CPM) improves survival among young women with breast cancer [2,3]. An increased risk of LR in triple-negative cancers is also apparent; however, this increased LR risk is present following surgical treatment with both BCT and mastectomy, highlighting the importance of future systemic therapies targeting the triple-negative subtype in improving local outcomes [4]. The strong association between BRCA mutation status and TNBC raises the possibility that poly ADP ribose polymerase inhibitors may be one such strategy; this concept is currently being tested in the adjuvant setting (NCT02032823). Surgical decision making for affected BRCA mutation carriers must take into account several competing risks: risk of ipsilateral breast cancer recurrence, risk of contralateral breast cancer (CBC), and the potential benefit of CPM and/or prophylactic oophorectomy on survival. Studies comparing risk of ipsilateral breast cancer recurrence between carriers and non-carriers have generated conflicting results, however; a recent meta-analysis suggests that the increased risk is only realized in studies with longer follow-up (>7 years), raising the question of new primary cancers versus true in-breast recurrences. In contrast, the risk of CBC is consistently higher in carriers than non-carriers, warranting a full discussion of strategies to reduce risk of CBC, including oophorectomy in premenopausal patients and the use of endocrine therapy in patients with estrogen receptor-positive index cancers. For both age and subtype, it appears that the intrinsic biology which imparts inferior outcomes is not overcome with mastectomy; therefore, a recommendation for more extensive surgical therapy among these higher-risk groups is not warranted. For those at inherited risk, a more aggressive surgical approach may be preferable, however; patient age, ER status, stage of the index lesion, and individual patient preferences should all be considered in the surgical decision-making process.

Reference(s)

[1] Azim HA et al. Breast Cancer Res 2014; 16: 427.
[2] Cao JQ et al. Int J Radiat Oncol Biol Phys 2014; 90: 509–17.
[3] Pesce C et al. Ann Surg Oncol 2014; 21: 3231–9.
[4] Lowery AJ et al. Breast Cancer Res Treat 2012; 133: 831–41.

Disclosure of Interest: No significant relationships.

PG 9.02
Feasibility of sentinel node biopsy in breast cancer after neoadjuvant treatment

V. Galimberti*. *Department of Senology, Istituto Europeo di Oncologia, Milano, Italy*

Background: Initially SNB was only indicated for early breast cancer. Patients scheduled for neoadjuvant treatment generally had large cancers, and often a clinically positive axilla, so SNB was not relevant. There was fear also that lymphatic drainage would be altered by the chemotherapy and the 'real' sentinel node would not be found. However, the 2014 ASCO guidelines noted that most breast cancer patients should have SNB [1], and, based on a systematic review of selected studies, recommended SNB after neoadjuvant treatment. The guidelines do not, however, recommend SNB in women who are cN1/2 before chemotherapy, even if they become cN0 afterwards, since the false negative rate (FNR) could be 'unacceptably high'. Thus, in arm C of the prospective SENTINA study [2] – consisting of cN1 women who became cN0 after chemotherapy and received SNB followed by axillary dissection (AD) – the FNR was 14.2%. And in the prospective Z1071 study [3], which enrolled cN1 women scheduled for neoadjuvant chemotherapy, the FNR was 12.6%. Other studies, by contrast, found FNRs below 10% for SNB after systemic neoadjuvant treatment in women with proven axillary disease prior to treatment [4,5].
Methods: To address this issue we retrospectively analyzed outcomes after a median of 61 months (IQR 38–82) in 396 patients who were cN0 or cN1/2 before neoadjuvant treatment, became or remained cN0 after, and received SNB (paper submitted).
Results: Five-year OS was 90.7% (95% CI 87.7–93.7%): 93.3% (95% CI 90.0–96.6) in those initially cN0, and 86.3% (95% CI 80.6–92.1) in those initially cN+ ($P = 0.12$). In initially cN0 patients, and also initially cN+ patients who responded well to neoadjuvant treatment (pT0/pTx), SN negativity was a significant predictor of good outcome, consistent with the known prognostic significance of axillary status, and suggesting that SN status accurately reflected axillary status (low FNR). By contrast, in initially cN+ patients found to be pT1/pT2–3, SN status (and whether or not AD was performed) had no influence on survival and thus did not accurately reflect axillary status (high FNR).

Conclusions: Our findings suggest that SNB is acceptable in cN+ patients who become cN0 after neoadjuvant therapy: in those who are pT0/pTx because SN status has it usual prognostic role (FNR low), but also in those who are pT1/2/3 because AD has no influence on outcome.

Reference(s)

[1] Lyman GH, Temin S, Edge SB, et al. Sentinel lymph node biopsy for patients with early-stage breast cancer. American Society of Clinical Oncology Clinical Practice. J Clin Oncol 2014; 32: 1365–83.
[2] Kuehn T, Bauerfeind I, Fehm T, et al. Sentinel-lymph-node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (SENTINA): a prospective, multicentre cohort study. Lancet Oncol 2013; 14: 609–18.
[3] Boughey JC, Suman VJ, Mittendorf EA, et al. Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node-positive breast cancer: the ACOSOG Z1071 clinical trial. JAMA 2013; 310: 1455–61.
[4] Newman EA, Sabel MS, Nees AV, et al. Sentinel lymph node biopsy performed after neoadjuvant chemotherapy is accurate in patients with documented node-positive breast cancer at presentation. Ann Surg Oncol 2007; 14: 2946–52.
[5] Canavese G, Dozin B, Vecchio C, et al. Accuracy of sentinel lymph node biopsy after neo-adjuvant chemotherapy in patients with locally advanced breast cancer and clinically positive axillary nodes. Eur J Surg Oncol 2011; 37: 688–94.

Disclosure of Interest: No significant relationships.

PG 9.03
Surgical management after neoadjuvant chemotherapy

P. Dubsky*. *Brustambulanz Akg Wien, Medical University of Vienna, Vienna, Austria*

Neoadjuvant (= preoperative) chemotherapy (NACT) is a standard option in both locally advanced- and primary, operable breast cancer. Chemotherapeutic regimens from adjuvant treatment can safely be delivered preoperatively and deliver comparable survival rates. NACT can lead to various forms of tumour shrinkage. In comparison to upfront surgery this entails higher rates of breast conservation (BCT). Despite increasing pCR rates due to new treatment regimens especially in hormone receptor negative or HER-2 overexpressing types of breast cancer, published reports do not show a clear increase of BCT. This phenomenon is all the more surprising since the indication for NACT is increasingly set according to aggressive tumour biology rather than increased tumour size. This may reflect uncertainties (both from the patient and the physician side) especially concerning local recurrence risk. Successful surgical management aiming toward breast conservation has two major objectives when carried out after chemotherapy:

- Resection within new tumour margins adjusted for therapy response and/or
- An operative assessment that secures the pathologic diagnosis of complete tumour remission (pCR).

First, in order to better guide surgical management it is important to define surgical pitfalls: These include a failure to resect residual invasive tumour foci possibly due to primary multifocality/centricity or to disseminated tumour response patterns. Residual ductal carcinoma in situ may lead to repetitive resections, poor cosmetic outcome and ultimately to mastectomy. Finally, mastectomy in cases of complete pathologic remission must be avoided. Preoperative surgical management is a typical example of an interdisciplinary task in women undergoing NACT: Safe surgery includes multiple tasks to be performed at three major time points:

1. Diagnostic assessment of tumour focality, intraductal components, tumour type and of hormone receptor and HER-2 status. All are major determinants of response patterns during and after chemotherapy. Clinical breast (and axillary) examination (CBE) in conjunction with mammography and ultrasound inform further radiologic means to improve ultimate diagnostic accuracy. Multiple technologies to mark biopsy-loci and/or tumour foci are available and have to be considered mandatory to guide surgery that will take place 4 to 6 months later.
2. The second major time point to plan surgery is response assessment after or close to the end of the chemotherapeutic regimen. The initial diagnostic assessment informs the radiologic means necessary to assess response. It is important to plan for potential pitfalls and use multiparametric MRT assessment in select cases. However, accurate information for surgery can be acquired via repetitive CBE, ultrasound and mammography.
3. Finally, several intraoperative/preoperative tools may be helpful to reduce repetitive surgery due to incomplete resections. Wire localization via appropriate radiologic guidance is an important means to guide breast conservation. Several marker technologies and ultrasound can instruct resection intraoperatively. In select cases, specimen mammography/ultrasound or the aid of frozen section analysis are considered helpful means in many environments.

Contemporary published evidence supports breast conservation even in cases of multicentric disease with low recurrence rates. Furthermore, oncoplastic surgery and even higher-level reconstructive surgery is compatible with NACT in select cases. The key to safe and successful surgical management lies with individualized surgical planning in an interdisciplinary setting. It is the context of radiology, medical oncology and pathology that instructs beyond surgical technique and is most likely to provide optimal surgical care.

References will be presented at the time of presentation.

Disclosure of Interest: No significant relationships.

PG 9.04
Conservative surgery for multifocal/multicentric disease

E.J.T. Rutgers*. *Dept. Surgery, Netherlands Cancer Institut, Amsterdam, Netherlands*

Multifocal (MF) and multicentric (MC) breast cancer is regularly considered a relative contraindication for breast-conserving therapy (BCT). There are two reasons for this wide spread notion:

- Perceived higher risk for in-breast recurrence since it is assumed that in MF/MC cancer the risk of more invasive foci in the breast is greater, and therefore radiotherapy possibly less effective.
- Less good cosmetic outcome due to wider excisions, either segmental resection or quadrantectomy in multifocal, or multiple wide local excisions in multicentric disease.

However, I concur that if optimal 'cytoreductive surgery' is achieved this will result in good local control (i.e. in-breast relapse <10% at 10 years). This can only be achieved on the basis of the right imaging, image guidance for non-palpable foci, and tumor free (invasive as well as ductal carcinoma in situ) margins after adequate pathological assessment. Surgery must then be followed by whole breast irradiation and systemic treatments as indicated by primary cancer biology. Careful planning and adaptive application of oncoplastic techniques will result in an optimal cosmetic result. The meticulous work of Roland Holland and coworkers [1] in the early 1980s on whole breast specimen showed invasive foci at more than 2 cm distance from the invasive primary cancer in more than 40% of specimen. Although multiple tumor foci may occur in up to 60% of mastectomy specimens, equivalent survival outcomes were observed in prospective trials comparing BCT and mastectomy for clinically unifocal lesions, suggesting that the majority of these foci are not, or do not become, biologically relevant or clinically significant with appropriate treatment.

As diagnostic tools advance, MF and MC tumors are more commonly diagnosed. Cancers that previously would have been classified as unifocal now can be detected as MF or MC. In addition, locoregional

Table 1 (abstract PG 9.04). Recurrence rates in studies with MF/MC patients treated with breast-conserving surgery

Study	Publication year	MF or MC	Patients (n)	Median FU (months)	Local recurrence (%)	Remark
Leopold	1989	MF/MC	10	64	40	
Kurtz [2]	1990	MF/MC	61	71	25	
Wilson [3]	1993	MF	13	72	25	
Hartsell	1994	MC	27	53	3.7	
Nos	1999	MF	56	60	11	
Cho [4]	2002	MF/MC	15	76	0	
Kaplan [5]	2003	MF/MC	36	45	3	
Okumura [6]	2004	MF/MC	34	58	0	
Oh [7]	2006	MF/MC	97	66	6	Neoadjuvant trial
Gentilini [8]	2008	MF/MC	476	73	5	
Cabioglu [9]	2009	MF/MC	30	55	5.4	
Lim [10]	2009	MF	147	59	2	
Bauman [11]	2010	MF/MC	22	42	4.5	
Yerushalmi [12]	2011	MF/MC	300	94	4.3	
Chung [13]	2012	MF	164	112	6.1	
Lynch [14]	2013	MF/MC	256	52	2	
Ataseven [15]	2014	MF/MC	617	36	5.2	Neoadjuvant trial
Tan [16]	2014	MF/MC	35	45	0	

treatment modalities have improved significantly over the past decade. More recent studies reflect these advances in diagnosis and treatment (Table 1). Studies evaluated staging MRI showed that up to 19% of women with diagnosed breast cancer harbor a second malignant ipsilateral lesion. These findings should only have consequences when additional lesions are proven cancer. Multiple enhancing lesions on MRI are in itself not an indication for a mastectomy.

Recent studies supplement the growing evidence that treatment of patients with MF/MC breast cancer with BCS, radiotherapy, and adjuvant systemic therapy can result in low rates of in-breast recurrence (Table 1).

References will be available in the main manuscript or, on request, from the author.

Disclosure of Interest: No significant relationships.

PG 9.05
Breast conservative surgery and local recurrence

M. Rezai[1]*, S. Kellersmann[2], S. Knispel[2], R. Kimmig[2], P. Kern[2].
[1]Surgery, Louise-Hospital, Breast Center Duesseldorf, Duesseldorf, Germany, [2]Women's Department, University Hospital of Essen, Essen, Germany

Introduction: Breast conservation is a legacy of Umberto Veronesi who laid the groundwork for the preservation of the body image of women affected by breast cancer (BC) with the Milan I study in the late 1970s [1,2]. In the EBCTCG-Meta-Analysis 2011, local control achieved by BCS and adjuvant radiotherapy led to a recurrence free survival of 84.4% at 10 years in nodal-negative BC [3]. BCS has two aspects: oncological safety with a resection of the tumor with free margins and esthetic outcome [4]. Free margins have been defined as 'no ink on margin' in the most recent 2014 SSO-ASTRO-Guidelines [5]. Determinants of local control used to be T-size, nodal and receptor status, tentatively resection margins – until a biologically based concept of Sorlie derived from molecular portraits defined risk of recurrence and mortality from breast cancer [6], approximated by IHC properties by St.Gallen [7,8]. We explored whether this concept proves at large scale in the context of BCS, and which other risk factors were predictive for recurrence. Furthermore we examined risk factors for unclear margins and for conversion to mastectomy.

Patients and Methods: We analysed 1035 patients with BCS (2004–2009) and local recurrence related to age, intrinsic subtypes, tumor size, histology, grading and margins.

Results: 944 patients with primary unilateral breast cancer were eligible for analysis. At a median follow-up of 5.2 years, LRR was 4.0%, 5-year-DFS of 90.9%, 5-year-OS of 94.5%. TNBC and Her2 non-luminal BC had the highest recurrence: LRR TNBC 11.3%, Her2+ non-lum. 9.3%, Lum.A 2.5% ($p < 0.001$). Age <40 vs. >40 years had a two-fold risk of recurrence (8.3% vs. 3.8%). In 11.4% (108/944), margins were unclear, out of which 89.8% (97/108) were re-excised. However 10.2% (11/108) did not undergo a re-excision. 1.5% (14/944) remained with unclear margins, none of them with recurrence. Factors influencing margins were multicentricity/multifocality of tumors ($p < 0.001$).

Conclusion: The intrinsic subtype concept was confirmed. T-size, nodal status and margins did not govern the prognosis. Neither T-stage nor resection volume had an impact on margin status ($p > 0.05$). Mastectomy rates were only 7.2% (68/944). We identified DCIS ($p = 0.001$) with/without invasive subtype and lobular histology ($p = 0.001$) as an independent risk factor for a mastectomy. Lobular histology, multicentricity and DCIS were predictive for breast preservation failure and conversion to mastectomy.

Reference(s)

[1] Veronesi U et al., Conservative treatment of breast cancer. A trial in progress at the Cancer Institute of Milan. Cancer 1977, 39(6 Suppl): 2822–2826.
[2] Veronesi U et al., Comparing radical mastectomy with quadrantectomy, axillary dissection, and radiotherapy in patients with small cancers of the breast. N Engl J Med 1981 Jul 2; 305(1): 6–11.
[3] EBCTCG: Effect of radiotherapy after breast-conserving on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10801 women in 17 randomised trials. Lancet. 2011 Nov 12; 378(9804): 1707–16.
[4] Rezai M, Kern P., New surgical techniques – problems and their solutions, Journal of Aesthetic Surgery, Springer, 1/2012.
[5] Moran MS, Morrow M. et al., Society of Surgical Oncology–American Society for Radiation Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in stages I and II invasive breast cancer. J Clin Oncol. 2014 May 10; 32(14): 1507–15.
[6] Sørlie T et al.: Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. Proc Natl Acad Sci USA 2001; 98: 10869–10874.
[7] Goldhirsch A et al.: Strategies for subtypes – dealing with the diversity of breast cancer: highlights of the St. Gallen International Expert Consensus on the primary therapy of early breast cancer. Ann Oncol 2011; 22: 1736–1747.
[8] Goldhirsch A et al., Personalizing the treatment of women with early breast cancer: highlights of the St Gallen International Expert

Consensus on the Primary Therapy of Early Breast Cancer 2013. Ann Oncol. 2013 Sep; 24(9): 2206–23.

Disclosure of Interest: No significant relationships.

Friday, 20 March 2015 **10.00–11.00**

Session 10: Radiotherapy: Innovation and long term effects in early breast cancer

PG 10.01

Hypofractionated radiotherapy in early breast cancer: clinical, dosimetric and radio-genomic issues

J. Yarnold*. *Institute of Cancer Research, Royal Marsden NHS Foundation Trust, Sutton, United Kingdom*

The effectiveness of curative radiotherapy (RT) is enhanced by partitioning the total dose into daily dose increments, called fractions. As a general rule, cancers respond to the total dose more strongly than to the size of daily fractions used to deliver it. This contrasts with the response of late-reacting, dose-limiting healthy tissues, which are sensitive both to the total dose and to the fraction size. These differences underpin the historical use of 'small' fractions, classically ≤2.0 Gy, to deliver the highest total dose tolerated by patients, thereby ensuring the greatest impact on cancerous tissue. The general rule has been challenged by randomised clinical trials over the last 20 years providing high level evidence that breast cancer is, against earlier assumptions, equally sensitive to fraction size as the dose-limiting healthy tissues [1–4]. Even though the a/b value for breast cancer of around 3 Gy confirms fractionation sensitivity of the population of breast cancers as a whole, it is not known if wide inter-tumoral variation exists that could form the basis of patient stratification to different fraction sizes. Meanwhile, the use of fractions >2.0 Gy (hypofractionation) in breast cancer RT is standard in the UK, and increasingly, internationally. Theoretical concerns about the effects of dose inhomogeneity are much too small to have any discernible clinical impact, regardless of how RT is fractionated. Full exploitation of differences in fractionation sensitivity between tumours and dose-limiting healthy tissues depends on understanding the underlying molecular mechanisms, and being able to manipulate them appropriately in tumours and dose-limiting normal tissues. In this respect, it has long been understood that DNA is the critical target of therapeutic ionising radiation, and that a critical lesion responsible for cell death is the unrepaired DNA double strand break (DSB). Non-homologous end joining (NHEJ) repairs the majority of DSB, but homologous recombination (HR) repair is important for repairing a minority of DSB in the heterochromatin of G2/S phase cells. The relevance to fractionation is that we postulate a dominant role for NHEJ and HR in explaining differences in tissue sensitivity to fraction size [5,6]. The important feature of this model is that it explains the tight association between proliferative indices and sensitivity to fraction size in healthy tissues, which is likely to be affected by extensive epigenetic and epigenetic modifications to DNA damage signalling and repair that are typical of human cancer.

Reference(s)

[1] Yarnold J, Ashton A, Bliss J, et al. Fractionation sensitivity and dose response of late adverse effects in the breast after radiotherapy for early breast cancer: long-term results of a randomised trial. Radiother Oncol 2005; **75**(1): 9–17.
[2] Owen JR, Ashton A, Bliss JM, et al. Effect of radiotherapy fraction size on tumour control in patients with early-stage breast cancer after local tumour excision: long-term results of a randomised trial. Lancet Oncol 2006; **7**(6): 467–71.
[3] Whelan TJ, Pignol JP, Levine MN, et al. Long-Term Results of Hypofractionated Radiation Therapy for Breast Cancer. N Engl J Med 2010; **362**(6): 513–20.
[4] Haviland JS, Owen JR, Dewar JA, et al. The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials. Lancet Oncol 2013; **14**(11): 1086–94.
[5] Somaiah N, Yarnold J, Daley F, et al. The relationship between homologous recombination repair and the sensitivity of human epidermis to the size of daily doses over a 5-week course of breast radiotherapy. Clin Cancer Res 2012; **18**(19): 5479–88.
[6] Somaiah N, Yarnold J, Lagerqvist A, Rothkamm K, Helleday T. Homologous recombination mediates cellular resistance and fraction size sensitivity to radiation therapy. Radiother Oncol 2013; **108**: 155–61.

Disclosure of Interest: No significant relationships.

PG 10.02

Evolving standards in breast cancer radiotherapy: who should receive locoregional RT?

T. Whelan*. *Department of Oncology, McMaster University, Hamilton Ontario, Canada*

Following mastectomy there may remain microscopic residual disease in the chest wall or regional nodes, which if untreated may recur and spread distantly. Randomized trials have shown that locoregional RT to the chest wall and regional lymph nodes following mastectomy and adjuvant systemic therapy reduces recurrence and breast cancer mortality in women with node positive and high risk node negative breast cancer [1–3]. There continues to be some uncertainty about the role of locoregional RT for patients with 1 to 3 positive axillary nodes, because of the relatively lower risk of locoregional recurrence and lack of effectiveness demonstrated in subgroup analyses of these trials. A recent update of the Early Breast Cancer Trialists' Collaborative Group Overview demonstrated that locoregional RT post-mastectomy reduced locoregional recurrence ($p < 0.001$), overall recurrence [hazard ratio (HR) = 0.67, $p < 0.001$] and breast cancer mortality (HR = 0.78, $p = 0.01$) in patients with 1–3 positive axillary nodes treated with adjuvant systemic therapy [4]. These results were also consistent with further updates of the original post-mastectomy RT trials [5,6].

The role of regional nodal RT in addition to whole breast RT following breast conserving surgery was recently addressed in two randomized trials. The EORTC 22922 trial randomized 4,004 patients with node negative breast cancer with medial tumors (N = 2002) and node positive (N = 2002) breast cancer to internal mammary plus medial supraclavicular nodal RT or no such treatment following breast conserving surgery (76%) or mastectomy [7]. Patients in either arm received whole breast or chest wall RT. At a median follow-up of 10 years regional nodal RT was shown to reduce distant recurrence (HR = 0.86, $p = 0.02$), overall recurrences (HR = 0.89, $p = 0.04$), and deaths (HR = 0.87, $p = 0.056$). In a similar trial (MA.20) 916 patients were randomized to regional nodal RT (to the supraclavicular, axillary and internal mammary nodes) plus whole breast RT or whole breast RT alone in node positive (90%) or high risk node negative breast cancer (10%). At 5 years median follow-up regional nodal RT reduced distant recurrence (HR = 0.67, $p = 0.002$) and overall recurrences (HR = 0.68, $p = 0.003$) [8]. The majority of node positive patients in both these trials had 1 to 3 positive axillary nodes.

Based on the results of these recent studies it is reasonable to consider locoregional RT following mastectomy or regional nodal RT following breast conserving surgery in patients with 1 to 3 positive axillary nodes. Such treatments can be associated with modest increased risks of pneumonitis, lymphedema and cardiac disease, but these effects are less common with modern RT approaches. There may be patients with 1 to 3 positive axillary nodes who with modern systematic therapy have limited benefits associated with

locoregional RT, but it is difficult to identify such patients at the present time.

Reference(s)

[1] Overgaard M, Hansen PS, Overgaard J, et al. Postoperative radiotherapy in high-risk premenopausal women with breast cancer who receive adjuvant chemotherapy. Danish Breast Cancer Cooperative Group 82b Trial. N Engl J Med 1997; 337(14): 949–55.
[2] Ragaz J, Jackson SM, Le N, et al. Adjuvant radiotherapy and chemotherapy in node-positive premenopausal women with breast cancer. N Engl J Med 1997; 337(14): 956–62.
[3] Overgaard M, Jensen MB, Overgaard J, et al. Postoperative radiotherapy in high-risk post-menopausal breast-cancer patients given adjuvant tamoxifen: Danish Breast Cancer Cooperative Group DBCC 82c randomized trial. Lancet 1999; 353(9165): 1641–8.
[4] Early Breast Cancer Trialists' Collaborative Group (EBCTCG) Darby S, et al. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. Lancet 2014; 383(9935): 2127–35.
[5] Overgaard M, Nielsen HM, Overgaard J. Is the benefit of postmastectomy irradiation limited to patients with four or more positive nodes, as recommended in international consensus reports? A subgroup analysis of the DBCG 82 b and c randomized trials. Radiother Oncol 2007; 82: 247–53.
[6] Ragaz J, Olivotto IA, Spinelli JJ, et al. Locoregional radiation therapy in patients with high-risk breast cancer receiving adjuvant chemotherapy: 20-year results of the British Columbia randomized trial. J Natl Cancer Inst 2005; 97(2): 116–26.
[7] Poortmans P, Struikmans S, Collette S, et al. Lymph node radiotherapy improves survival in breast cancer: 10 year results of the EORTC Radiation Oncology and Breast Cancer Groups phase III trial 22922/10925. ESTRO 33 Congress report 2013, page 6, available at www.estro.org.
[8] Whelan T, Olivotto I, Ackerman I, et al. NCIC-CTG MA.20: An intergroup trial of regional nodal irradiation in early breast cancer. Proceedings of the American Society of Clinical Oncology 2011; 29(18S): 779s (Abstr LBA1003).

Disclosure of Interest: No significant relationships.

PG 10.03
Technical innovation in adjuvant radiotherapy: evolution and evaluation of new treatments for today and tomorrow

I. Kunkler*. *Edinburgh Breast Unit, Western General Hospital, The University of Edinburgh, Edinburgh, United Kingdom*

The disruptive impact of the role of radiotherapy in breast conserving therapy owes it origin to the work of Sir Geoffrey Keynes [1]. Following validation of safety and efficacy in clinical trials against mastectomy, there has been a progressive fall in local recurrence rates with breast conserving surgery (BCS) and postoperative whole breast radiotherapy (WBRT) down to 2–3% at 5 years [2]. The trade off in improving local control is the increased risks of radiation induced cardiac morbidity [3] and mortality and of second malignancy [4].

Over the last decade technical developments in breast radiotherapy (intensity modulated radiotherapy, brachytherapy and intraoperative radiotherapy) have facilitated studies of partial breast irradiation (PBI) evaluating the concentration of radiation dose in and close to the tumour bed. Some of the early results of trials of accelerated partial breast irradiation (ABPI) have been disappointing. An interim report [5] of the RAPID trial comparing standard WBRT to ABPI (38.5 Gy in 10 bd fractions) showed inferior cosmetic results in the ABPI arm, suggesting that this dose fractionation regime was too intense. Intraoperative electron beam therapy when compared in the ELIOT trial to conventional WBRT resulted in inferior local control with IORT [6]. IORT using 50 X-rays in the TARGIT A trial also showed inferior local control with IORT compared to WBI [7], although the absolute difference small and longer term follow up is needed. Radiation can be delivered precisely to a defined target volume using IMRT or image guided radiotherapy, shaping the high dose region to the tumour or even sub regions within the tumor, while limiting dose to surrounding normal tissue. While there is level 1 evidence that IMRT delivers better cosmesis than standard RT [8], there is no evidence as yet that local control is improved.

Looking forward, the main clinical dividends in local control and survival may come from three areas:

i. Identification of molecular signatures of breast cancer radiosensitivity, allowing the exclusion from RT of patients unlikely to respond. The Radiotype Dx molecular signature of breast cancer radiosensitivity [9] looks promising but will require further validation.
ii. Integrating stereotactic body radiotherapy (SBRT) with systemic therapy in the neoadjuvant setting represents a novel approach in which ablative doses of focal radiation are delivered in a limited number of fractions (typically 5 or fewer). The sharp dose gradients limit radiation dose to surrounding normal tissues. The integration of preoperative SBRT in escalating doses with neoadjuvant chemotherapy has been shown to be safe in a phase 1 study and does not the increase the risks of operative complications after breast conserving surgery [10]. It is likely to be from an understanding of the complex physiology and signaling pathways which influence tumour growth and metastatic spread that opportunities for exploiting drug-radiation synergies are likely to emerge [11].
iii. Real time sensing of the hypoxic tumour microenvironment is a research priority [12]. Targeting hypoxic subvolumes with drug–radiation combinations may provide a new direction for CMT research. Candidate targets are the pH regulatory mechanisms of the breast cancer cell. It has been suggested that acidosis contributes to radiation resistance [13] and it has been shown that knock down of hypoxia induced CA IX and CA XII sensitises Chinese hamster fibroblasts to radiation by increasing intracellular acidosis. Inhibition of carbonic anhydrase IX shows promise in preclinical breast cancer models including explants [14]. These might lead to preoperative 'window of opportunity' studies of inhibitors of pH regulatory mechanisms (including CA IX, CA XII, CA 11, MCT 4) in combination with neoadjuvant systemic therapy and image guided RT.

Reference(s)

[1] Keynes G. Radium treatment of primary carcinoma of the breast. Lancet 1928; 212: 108–111.
[2] Mannino M, Yarnold JR. Local relapse rates are falling after breast conserving surgery and systemic therapy for early breast cancer: can radiotherapy ever be safely withheld? Radiother Oncol. 2009; 90: 14–22
[3] Darby SC, Ewertz M, McGale P et al. Risk of ischemic heart disease in women after radiotherapy for breast cancer. N Engl J Med. 2013 Mar 14; 368(11): 987–98.
[4] Grantzau T, Thomsen MS, Vaeth M, Overgaard J. Risk of second primary lung cancer in women after radiotherapy for breast cancer. Radiother Oncol 2014; 111: 366–373.
[5] Olivotto IA, Whelan TJ, Parpia S et al. Interim cosmetic and toxicity results from RAPID. A randomized trial of accelerated partial breast irradiation using three dimensional conformal external beam irradiation therapy. J Clin Oncol 2013; 31: 4038–4045.
[6] Veronesi U, Orecchia R, Maisonneuve P et al. Intraoperative radiotherapy vs external radiotherapy for early breast cancer (ELIOT): A randomised controlled equivalence trial. Lancet Oncol 2013; 14: 1269–1277.
[7] Vaidya JS, Wenz F, Bulsara M et al. Risk-adapted targeted intraoperative radiotherapy for breast cancer:5 year results for local control and overall survival from TARGIT-A randomised trial. Lancet 2014; 383: 603–613.
[8] Mukesh R, Barnett GC, Wilkinson JS et al. Randomised controlled trial of intensity modulated radiotherapy for early breast cancer: 5 year results confirm superior overall cosmesis. J Clin Oncol 2013; 31: 4488–95.

[9] Speers C, Balbin OA, Liu M et al. RadiotypeDx: Identification and validation of a radiation sensitivity signature in human breast cancer. Cancer Research December 15, Abstract P6-06-5, SABCS 2013.
[10] Bondiau PY, Bahadoran, Lallement M et al. Robotic stereotactic radioablation concomitant with neoadjuvant chemotherapy for breast tumors. Int J Rad Oncol Biol Phys 2009; 75: 1041–1047.
[11] Giaccia AJ. Molecular radiobiology: the state of the art. J. Clin Oncol 2014; 32: 2871–2878.
[12] Eccles SA, Aboagye EO, Ali S et al. Critical research gaps and translational priorities for the successful prevention and treatment of breast cancer. Breast Cancer Res. 2013; 15: R92.
[13] Vaupel P.Tumour microenvironmental physiology and its implications for radiation oncology. Sem Radiat Oncol 2004; 14: 198–206.
[14] Pettersen EO, Ebbesen P, Gieling RG et al. Targeting tumour hypoxia to prevent cancer metastasis. From biology, biosensing and technology to drug development: the METOXIA consortium. J Enzyme Inhib Med Chem. 2014: 1–33.

Disclosure of Interest: No significant relationships.

Friday, 20 March 2015 **11.30–12.30**

Session 11: Adjuvant systemic treatment for the individual patient I: Endocrine therapies: New aspects for old treatments

PG 11.01
Endocrine therapy for premenopausal women: type and duration

N.E. Davidson*. *Cancer Institute and UPMC Cancer Center, University of Pittsburgh, Pittsburgh, PA, United States of America*

Multiple strategies for endocrine treatment of premenopausal women with hormone-responsive breast cancer have been assessed and results have been presented over the last two years. These include tamoxifen for 5–10 years (ATLAS and aTTom), tamoxifen for 5 years followed by aromatase inhibitor for 5 years for women who have become postmenopausal (MA-17); ovarian ablation (OA) by surgery (EBCTCG overview); ovarian function suppression (OFS) by LHRH agonist (LHRH agonist metaanalysis); or combinations of approaches including OFS plus tamoxifen or aromatase inhibitor (AI) (SOFT, TEXT, ABCSG 12 and E3193). Many of these trials have taken place in the backdrop of (neo)adjuvant chemotherapy which can confound interpretation because such therapy can suppress ovarian function either transiently or permanently. Nonetheless these trials suggest in aggregate that 10 years of tamoxifen are better than 5 years and that a program of extended adjuvant therapy of tamoxifen for 5 years followed by aromatase inhibitor for 5 years is effective for suitable candidates. The SOFT and E3193 trials do not show a major advantage for use of OFS + tamoxifen compared to tamoxifen alone. The joint SOFT/TEXT analysis and ABCGS12 trials both suggest that outcomes can be excellent with the use of combined endocrine therapy alone in properly selected patients but give conflicting results with regard to potential benefits for OFS + AI compared with OFS + tamoxifen. Given the long natural history of endocrine-responsive breast cancer, longer follow-up of all trials will be critical to ascertain benefit and document unexpected late toxicities, if any. A pressing need is the identification of markers that can identify patients who need extended adjuvant endocrine therapy as well as markers that might allow selection of those that would benefit from a combination strategy like OFS + AI. Finally, most trials have used OFS and oophorectomy interchangeably, but the equivalence of these therapies in the adjuvant setting especially in combination therapy is not certain and may require further assessment through followup of the completed trials. What has become clear is that adjuvant endocrine therapy is a vital part of the adjuvant regimen for most premenopausal women with hormone-responsive breast cancer and a subset of these women with luminal A-type tumors can be safely treated with endocrine therapy alone.

Disclosure of Interest: No significant relationships.

PG 11.02
Endocrine therapy for post-menopausal patients: type and duration

H.J. Burstein*. *Breast Oncology Center, Dana-Farber Cancer Institute, Harvard Medical School, Boston, United States of America*

Because the vast majority of breast cancers diagnosed across the globe are ER positive tumors arising in postmenopausal women, careful attention to adjuvant endocrine therapy has dramatically improved breast cancer outcomes worldwide. Treatment options for postmenopausal women include either tamoxifen (Tam) or an aromatase inhibitor (AI) or a sequence of the two, given for 5 or 10 years. Tamoxifen and AIs differ with respect to side effect profiles. Both can cause menopausal symptoms such as hot flashes and night sweats. Tamoxifen contributes to rare risks of uterine cancer and thromboembolism. AIs cause accelerated osteoporosis and bone fracture, a musculoskeletal syndrome associated with achiness and stiffness, and vaginal atrophy with associated sexual dysfunction.

In comparison to 5 years of tamoxifen monotherapy, the incorporation of an AI into the treatment program either as initial treatment, or as sequential therapy after 2–3 years of tamoxifen, lowers the risk of cancer recurrence. Randomized trials demonstrate equivalence for TAM2–3 → AI3–2 as for AI5. Patient preferences factoring in side effect profiles and individual tolerability are important in choosing one strategy or the other. Extended adjuvant endocrine therapy further reduces the risk of recurrence. Longer durations of treatment such as TAM5 → TAM5 or TAM5 → AI5 improve on outcomes seen with TAM5 alone, but also carry risks of ongoing side effects. There are no data for the safety or efficacy of AI therapy beyond a total duration of 5 years though clinical experience does not suggest emerging toxicity concerns. Studies have shown equivalence between commercially available brands of AIs though anecdotally, patients sometimes tolerate one product better than another.

Similar to rates of non-adherence with other chronic medications, studies have documented high rates of non-compliance with adjuvant endocrine therapy often owing to treatment-related symptoms. Clinicians should gauge compliance and mitigate symptoms using a variety of available interventions.

Predictors of recurrence in ER positive breast cancer include tumor and nodal stage at presentation, tumor grade, measures of proliferation such as Ki67, quantitative degrees of ER/PR expression, intrinsic subtype, and molecular diagnostic profiles. These pathobiological variables are highly interrelated across a spectrum. Tumors that are low grade typically have high degrees of ER and PR expression, lower proliferation measures, lower OncotypeDX recurrence scores, and tend to cluster as luminal A tumors. Tumors with higher grade features tend to have lower levels of ER and/or PR expression, higher proliferation measures, higher OncotypeDX scores, and tend to cluster as luminal B tumors. To date, there are no markers that selectively predict early vs late recurrence, nor suggest treatment with tamoxifen vs AI, nor determine who benefits from longer duration of therapy.

Almost all women diagnosed with ER positive tumors should consider endocrine therapy. Even subcentimeter, node-negative cancers have a lower risk of recurrence with use of endocrine treatment. Whether good prognosis tumors, especially stage 1 cancers with favorable histological features, require more than 5 years of treatment is not known.

Reference(s)

Early Breast Cancer Trialists' Collaborative Group. Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. Lancet 2011; 378: 771–84.

Davies C, et al. Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. Lancet 2013; 381: 805–16.

Dowsett M, et al. Meta-analysis of breast cancer outcomes in adjuvant trials of aromatase inhibitors versus tamoxifen. J Clin Oncol 2010: 28: 509–18.

Burstein HJ, et al. Adjuvant endocrine therapy for women with hormone receptor-positive breast cancer: american society of clinical oncology clinical practice guideline focused update. J Clin Oncol 2014; 32: 2255–69.

Disclosure of Interest: No significant relationships.

PG 11.03
Predicting benefit of endocrine therapy

M. Regan*. *Dept. Biostatistics and Computational Biology, Dana-Farber Cancer Institute, Boston, United States of America*

Adjuvant endocrine therapy is a mainstay of treatment for patients with endocrine-responsive early breast cancer. Questions remain concerning which patients should receive what type of endocrine therapy and for how long. Several factors have been considered as potential indicators to predict benefit of endocrine therapy, including patient factors, clinico-pathological factors and multigene assays. To date, factors associated with risk of recurrence have been the most widely adopted to influence treatment selection. In this presentation I will examine data available from BIG 1-98 for postmenopausal women, and from SOFT and TEXT for premenpausal women with the goal to shed light on who should receive which type of adjuvant endocrine therapy and for how long.

Disclosure of Interest: Grants/research support: Veridex LLC, OncoGenex via Hoosier Cancer Research Network; Prostate Cancer Foundation. IBCSG trials include funding from: Novartis, Pfizer, Ipsen, Celgene, Ferring, Merck. Honoraria or consultation fees: American Association for Cancer Research, LEIDOS Biomedical Research Inc.

Friday, 20 March 2015 **14.00–15.30**

Session 12: Adjuvant systemic treatment for the individual patient II: Cytotoxic chemotherapy and targeted agents

PG 12.01
Tailoring the chemotherapy regimen in patients with triple negative subtypes

E. Winer*. *Division of Women's Cancer, Dana-Farber Cancer Institute, Boston, United States of America*

Triple negative breast cancer accounts for approximately 10–15% of all breast cancer in North America and Europe, and may be responsible for a higher proportion of cases in developing countries. By definition, all triple negative cancers do not have estrogen and progesterone receptors and they are not amplified for HER2. As a result, the only available adjuvant treatment consists of chemotherapy. For patients with stage II and III triple negative disease, regimens that contain anthracyclines and taxanes are the standard approach. Those with stage I disease are often treated with shorter and/or somewhat less toxic regimens. In general, chemotherapy reduces the overall risk of disease recurrence in the triple negative setting by as much as 35–50%. In spite of the impact of chemotherapy, triple negative disease accounts for a disproportionate share of breast cancer mortality. Some triple negative cancers are exquisitely sensitive to chemotherapy and others have a high degree of intrinsic resistance to the same therapy.

It has become clear that triple negative disease is remarkably heterogeneous. While almost all triple negative cancers are poorly differentiated have a high degree of genomic instability, there are important different across triple negative tumors. A variety of investigators have attempted to sub-classify triple negative cancers, and there do appear to be substantial differences in the genetic make-up of triple negative cancer, but the clinical significance of these genomic sub-classifications remain unclear. The subgroup of triple negative cancers that have a high proportion of tumor infiltrating lymphocytes (TILS), have a better overall prognosis, probably in part because of an increased sensitivity to cytotoxic chemotherapy. A number of investigators are examining the subgroup of tumors that have a defect in homologous recombination, a feature of BRCA1-associated triple negative cancers. Several studies are attempting to determine if these tumors are more sensitive to platinum-based therapy.

At present, we cannot use investigational classifications of triple negative breast cancer to determine appropriate systemic therapy. These approaches are in the early phases of investigation in clinical trials. While it is hoped that one or more sub-classifiers will be useful in the clinical setting, we will have to wait at least 2–3 years before utilizing these approaches outside of clinical trials.

Disclosure of Interest: Grants/Research support: Genentech, Roche.

PG 12.02
Defining optimal duration and predicting benefit from chemotherapy in patients with luminal-like subtypes

C.D. Hart, A. Di Leo*. *Dept. of Medical Oncology, Hospital of Prato "Sandro Pitigliani", Prato, Italy*

Luminal B breast cancer is a distinct molecular subtype of estrogen receptor (ER) positive breast cancer, with a notably poorer prognosis than its Luminal A counterpart, and represents a subgroup with limited specific evidence for optimal management. Molecular studies with gene expression profiling have identified this subtype as having lower expression of ER and progesterone receptor (PR) genes, and higher expression of genes associated with proliferation and cell cycle activation, and thus distinguished it from Luminal A. A proportion also display HER2 overexpression, and are classified as Luminal B-like. Further molecular studies, notably through the Cancer Genome Atlas, have discovered a multitude of genetic aberrations specific to Luminal B cancer, clearly identifying it as a distinct disease [1]. Yet, despite this recognition, little is known on how to tailor treatment accordingly, and latest-technology molecular classification is unattainable for most treating teams. Immunohistochemical classification is a more accessible surrogate for defining luminal B disease, where it characterised by lower ER positivity, lower or absent PR positivity, and higher proliferation rates and histological grade. The 13th St Gallen consensus defines it as being ER and PR positive, HER2 negative, and with a Ki67 level of ≥20–25%, although Ki67 remains a controversial biomarker due to inter-observer variation and difficulty in defining an optimal cut-off [2]. Luminal B cancer has been shown to have a more aggressive clinical course, with higher rates of relapse in the first 5 years than luminal A, making them more similar in clinical behaviour to basal-like and Her2 enriched subtypes [1]. Prognostic algorithms such as Oncotype DX typically classify luminal B as high risk, essentially as a consequence of the higher proliferation rates, and thus more likely to derive benefit from chemotherapy in addition to endocrine therapy [3]. However within the luminal B cohort, there is no tool to determine prognosis, or define those for whom adjuvant chemotherapy might be omitted. The place for

adjuvant chemotherapy in luminal B disease is not well delineated. Extrapolation from previous clinical trials is limited by difficulties in defining the luminal B subgroup, and relies on surrogate markers. For the most part, chemotherapy is thought to be more active in this population, although the optimal choice of chemotherapeutic agent, and the preferred duration of treatment, is unknown. Current trials aim to address these problems however: the RxPONDER, MINDACT and TAILORx prosepective trials will examine gene signatures of early breast cancers as predictors of chemotherapy response. Targeted agents that address endocrine resistance are already in clinical practice (everolimus) or development (PI3K inhibitors, FGF inhibitors, CDK4/6 inhibitors). Their specific role in luminal B disease is yet to be defined, and again rely on prospective trials that molecularly define the subgroup.

Reference(s)

[1] Ades F, Zardavas D, Bozovic-Spasojevic I et al. Luminal B breast cancer: molecular characterization, clinical management, and future perspectives. J Clin Oncol. 2014; 32: 2794–803.
[2] Harbeck N, Thomssen C, Gnant M. St. Gallen 2013: brief preliminary summary of the consensus discussion. Breast Care (Basel). 2013; 8: 102–9.
[3] Fan C, Oh DS, Wessels L, et al. Concordance among gene-expression-based predictors for breast cancer. N Engl J Med. 2006; 355: 560–9.

Disclosure of Interest: No significant relationships.

PG 12.03
Targeting HER2 in 2015

M. Piccart-Gebhart[1] *, D. Zardavas[2]. [1]*Medicine, Institut Jules Bordet, Bruxelles, Belgium,* [2]*Breast International Group (BIG) AISBL, Bruxelles, Belgium*

The introduction of trastuzumab revolutionized the treatment of patients with HER2-positive breast cancer (BC), with both early- and metastatic-stage disease, coupled with cytotoxic chemotherapy [1]. Lapatinib, a dual EGFR/HER2 small molecule inhibitor, was another step forward in the treatment of metastatic HER2 positive BC [2]. More recently, two additional HER2 blocking agents became part of our therapeutic armamentarium: trastuzumab-DM1, an antibody-drug conjugate, delivering potent cytotoxic chemotherapy to HER2-overexpressing cancer cells, while retaining the biologic actions of trastuzumab [3]; and pertuzumab, an anti-HER2 monoclonal antibody, which when coupled with trastuzumab achieves a more thorough HER2 blockade, capitalizing on the concept of dual HER2 blockade [4]. Despite these advances, patients with HER2-positive BC still experience relapse of their disease, with the resistance being almost inevitable in the metastatic stage. To this end, currently ongoing research efforts try to further improve the clinical outcomes within this patient population, focusing on the following areas: (i) assessment of different dual HER2 blockade strategies, (ii) development of TDM1 in the early stage disease, (iii) co-targeting of HER2 with other molecules perceived as anti-HER2 treatment resistance mediators, and (iv) identification of predictive biomarkers. With regard to the last one, it must be noted that so far apart from HER2 itself, no other predictive biomarker has been validated for treatment guidance among patients with HER2-positive BC. Promising data indicating that lymphocytic infiltration of the tumour could be a predictor of sensitivity to trastuzumab-based treatment were recently refuted by an analysis of TILS in NCCTG 9831. Of note, clinical trials assessing the potential added value of immunologic checkpoint inhibitors given concurrently with trastuzumab are about to start recruitment. Despite the strong preclinical rationale indicating that activation of the PI3K signaling pathway mediates trastuzumab resistance, the clinical results concerning the potential predictive value of alterations affecting this pathway have not been consistent and are thus not ready for implementation in the clinical practice. The respective development of PI3K blocking agents, still ongoing, has not led to the registration of a new drug so far. Everolimus just failed to improve progression free survival in the Bolero1 trial – when given in combination with paclitaxel; however, there was a suggested benefit in the hormone receptor negative subgroup Numerous other potentially relevant alterations are being assessed as predictive biomarkers for HER2 blockade, with extensive molecular profiling initiatives currently ongoing. These are particularly important in view of the recent negative results of the large ALTTO trial which tested 4 different anti-HER2 in combination or in sequence with adjuvant chemotherapy: trastuzumab or lapatinib alone, the sequence and the combination of the 2 agents. In the era of personalized oncology, rigorous translational and clinical collaborative efforts are needed to further advance the field of treatment of patients with HER2-positive breast cancer.

Reference(s)

[1] Hudis, C.A. Trastuzumab – Mechanism of Action and Use in Clinical Practice. N. Engl. J. Med. **357**, 39–51 (2007).
[2] Geyer, C.E. et al. Lapatinib plus capecitabine for HER2-positive advanced breast cancer. N. Engl. J. Med. **355**, 2733–2743 (2006).
[3] Krop, I.E. et al. Trastuzumab emtansine versus treatment of physician's choice for pretreated HER2-positive advanced breast cancer (TH3RESA): a randomised, open-label, phase 3 trial. Lancet Oncol. **15**, 689–699 (2014).
[4] Swain, S.M. et al. Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA study): overall survival results from a randomised, double-blind, placebo-controlled, phase 3 study. Lancet Oncol. **14**, 461–471 (2013).

Disclosure of Interest: Board member: PharmaMar. Consultant (honoraria) : Amgen, Astellas, AstraZeneca, Bayer, Eli Lilly, Invivis, MSD, Novartis, Pfizer, Roche-Genentech, sanofi Aventis, Symphogen, Synthon, Verastem. Research grants to my Institute: most companies.

PG 12.04
Long term side effects of adjuvant chemotherapy in patients with early breast cancer

A.C. Wolff*. *Breast Cancer Program, The Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, United States of America*

Breast cancer outcomes continue to improve, in great part due to the broader use of screening and earlier detection and of more proficient multimodality care that result in improved local control and in lower risk of systemic recurrence. Chemotherapy remains the primary systemic adjuvant modality for most women with HER2-positive (combined with trastuzumab) and with triple-negative disease, while endocrine therapy forms the core of adjuvant recommendations for the two-thirds of patients with early breast cancer (EBC) diagnosed with hormone receptor-positive (ER-positive) disease. However, beginning in the mid-1980s evidence from large randomized trials and from large systematic reviews/meta-analyses showed a significant relative improvement in the average risk of recurrence regardless of stage and ER status. Policy statements also heavily influenced the adoption of systemic chemotherapy for most patients with EBC, and patients expressed their willingness to consider adjuvant chemotherapy even if the expected absolute survival benefit did not exceed one or two per cent points. As a result, adjuvant chemotherapy was widely adopted for patients with ER-positive, including those with small, node-negative tumors. However, there is now a growing awareness that most patients with EBC, especially those diagnosed with small, stage 1 disease, are expected to survive their breast cancer diagnosis. Most are then expected to live long enough that other competing causes of death such as cardiovascular disease eventually become more important than their previous breast cancer diagnosis. Even among patients with ER-negative disease,

long-term follow-up data from the observation arms of adjuvant chemotherapy trials conducted 25 years ago show that most of them are expected to remain disease-free long-term. There is also a growing understanding about the small, but not insignificant short- and long-term risk of complications associated with the most commonly used chemotherapy regimens. This is particularly important as breast cancer is a disease of older women, many who have other comorbid conditions. Older women are also at greater risk for loss of function complications associated with use of adjuvant chemotherapy. As a group, they are less likely to be offered adjuvant chemotherapy, even though age alone is a poor predictor of complications and the observed reduction in breast cancer recurrence offered by adjuvant chemotherapy is equally observed across all age groups. Large datasets and long term follow-up of adjuvant trials have allowed investigators to ask clinical questions involving rare outcomes that are of direct interest to patients, practicing oncologists, cancer researchers, and policy makers, even though few studies included patient-reported outcome measures. Younger and otherwise healthier patients are more likely to be offered adjuvant chemotherapy, but many will remain at risk for late complications, such as cardiomyopathy and marrow neoplasms. Greater awareness of short- and long-term complications from established adjuvant chemotherapy regimens will allow patients and their health care providers to have more careful discussions on the merits of proposed therapies. High quality tools (including standard pathology measures and new molecular measures will continue to aid treatment decisions, which must take into account individual risk of recurrence, expected absolute improvements in outcome, and absolute risks of toxicities.

Reference(s)

Risk of Marrow Neoplasms After Adjuvant Breast Cancer Therapy: The National Comprehensive Cancer Network Experience. Wolff AC, Blackford AL, Visvanathan K, et al. J Clin Oncol. 2014 Dec 22. PMID: 25534386.

Adjuvant chemotherapy in older women with breast cancer: who and what? Muss HB. J Clin Oncol. 2014 Jul 1; 32(19): 1996–2000. PMID: 24868030.

Enhancing therapeutic decision making when options abound: toxicities matter. Kuderer NM and Wolff AC. J Clin Oncol. 2014 Jul 1; 32(19): 1990–3. PMID: 24868027.

Disclosure of Interest: No significant relationships.

Friday, 20 March 2015 **16.00–17.15**

Session 13: Adjuvant systemic treatment for the individual patient III: Special patient populations and patient needs

PG 13.01
Management of breast cancer in very young women

A. Partridge*. *Department of Medicine, Dana-Farber Cancer Institute, Boston, United States of America*

Breast cancer is the leading cause of cancer-related deaths in women age 40 and younger in developed countries, and although generally improving, survival rates for young women with breast cancer remain lower than for older women. Young women are more likely to develop more aggressive subtypes of breast cancer (more triple negative and more Human Epidermal Growth Factor Receptor 2 [HER2]-positive disease) and present with more advanced stage disease. Previous research has demonstrated that young age is an independent risk factor for disease recurrence and death, although recent data suggest this may not be the case in certain tumor molecular subtypes. Recent preliminary evidence suggests potential unique biologic features of breast cancer that occurs in young women although this has yet to have been translated into treatment differences. There are clearly host differences that affect the management of breast cancer for young patients including generally being very premenopausal at diagnosis, and concerns regarding fertility, genetics, and social/emotional issues that should be considered. Despite an increased risk of local recurrence, young age alone is not a contraindication to breast conserving therapy given the equivalent survival seen in this population with either mastectomy or breast conservation. However, many young women in recent years are choosing bilateral mastectomy, even without a known hereditary predisposition to the disease. For systemic therapy, endocrine therapy, multi-agent chemotherapy and/or biologic therapy decisions should target the tumor similar to the treatment in older women. Select young women will do well with hormone therapy only. Recent data from the TEXT and SOFT trials evaluating the optimal endocrine therapy for the first 5 years, and the ATTom and ATLAS trials demonstrating benefit from extended duration of tamoxifen (10 vs. 5 years), have further defined options for adjuvant endocrine therapy for young women with early breast cancer. Attention to adherence with endocrine therapy may be particularly important to improve outcomes in young survivors who are at increased risk of non-adherence compared to older women.

Disclosure of Interest: No significant relationships.

PG 13.02
Management of breast cancer in older and frail patients

I. Smith. *The Royal Marsden, Breast Unit (Medical Oncology), London, United Kingdom*

The incidence of breast cancer continues to rise, particularly in the elderly, In 2005–2009 around 18,000 breast cancer registrations per annum in women >65 were made in the UK. The median life expectancy of a 70 year old European woman is 16 years and an 80 year old almost 10 years. The challenge in older patients is to balance effective treatment against potential comorbidities and to minimize both under-treatment and over-treatment. An additional important issue is that older patients are under-represented in clinical trials, such that a strong evidence base for therapeutic decisions is often lacking. For example, in an EBCTCG overview of 60 adjuvant chemotherapy trials only 4% were 70 or older, and population-based data show that the use of both surgery and chemotherapy is proportionately less in this age group.

Avoidance of, or minimizing, surgery simply because of age is bad management: trials have shown that tamoxifen alone in women over 70 is associated with both increased risk of local recurrence and worse survival than with surgery as well.

Likewise adjuvant chemotherapy should not be withheld on the basis of age alone. The EBCTCG has shown that this achieves a significant reduction in the risk of death in those aged 70 or over. Patient selection is however as important as in other age groups. In an analysis of 41,000 aged 65 or over with Stage 1–3 breast cancer, adjuvant chemotherapy was not associated with improved survival in node negative or ER positive node positive disease. However women with ER negative, node positive disease had a significant reduction in breast cancer mortality with chemotherapy (hazard ratio 0.72). Treatment related mortality however is higher in women over 65 (1.5%) compared with those <50 (0.2%) in 4 CALGB trials. Balanced against this, conventional chemotherapy in the elderly is more effective than less toxic single agent oral treatment. Further trials of less toxic and simpler chemotherapy in the elderly are urgently needed. The assessment of comorbitities, general frailties and their prognostic influence is therefore important. Measures available include Comprehensive Geriatric Assessment (CGA) and

Charlston index are available to assess prognosis independent of cancer and fitness for treatment.

In contrast to surgery and chemotherapy, post surgical radiotherapy may be overused in older women. Many of the studies on which this practice is based excluded patients aged 70 or older, and older age is a recognised factor predicting a lower risk of local recurrence following breast conserving surgery. Randomised trials strongly suggest that older women with small breast cancers on tamoxifen after surgery may gain little or nothing from adjuvant radiotherapy.

In conclusion, further trials of less toxic/less morbid therapeutic approaches that still sustain efficacy are now urgently needed for older/frail patients, with the long term hope that these might subsequently prove useful in younger fitter patients as well.

Disclosure of Interest: No significant relationships.

PG 13.03
Survivorship care after early breast cancer

S. Kyriakides*. *Europa Donna Cyprus, Nicosia, Cyprus*

The number of breast cancer survivors, women and men who have had a breast cancer experience at any point in their lives, has increased significantly over the last years, this being evidence of the great strides that have been made in early diagnosis, treatment and follow up care. Today, most patients that have been through breast cancer live very fulfilling and productive lives, in all areas. For many patients diagnosed with breast cancer the disease may never return. However, one must not ignore the fact that the treatment of early breast cancer may have dramatically changed the specific emotional and psychological end points for the patient. This change has necessarily meant that the scientific and advocacy community have had to address a whole range of different issues and concerns, relevant to the patients and their families. Following a breast cancer diagnosis, no matter how early this is, uncertainties and psychosocial needs become part of the reality of the patients life after the end of treatment, of the realities of those living with this experience. Fear of recurrence is most commonly initially paramount, leading patients – survivors to exhibit various levels of anxiety, commonly considered not related to the earlier diagnosis by the patients environment who may not be aware of the impact that the actual diagnosis had. Additionally, survivorship necessarily entails addressing quality of life issues that are a direct result of the treatment that the patient has undergone or is undergoing, the emotional, social and psychological impact of the disease, the changing life realities for the patient and the family members. The long term survival of patients following a diagnosis of early breast cancer has led to the need to dispelling a number of myths that have prevailed for many years. Furthermore, questions related to sexuality, relationships, fertility, pregnancy, quality of life, employment, insurance have become part of the patients and family's agenda, and, necessarily, part of the agenda of the multidisciplinary team from the very beginning of treatment. The knowledge of these new, varying challenges, is what renders the value of guidelines in diagnosis, treatment, diagnosis and follow up care so vital. One needs to see the experience of early breast cancer as part of a life continuum with a variety of challenges arising along the way, a journey that is never static, and that necessitates an individualistic treatment and followup care plan at all levels.

Reference(s)

Personalizing the treatment of women with early breast cancer: highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2013. A. Goldhirsch, E.P. Winer, A.S. Coates, R.D. Gelber, M. Piccart-Gebhart, B. Thürlimann and H.-J. Senn and Panel Members.

Europa Donna, Breast Cancer Network Australia, Susan G Komen the Breast, Cancer World and other advocacy articles and materials.

Implementing a Survivorship Care Plan for Patients With Breast Cancer. Patricia A. Ganz and Erin E. Hahn.

Meeting Highlights: International Expert Consensus on the Primary Therapy of Early Breast Cancer 2005. A. Goldhirsch, J.H. Glick, R.D. Gelber, A.S. Coates, B. Thürlimann, H.-J. Senn7 & Panel Members.

Disclosure of Interest: No significant relationships.

The Breast 24S1 (2015) S26–S86

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Poster Abstracts I

Biology/Pathology/Basic Research

P001
Predicting positive sentinel nodes and assessing feasibility for intra-operative lymph node assessment

S. Ahmad*, E. Copley. *Breast Surgery, Kettering General Hospital NHS Foundation Trust, Kettering, United Kingdom*

Goals: In centres not practicing intra-operative lymph node assessment with one step nucleic acid amplification for CK19 messenger RNA (OSNA), the question is often posed, as to how to accurately plan theatre list, in cases of positive sentinel lymph node biopsy (SLNB) requiring additional theatre time for Axillary lymph node dissection (ALND). OSNA eliminated the wait for identifying positive SLNB and the need for re-admission and delay for ALND. This has significant benefits for patients, surgeon and institution. In addition to identifying positive sentinel nodes for ALND, OSNA will continue to have psychological relief for the SLNB negative cases in the immediate post operative period.
Methods: We undertook a retrospective study of histological data for all 363 SLNB cases, at our centre from 13/12/2006 to 10/02/2010. The percentage of Positive SLNB was determined in relation to the size and grade of invasive tumour. Histology of 10 patients was not included as 9 were pure ductal carcinoma in situ, and SLNB failed in one. Data for all the remaining 353 cases was included.
Results: The SLNB positivity in the mastectomy and wide local excision (WLE) groups was correlated with size and grade of invasive cancer. A mastectomy patient is twice as likely to be SLNB positive than a WLE patient reflecting the correlation of large tumour size with higher stage. In WLE patients with a higher-grade tumour, there is a direct correlation between tumour size and SLNB positivity. 29.3% (17/58) of GII/III cancers 21–30 mm, and about 50% (14/25) of tumours above 31 mm on histology are associated with SLNB metastases. More recent large centre study shows that over a third of their SLNB cases are positive for metastases on OSNA.
Conclusion: Our retrospective data of SLNB cases supports the concept, that if we were to use our own tumour profile (Large tumour size 3 cm and above, particularly Grade II/III cancers) to predict sentinel node metastasis, we would have correctly predicted in a large number of cases and planned theatre list. We could have refined our prediction of SLNB positivity using Memorial Sloan Kettering Nomogram. Our figures have their limitations, as these were retrospective figures based on conventional histology, and at a time when some surgeons were going through new start validation phase.
Disclosure of Interest: No significant relationships.

P002
Biological profile of invasive lobular carcinoma in a medical oncology department – Algeria

S. Sakhri*, R. Ferhat. *CHU Tizi Ouzou, Algiers, Algeria*

Goals: Invasive lobular cancers (ILC) constitute 5–15% of all invasive breast tumors, less common than invasive ductal carcinoma (IDC), and appear to have a distinct biology. The aim of our study is to determine the ILC biological profile collected in the department of oncology medical Tizi Ouzou hospital Algeria.
Methods: We recorded the cases of 73 patients with ILC between January 2010 and January 2012. The aim of this study is to evaluate the clinical and pathological response, molecular profiling using RE, RP, KI67, HER2, and the follow up between 2012 and 2014.
Results: The average age of patients with ILC is 52 years, 40% women have postmenopausal status, all patients underwent mammography, diagnosed by a core needle biopsy, the commonest stage at presentation was stage III (42%). 10 patients (13%) underwent a breast conserving surgery, and 87% a mastectomy.
The majority of cases were histologic grade II (SBR II), 50% of the tumors were estrogen and progesterone receptor positive, Her2 neu was reported to be negative in 60%. The treatment consisted of: neoadjuvant chemotherapy in 28 cases (38%), adjuvant chemotherapy in 42 cases (57%), followed by radiotherapy, and hormonal therapy (HT) was given to 47 patients (64%), and target therapy to 40%.
At the follow up after 2 years, 12% had metastatic or locoregional recurrence: bone (60%), lung (30%), and liver (10%); 88% of the cases remain in complete remission.
Conclusion: ILC are a heterogeneous group of tumors and the management decisions should be based on individual patient and biologic characteristic of the tumor.
Disclosure of Interest: No significant relationships.

P003
Shifts in miRNA expression affect DNA repair mechanisms in breast cancer cells

V. Halytskiy*. *Molecular Immunology Department, Palladin Institute of Biochemistry of the National Academy of Sciences of Ukraine, Kiev, Ukraine*

Goals: Genome instability, high mutation rate as well as high variability is typical of many cancer cells. Also, tumor growth is tightly associated with regular shifts in miRNA expression pattern. Usually, expression of miRNAs miR-18a/b, miR-19, miR-21, miR-23a/b, miR-29a, miR-155, miR-181, miR-206, miR-210, miR-221/222 and miR-375 is up-regulated in breast cancer cells. This investigation aims to identify in what way these shifts in miRNA expression pattern contribute to the abnormalities in DNA repair.
Methods: miRNA targets within gene transcripts were predicted in silico using TargetScan software.

Results: Transcripts of around 60% of the genes involved in DNA repair carry targets for at least one of the up-regulated miRNAs (see table).

Table: miRNA targets in 3′-UTR regions of gene transcripts encoding the DNA damage response proteins

miRNA	Targets
miR-18a/b	UNG, TDP1, MLH3, DDB1, GTF2H5 (TTDA), ERCC1, RBBP8, FANCG (XRCC9), FANCI (KIAA1794), DCLRE1C (Artemis), ATM
miR-19	SMUG1, MBD4, APLF, TDP1, RAD23B, GTF2H1, GTF2H5 (TTDA), ERCC4 (XPF), RAD51D, RBBP8, FANCC, BRCA2, FAAP20
miR-21	TDP2, MSH2, RPA2, GTF2H5 (TTDA), ERCC4 (XPF), RAD51B/D, GEN1, FANCI (KIAA1794), BRIP1 (FANCJ), FANCM, ATM
miR-23a/b	NEIL1, MLH3, RAD23B, DDB1, GTF2H5 (TTDA), CCNH, ERCC4 (XPF), UVSSA (KIAA1530), MRE11A, GEN1, FANCA/D2, FANCG (XRCC9), FANCI (KIAA1794), DCLRE1C (Artemis)
miR-27	NTHL1 (NTH1), PARP3, TDP1, DDB1, RPA2, GTF2H2, GTF2H5 (TTDA), ERCC8 (CSA), MRE11A, FANCG (XRCC9), BRIP1 (FANCJ), FANCM, XRCC5 (Ku80)
miR-29a	TDG, NEIL2, ALKBH3 (DEPC1), TDP1, MLH3, RPA1, ERCC2 (XPD), GTF2H5 (TTDA), ERCC6 (CSB), RAD52, MRE11A, FANCC/E
miR-155	APLF, GTF2H5 (TTDA), ERCC6 (CSB), MRE11A, GEN1, FANCD2/F, RAD51C (FANCO), PRKDC
miR-181	MBD4, APLF, RAD23B, GTF2H1/2, GTF2H5 (TTDA), UVSSA (KIAA1530), MRE11A, NBN (NBS1), GEN1, BRIP1 (FANCJ), FANCM, BTBD12 (SLX4), FAAP20, DCLRE1C (Artemis), ATM
miR-206	TDG, TDP1/2, MLH3, RPA1, ERCC4 (XPF), RAD50/51/51B/54B, NBN (NBS1), GEN1, PRKDC
miR-221/222	GTF2H5 (TTDA), ERCC4 (XPF), RAD50/51, MRE11A, FANCD2, ATM
miR-375	OGG1, APEX1 (APE1), MSH3, MLH3, RAD51B, XRCC2, MRE11A, EME1

Silenced genes encode DNA repair enzymes as well as other DNA damage response proteins that are key elements of all DNA repair systems – base excision repair, direct reversal of damages, repair of DNA-topoisomerase crosslinks, mismatch excision repair, nucleotide excision repair, homologous recombination and non-homologous end-joining.

Conclusion: miRNAs, hyperexpression of which is essential for abnormal proliferation and surviving of breast cancer cells, silence also genes encoding DNA repair enzymes as well as other key elements of the DNA damage response network. This results in an increase of genetic instability and can lead to cancer progression. Moreover, miRNA-mediated silencing of DNA repair genes may cause higher risk of oncogene mutations and, therefore, underlie the initial stage of carcinogenesis.

Disclosure of Interest: No significant relationships.

P004

Reliability of Ki67 value according to histological grade and hormone status

M. Izquierdo[1]*, F. Tresserra[2], I. Rodriguez[2], R. Fabregas[2]. [1]*Gynecology, Hospital Universitario Quiron Dexeus, Barcelona, Spain,* [2]*Hospital Universitario Quiron Dexeus, Barcelona, Spain*

Goals: Proliferative tumor activity measured immunohistochemically by Ki67 has high interobserver variability. Its clinical use can be improved if it is considered together with histological grade, estrogen (ER) and progesterone receptor (PR) levels.

Methods: Ki67 value has been studied in 566 breast cancers since 2007 to 2013 at our Institution using MIB 1 monoclonal antibody. The histological grade and hormone receptor status were also evaluated. The value was assessed optically in percentage of stained nuclei.

Results: Histological grade I was in 293 (51.7%) tumors, II in 219 (38.7%) and III in 54 (9.6%). Estrogen receptor was positive in 455 (80.53%) and progesterone receptor was positive in 341 (60.67%) tumours. None of the tumours with Ki67 value lower than 10% had grade III. There were no tumours with histological grade I, positive estrogen and negative progesterone receptor with histological grade I, positive estrogen and negative progesterone receptor with Ki67 higher than 25%. Only 7% of tumours with histological grade I and positive estrogen and progesterone receptors has a Ki67 higher than 25%.

Conclusion: It has to be considered to repeat or confirm the values of Ki67 higher than 25% in those tumors with histological grade I mainly with estrogen receptor positive, and Ki67 values lower than 10% in those tumors with histological grade III.

Disclosure of Interest: No significant relationships.

P005

Cancer-associated fibroblasts induce trastuzumab resistances in HER2-positive breast cancer

Y. Mao[1]*, Q. Qu[2], Y. Zhang[1], J. Liu[1], K. Shen[1]. [1]*Comprehensive Breast Health Center, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China,* [2]*Department of Oncology, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China*

Goals: HER2 positive breast cancer is characterized by aggressive biology and poor prognosis, which accounts for about 25% of breast cancer. Trastuzumab, an anti-HER2 targeted agent, has improved the prognosis of these patients. However, at least 30% of them will develop trastuzumab resistance during 1 to 2 years treatment. Cancer-associated fibroblasts (CAFs), one major component of tumor microenvironment, have related to cancer development and progression, but whether and how they mediate trastuzumab resistance in HER2 positive breast cancer remain unclear.

Methods: CAFs and normal fibroblasts (NFs) were isolated from fresh HER2+ breast samples obtained from Ruijin hospital. Conditional medium (CM) were collected from cultured CAFs and NFs. Different secreted proteins were analyzed by RayBio human cytokine antibody Array. Cell proliferation was determined by XTT assay and colony formation assay. Gene expression was analyzed by real-time PCR. Protein expression was determined by western-blotting. Gene transcriptional activity was determined by luciferase reporter assay. Cancer stem cells were evaluated by tumor sphere assay.

Results: CAFs mediated trastuzumab resistance in two HER2+ cell lines, BT474 and SK-BR3. Moreover, higher level of interleukin 6 (IL6) was secreted from CAFs compared with NFs, and induced trastuzumab resistance in both cell lines. Also, this phenomenon was accompanied by PTEN downregulation and cancer stem cells expansion. Moreover, IL6 expands cancer stem cells population by PTEN downregulation through decreasing its transcriptional activity. Interestingly, a neutralizing IL-6 antibody and IL6 pathway inhibitor (S3I-201) can partly decrease the number of cancer stem cells and reverse trastuzumab resistance.

Conclusion: CAFs secrete high level of IL6, mediate trastuzumab resistance through degrading PTEN by decreasing its transcriptional activity. Decreasing IL6 level and inhibiting its pathway may partly rescue trastuzumab sensitivity in HER2+ breast cancer cell lines, serving as novel therapeutic ways for trastuzumab-resistant breast cancer patients.

Disclosure of Interest: No significant relationships.

P006

Paracrine interaction between adipose-derived stem cells and breast cancer cells

W. Tsuji[1]*, R. Schweizer[2], J.A. Plock[2], K.G. Marra[1], J.P. Rubin[1]. [1]*Department of Plastic Surgery, University of Pittsburgh, Pittsburgh, United States of America,* [2]*Department of Plastic Surgery and Hand Surgery, University Hospital Zurich, Zurich, Switzerland*

Goals: Autologous fat grafting is a promising method for breast reconstruction due to ease of procurement, natural appearance, and low immuno-response. Fat graft implementation with Adipose-derived Stem Cells (ASCs) has been proposed to enhance fat retention. However, the interplay between ASCs and breast cancer

cells (BCCs) is still controversial and of utmost importance in the post-cancer setting. Epithelial–mesenchymal transition (EMT) has been investigated for a variety of tumors and thought to be involved in malignant transformation or progression. Herein we investigate the effects of human ASCs on human BCCs and whether they may induce EMT.

Methods: BT-474 and MDA-MB-231 BCC lines were co-cultured for 7 days using transwell basket systems to assess the paracrine interaction between ASCs and BCCs. Various ASC to BCC ratios were seeded and human fibroblasts used as a control. Change in morphology was assessed by microscopic evaluation. Any proliferative effect on BCCs was investigated by AlamarBlue. Co-culture supernatants were analyzed by ELISA to detect soluble factors involved in migration, inflammation and angiogenesis. RT-PCR was performed for EMT marker assessment.

Results: BT-474 changed from an epithelial- to a more mesenchymal-like morphology when co-cultured with ASCs and fibroblasts. Both BT-474 and MDA-MB-231 proliferation was tackled by ASCs and fibroblasts in indirect co-culture. TNF-α was highly expressed in supernatants of BT-474 co-cultured with ASCs. Vimentin and Snail were up-regulated in BT-474 under ASC influence to a higher extent than fibroblasts.

Conclusion: In vitro, ASCs switch BT-474 phenotype to a more malignant, mesenchymal-like breast cancer type as depicted by morphological changes and increased proliferation, as well as cytokine regulation and EMT marker up-regulation. Fibroblasts had only partly similar effects. In vivo experiments are needed to clarify the role of ASCs in cancer progression.

Disclosure of Interest: No significant relationships.

P007

c-MET aberration in triple negative breast cancers

H. Zhang*. *Pathology, the University of Texas M.D. Anderson Cancer Center, Houston, United States of America*

Goals: c-MET (mesenchymal–epithelial transition factor gene) is a proto-oncogene on chromosome 7q31 activating several downstream signaling pathways, including PI3K/AKT and MAPK pathways. High c-MET expression has been shown to be associated with poor prognosis in hormonal receptor positive and Her2 positive breast cancers. However, its significance in triple negative breast cancers has not been explicitly explored.

Methods: Archival paraffin-embedded tissue blocks were selected from one hundred and six female patients with diagnosis of triple negative invasive breast carcinoma that had surgeries at the University of Texas-MD Anderson Cancer Center. Medium follow up is 69.4 months (range 9–317 months). Expression of c-MET was assessed by IHC using rabbit monoclonal anti-total c-Met antibody (SP44 from Ventana). Staining intensity was scored on a scale of 0, 1+, 2+ and 3+. Samples that scored ≥2+ in ≥50% of tumor cells were considered to be positive for c-MET overexpression. FISH analysis was performed using MET (7q31) specific FISH probe (Kreatech). The chromosome 7 satellite enumeration (SE) probe is used for control. Sixty tumor cells were counted for each sample. c-MET gene copy numbers ≥4 per cell or c-MET/CEP7 ratio ≥2 is used as cut-off for c-MET amplification.

Results: FISH was successfully performed on 99 cases and IHC was successfully assessed on 103 cases. c-MET was overexpressed in 13 out of 103 cases by IHC. c-MET was amplified in 2 (c-MET/CEP7 ratio ≥2) and 3 (≥4 c-MET copies per tumor cell) out of 99 cases by FISH. Only one case met both criteria for c-MET amplification by copy number and c-MET/CEP7 ratio. Not a single case was identified as both over-expression by IHC and amplification by FISH. At the time of the analysis, 23 women (21.7%) had died, and 20 (18.9%) had experienced a recurrence. However, neither of c-MET overexpression or amplification is statistically significant to the relapse free survival (RFS) or overall survival (OS), even after being adjusted to age, tumor size, nodal status, and adjuvant chemotherapy drugs through multivariable Cox proportional hazard analysis. In addition, the status of c-MET does not correlate with IHC status of ER, PR and Her2 status of the tumors.

Conclusion: In this study, the frequency of c-MET dysregulation, including overexpression and amplification was assessed in a small cohort of triple negative breast cancers and the correlation of survival data was also explored. The insignificance of either c-MET overexpression by IHC and amplification by FISH correlating to the survival data might be due to the low incidence of c-MET aberration in this specific subtype of breast cancers.

Disclosure of Interest: No significant relationships.

P008

S-1 in combination with CPT-11 plus trastuzumab for pretreated HER2+ metastatic breast cancer

U. Toh[1]*, N. Iwakuma[1], M. Mishima[1], M. Furukawa[1], T. Fujii[1], E. Ogo[2], S. Nakagawa[3], M. Tanaka[4], Y. Akagi[1]. *[1]Surgery, Kurume University School of Medicine, Kurume, Fukuoka, Japan, [2]Radiology, Kurume University School of Medicine, Kurume, Fukuoka, Japan, [3]Breast Surgery, National Hospital Organization Kyushu Medical Center, Fukuoka, Japan, [4]Breast Surgery, Kurume General Hospital, Kurume, Japan*

Goals: Our previous phase II study using S-1 plus irinotecan (CPT-11) without Trastuzumab (Tr) have shown an overall response rate (ORR) of 44% in chemotherapy pretreated patients (pts) with metastatic breast cancer. The aim of this Phase II clinical trail is to evaluate efficacy and safety of S-1 in combination with CPT-11 plus Tr in pretreated pts with HER-2 positive metastatic breast cancer.

Methods: This is an open-label, multicentre, single-arm, phase II study. Major eligibility criteria are: pts with previously treated, advanced and/or metastatic measurable Her2 positive breast cancer. Pts receive S-1 (80 mg/m^2/day) orally on days 3–7, 10–14 and 17–21. CPT-11 (60 mg/m^2) is administrated on days 1, 8 and 15. Tr (4 mg/kg for the initial dosing and 2 mg/kg for subsequent administration) was administrated on days 1, 8, 15 and 22, treatment repeated every 4 weeks. The clinical trial registry number is UMIN000008647.

Results: So far, 20 of planned 32 pts have been evaluated for the first analysis. The response rate (CR+PR) was 25% (4/20) and the clinical benefit rate (CR+PR+SD) was 75% (155/20). The most commonly treatment-related AEs were bone-marrow suppression (60%), diarrhea (55%) and anorexia (50%). All of these toxicities were manageable and there were no unexpected toxicity. No cardiac events have yet to be reported on this Phase II trial.

Conclusion: The preliminary results of this study are encouraging, further studies should be considered to evaluate this regimen in advanced/metastatic BC and the enrollment is on-going.

Disclosure of Interest: No significant relationships.

P009

Expression of Six1 gene involved in apoptosis in MCF-7 cells sensitive and resistant to paclitaxel

M. Armat[1]*, T. Oghabi Bakhshaiesh[2], M.S. Hejazi[3], N. Samadi[4]. *[1]Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran, [2]Medical Biotechnology, Tabriz University of Medical Sciences, Tabriz, Iran, [3]Pharmaceutical Biotechnology, Tabriz University of Medical Sciences, Tabriz, Iran, [4]Biochemistry and Laboratory Medicine, Tabriz University of Medical Sciences, Tabriz, Iran*

Goals: Our goal in this study is to measure the level of Six1 mRNA expression in both resistant and sensitive MCF-7 cells in order to study the mechanism of Six1 signalling pathways and its influence on metastasis and proliferation of cancer cells.

Methods: We first established Paclitaxel-resistant MCF-7 cells in our lab. Morphological modifications in paclitaxel resistance cells were examined via light Microscopic images and Fluorescence Activated Cell Sorting (FACS) analysis. Using quantitative Real time PCR (qRT-PCR) we measured Six1 and p53 mRNA expression levels in both non-resistant and resistant cells.
Results: Our results demonstrate that Six 1 mRNA level increased significantly in resistant MCF-7 ($p < 0.05$) while expression of P53 was down regulated relative to non-resistant MCF-7 cells ($p < 0.05$).
Conclusion: Our results suggest that inhibition of Six1 signaling can improve the efficiency of chemotherapeutic agents in cancer patients with high expression of Six1 gene.
Disclosure of Interest: No significant relationships.

P010
An RNA based method to determine HER2 expression status in breast cancer patients

S. Baldacchino[1]*, K. Sacco[1], C. Saliba[1], J. Degaetano[2], C. Scerri[3], G. Grech[1]. *[1]Department of Pathology, University of Malta, Msida, Malta, [2]Department of Pathology, Histopathology, Mater Dei Hospital, Msida, Malta, [3]Department of Physiology and Biochemistry, University of Malta, Msida, Malta*

Goals: To develop an RNA based test to determine HER2 expression as part of breast cancer profiling and to compare it with the current HER2 immunohistochemistry (IHC) and FISH confirmatory techniques.
Methods: A Luminex-based magnetic bead assay was designed for HER2 expression detection using fresh or Formalin-Fixed Paraffin Embedded (FFPE) tissue derived RNA. The expression value of HER2 was normalised to the geomean of a selection of housekeeping genes and statistically compared to HER2 results using conventional amplification detection methods.
Results: The assay yielded highly reproducible results between replicates with correlation (R^2) values of 0.97–0.999 and also using the same samples across runs ($R^2 = 9.95–0.99$). The assay can detect HER2 amplification accurately when using as little as 50 ng of RNA with or without Haematoxylin and Eosin (H&E) staining. HER2 expression values were normalised to 3 selected housekeeping genes. Selection of normalisation genes was based on variation between control breast cell lines and standard error between runs. A threshold for determining positive and negative normalised HER2 cases was set to accurately classify retrospective cases including cases that were ambiguous with IHC. A pilot study classified 9/9 cell lines accurately (Kao, 2009) and also classified 22/24 breast cancer cases in consensus with the diagnosis. The two remaining cases did not give a definitive result with IHC and lacked confirmatory diagnostic testing but were classified with the Luminex-based assay.
Conclusion: The Luminex-based assay has proven to be a reliable and a highly sensitive technique. The results of both methods will be correlated with the clinical progression HER2 targeted therapy in cases of borderline HER2 amplification results. Heterogeneous tumours can be microdissected using H&E stained sections, prior to analysis. Moreover, this test can be easily multiplexed to provide individual molecular expression profiles for breast cancer.
Disclosure of Interest: No significant relationships.

P011
A new clinical cut-off of cytokeratin 19 mRNA copy number in sentinel lymph node of breast cancer

S. Buglioni[1]*, I. Terrenato[2], B. Casini[1], V. D'Alicandro[1], F. Di Filippo[3], M. Mottolese[1], E. Pescarmona[1]. *[1]Pathology, Regina Elena National Cancer Institute, Rome, Italy, [2]Biostatistics, Regina Elena National Cancer Institute, Rome, Italy, [3]Surgery, Regina Elena National Cancer Institute, Rome, Italy*

Goals: Since 2007, one-step nucleic acid amplification (OSNA) has been used as a diagnostic system for sentinel lymph node (SLN) examination in patients with breast cancer. The OSNA cut-off were set on the basis of volume of metastic foci of histopathologically positive lymph nodes for cytokeratin 19 (CK19) mRNA expression. The purpose of this study was to define a new clinical cut-off of CK19 mRNA copy number based on the calculation of the risk that an axillary lymph node dissection (ALND) will be positive. This new analysis could be more efficient than the traditional histological concept of micrometastasis and macrometastasis and provide a more objective evaluation of CK19 mRNA copy number.
Methods: 1529 SLN from 1140 patients were analysed with the OSNA assay. 318 patients with positive SLN for micrometastasis (250–5000 copies) and macrometastasis (>5000 copies) underwent ALND. Axillary non-SLN were routinely examined. ROC curves and Youden's index were performed in order to identify a new cut-off value. Logistic regression models were performed in order to compare OSNA categorical variables created on the basis of our and traditional cut-off to better identify patients with positive ALND.
Results: 69% and 31% of OSNA positive patients had a negative and positive ALND respectively. ROC analysis identified a cut-off of 2150 CK19 mRNA copies with 95% of sensibility and 51% of specificity. Positive and negative predictive values of this new cut-off were 47% and 96%. Logistic regression indicated that the cut-off of 2150 copies better detects patients with positive ALND (OR 19.6, 95% CI 7.7–50.2; $p < 0.0001$) in comparison to the conventional OSNA cut-off of 5000 copies (OR 4.83, 95% CI 2.8–8.4; $p < 0.0001$).
Conclusion: This cut-off identifies false positive and false negative cases and true-positive and true negative cases very efficiently, and therefore it better identifies which patients really need an ALND and which patients can avoid one. This is why we suggest that the negative cut-off should be raised from 250 to 2150. Furthermore we propose that for patients with a copy number that ranges between 2150 and 5000, there should be a multidisciplinary discussion concerning the clinical and biomorphological features of primary breast cancer before any decision is taken on whether to perform an ALND or not.
Disclosure of Interest: No significant relationships.

P012
Cost effectiveness and utility of vacuum assisted biopsy of breast in screen detected indeterminate lesions

S. Ahmad[1]*, A.E. Ginawi[2], M. Hajaj[3]. *[1]Breast Surgery, Kettering General Hospital NHS Foundation Trust, Kettering, United Kingdom, [2]General and Breast Surgery, Kettering General Hospital NHS Foundation Trust, Kettering, United Kingdom, [3]Director of Breast Screening, Kettering General Hospital NHS Foundation Trust, Kettering, United Kingdom*

Goals: We carried out the direct cost comparison and clinical utility of vacuum assisted biopsy (VAB) versus wire guided diagnostic excision biopsy under general anesthesia (GA) in the evaluation of screen detected lesions of indeterminate malignant potential (B3) of the breast at Kettering General Hospital NHS Foundation Trust.

Methods: We conducted a retrospective audit of screen detected B3 lesions from April 2009 to March 2014 at Kettering General Hospital (KGH). During this period over 1200 guided needle biopsies were performed, over 494 Breast cancers detected and 59 cases of B3 lesions were diagnosed. 23 of 59 (38.9%) cases of B3 had a final outcome of malignancy. The remaining had atypical hyperplasia, lobular neoplasia, benign and others including one case for which no data was found as the assessment moved to another hospital. One Patient had B3 Lesion with a concurrent malignant lesion in the same breast and chose mastectomy with no further assessment of B3 lesion 29 of 59 cases of B3 lesions had VAB as part of assessment process since the VAB has become available in 2010. 29 cases that had VAB as part of assesment, 14 were diagnosed with invasive cancer or ductal carcinoma in situ. 7 of 14 (50%) cancers in the VAB group had VAB only, and spared wire guided diagnostic excision. We compared direct costs of VAB with the costs of wire guided diagnostic excision obtained from Finance and Screening department at KGH. VAB costs approximately £200 (including £161 VAB probe). Wire guided diagnostic excision under GA costs approximately £1364 based on 535 ward minutes, 96 theatre minutes and costs of blood tests and wire. These costs comparison do not take into account the personnel costs of Radiology as these are assumed to be equal.

Results: The costs saving comparison show, £1164 direct costs saved to hospital for each case of B3 lesion obviated by VAB having wire guided diagnostic excision biopsy, as these were found to be malignant and went for therapeutic surgery. However this study does not take into account the cost savings in more than half the cases with benign outcome, having VAB as initial biopsy for indeterminate and suspicious findings on Radiology. Moreover this does not take into account the indirect socio-economic costs to individuals and community. The benefits to patients in being less invasive, shorter recovery time, less scaring on mammogram and better cosmetic outcome has been confirmed in many large scale studies.

Conclusion: VAB is known to have a high diagnostic accuracy. By adopting VAB, as part of the diagnostic assessment for breast lesions, there is a potential for huge direct and indirect costs savings as well as there is an enormous clinical utility and benefits to the patients and community. This makes good case for all those hospitals and units with no access to VAB, to acquire this technology for the benefit of their patients and institution.

Disclosure of Interest: No significant relationships.

P013

UNC45-A expression correlates with progesterone receptor status in invasive ductal breast cancer

S.S. Hatch[1]*, M.A. Eltorky[2], S. Li[2], G.S. Wilkinson[2], H.F. Epstein[2].
[1]*Radiation Oncologist, UTMB, Galveston, United States of America,*
[2]*UTMB, Galveston, United States of America*

Goals: UNC45-A chaperone represents a potential diagnostic and therapeutic target because mRNA and protein products are over expressed and show enhanced function in metastatic ductal breast carcinoma and breast cancer cell lines with diverse expression of other biomarkers. UNC45-A appears necessary for motor function of non-muscle myosin IIA, a protein essential to cell proliferation and invasion, and for transcriptional activity of the PR, a biomarker and therapeutic target in breast cancers. This study seeks to establish in human breast cancer biopsies the levels of UNC-45A expression with respect to steroid receptors, histological grade, proliferative rate, Her 2 neu status and patient age.

Methods: IHC studies were performed on 33 paraffin sections of invasive ductal carcinomas using mouse monoclonal UNC45-A Ab. After deparaffinization/rehydration, Ag retrieval was performed by Vector kit H-3300. The slides were treated with 3% H_2O_2 and washed. The non-specific streptavidin and biotin activities were blocked with Vector kit SP-2001. UNC45-A primary Ab was dissolved in PBS containing 5% horse serum (10 ug/ml) and incubated at room temperature. The 2nd Ab (BA-2000 Vector) was prepared 1:250 in PBS containing 5% horse Serum. Peroxidase reaction performed using Vector VECTASTAIN ABC kit PK-6100 and Substrate kit SK-4105. Slides were counterstained with hematoxylin QS H-3404 (Vector), dehydrated/mounted with H-5000 (Vector). The expression of UNC 45-A was scored by a single breast pathologist as background compared to 1+ to 3+. The results were statistically evaluated using a Pearson Correlation coefficient matrix.

Results: UNC45-A protein expression was elevated in human breast carcinoma samples with measurable PR and negatively correlated with Her 2 neu at a significance at 0.05. No significance was demonstrated with correlation of UNC 45-A expression with ER, Ki 67, grade of tumor, or age of patient.

Conclusion: After ligand binding the PR travels into the nucleus and functions as a transcription factor. The PR are escorted by molecular chaperones which regulate their function. The HSP-90 complex binding with chaperone maintains receptor in a folded and hormone-responsive state. Measure of UNC 45-A may be a surrogate for HSP90. This implies that if the PR is measurable and the UNC 45-A is overexpressed then HSP90 may be a potential therapeutic target for breast cancer treatment.

Disclosure of Interest: No significant relationships.

P014

Loss of LOC285194 is associated with poor prognosis in triple-negative breast cancer

X. Ni*, Z. Shao. *Breast Surgery, Fudan University Shanghai Cancer Center, Fudan University, Shanghai, China*

Goals: Triple-negative breast cancer (TNBC) is a highly aggressive tumor subtype associated with poor prognosis. The lack of obvious targets is a major challenge in treating patients with triple-negative breast cancer. Long non-coding RNAs are reported to be strongly correlated with poor patient prognosis, suggesting a potential role in cancer progression. Thus, identification of novel targets of long non-coding RNA is urgent for improving outcomes in triple-negative breast cancer.

Methods: Here we conducted HTA 2.0 microassay analyses in 200 triple-negative breast cancer patients, which include tumorous and adjacent normal tissues. The expression of LOC285194 was detected by quantitative real-time polymerase chain reaction in pairs of tumorous and adjacent normal tissues. In vitro and in vivo studies were used to analysis the function of LOC285194 in triple negative breast cancer.

Results: We identified for the first time that LOC285194, was significantly down-regulated in primary tumors than normal tissures in triple-negative breast cancer. Multivariate analysis showed that loss expression of LOC285194 was an independent predictor for poor disease-specific survival (DFS) in triple-negative breast cancer. Through in vitro assays, we confirmed that silencing of LOC285194 expression by shRNA in MDA-MB-231 and MDA-MB-468 breast cancer cells, can potentiate the proclivity to metastasize in transwell assay and enhance tumorigenesis in vivo by injection into the right flank of the nude mice. In a reverse-complimentary approach, we determined that elevated LOC285194 expression in highly metastatic breast cancer cell lines (MDA-MB-231Bo) can suppress the ability of invasion and metastasis in vitro and in vivo. Mechanistically, microassay reveals that the metastatic behavior strongly correlates with increased microRNA-24 levels and overexpression of TGF-β type II receptor (TGF-βR2). Dual luciferase reporter assay confirmed that long non-coding RNA LOC285194 was a target of microRNA-24.

Conversely, restoration of LOC285194 can inhibit the activation of this pathway in MDA-MB-231Bo cells.
Conclusion: By utilizing a series of mammary tumor cell lines and animal models, we demonstrate that long non-coding RNA LOC285194 acts as a tumor suppressor in triple-negative breast cancer through regulating microRNA-24/TGF-β signaling pathway which might be a potential prognostic indicator and therapeutic target for triple-negative breast cancer.
Disclosure of Interest: No significant relationships.

P015
Metabolic syndrome and statin use are associated with pro-estrogenic breast inflammation

N.M. Iyengar[1]*, A. Gucalp[1], X.K. Zhou[2], P.G. Morris[1], D. Giri[1], K. Subbaramaiah[2], M. Pollak[3], M. Morrow[4], C. Hudis[1], A.J. Dannenberg[2]. *[1]Medicine, Memorial Sloan Kettering Cancer Center, New York, United States of America, [2]Weill Cornell Medical College, New York, United States of America, [3]McGill University, Montreal, Canada, [4]Breast Surgery, Memorial Sloan Kettering Cancer Center, New York, United States of America*

Goals: Metabolic syndrome is associated with increased breast cancer (BC) risk. After menopause, obesity confers increased risk of hormone receptor (HR)-positive BC. We previously demonstrated an obesity→inflammation→aromatase axis in breast white adipose tissue (WAT) where inflammation is defined by the presence of crown-like structures (CLS) consisting of a dead or dying adipocyte encircled by macrophages. CLS in the breast (CLS-B) are associated with elevated body mass index (BMI), postmenopausal status, increased tissue levels of proinflammatory mediators, and increased estrogen signaling. Here, we compared levels of relevant circulating factors in women with and without breast WAT inflammation.
Methods: We prospectively collected paired WAT and fasting serum and plasma from women undergoing mastectomy. WAT inflammation was detected by CD68 immunohistochemistry to identify CLS-B. Plasma levels of glucose, insulin, hsCRP, leptin, IL-6, and branched chain amino acids (BCAAs) were measured. Serum levels of total cholesterol, triglycerides (TG), HDL and LDL cholesterol were determined. Insulin resistance (IR) was assessed using the updated Homeostasis Model Assessment (HOMA2-IR). Associations between CLS-B and clinical features, including medication usage, were analyzed using logistic regression and Fisher's exact test. Serum/plasma endpoints were evaluated using Student t-test and nonparametric Wilcoxon rank-sum test.

	Fasting level, mean (SD)		
	CLS-B − (N = 48)	CLS-B + N = 52	P
Glucose (mg/dL	73.2 (8.0)	84.3 (37.6)	0.04
Insulin (mU/L)	4.3 (2.1)	5.6 (2.9)	0.01
LDL (mg/dL)	105.9 (31.0)	119.4 (32.4)	0.04
HDL (mg/dL)	71.9 (15.8)	62.1 (16.1)	0.003
TG (mg/dL)	69.2 (26.3)	104.9 (50.6)	<0.001
Leptin (pg/mL)	12.0 (10.1)	22.6 (19.7)	<0.001
hsCRP (ng/mL)	1.0 (1.4)	2.3 (2.7)	0.003

Results: From 2011 to 2013 we accrued 100 patients (pts); median age 47 years (range 27–70). Overall, CLS-B were found in 52/100 (52%) pts: 18/19 (95%) obese pts, 17/33 (52%) overweight pts, and 17/48 (35%) normal BMI pts. A clinical diagnosis of dyslipidemia was present in 14/52 (27%) pts with CLS-B and 1/48 (2%) pts without CLS-B ($P < 0.001$). CLS-B were found in 10/11 (91%) statin users, but in only 42/89 (47%) non-users ($P = 0.008$). Fasting glucose, insulin, LDL, TG, leptin, hsCRP, and IL-6 levels were higher in pts with CLS-B (Table). BCAA levels were also greater in pts with CLS-B ($P < 0.001$). HOMA2-IR was greater in pts with CLS-B (mean 0.63±0.34) versus those without CLS-B (mean 0.46±0.23; $P = 0.006$).
Conclusion: Breast WAT inflammation, which we previously linked to increased aromatase activity, is associated with biochemical changes that occur in the metabolic syndrome, a risk factor for BC. Statin use is more common in patients with breast WAT inflammation and metabolic syndrome. These findings may account for the variability in results of prior studies examining statin use and breast cancer risk due to elevated baseline risk in statin users compared to non-users.
Disclosure of Interest: No significant relationships.

P016
Impact of ki 67/Topo IIa combined expression in HER2 amplified breast ductal adenocarcinomas

N.S. Salemis[1]*, E. Tsiambas[2], A. Karameris[3], G. Vilaras[3], E. Patsouris[4]. *[1]Breat Surgery Unit, 401 Army General Hospital, Athens, Greece, [2]IHC & Molecular Biology Lab, 401 Army General Hospital, Athens, Greece, [3]Pathology Department, 417 NIMTS, Athens, Athens, Greece, [4]Pathology Department, Medical School, University of Athens, Athens, Greece*

Goals: HER-2 depended signalling pathway is deregulated in a subset of breast adenocarcinomas. Furthermore, Topoisomerase IIa and ki 67 protein expression demonstrate a broad diversity in those tumours. Our aim was to investigate the co-expression of those proliferation markers in HER2 positive (score 2+/3+) cases.
Methods: Fifty (n = 50) paraffin-embedded primary breast ductal adenocarcinomas were cored at 1 mm diameter and transferred to the recipient tissue microarray block (TMA). Immunohistochemistry (IHC) was performed using anti-HER2/Topo IIa/ki 67 antibodies (DAB/fast red chromogens). Dual (green/red) Fluorescence in situ hybridization (FISH) was performed using HER2 gene/chromosome 17 centromeric probes. Digital image analysis was also applied calculating combined ki 67/Topo IIa expression (isolated and double stained nuclei).
Results: HER2 protein over expression (score: 2+/3+) was observed in 18/50 (36%) cases. FISH analysis detected 11/18 (61%) amplified cases. Combined Ki 67 and Topo IIa increased expression (<10 stained nuclei pof at 200× original magnification) was detected in 8/11 cases. Double staining analysis identified a subset of mixed reddish/brown nuclei associating to specific cell cycle phases.
Conclusion: A subset of HER2 positive (gene amplified) breast cancer cases demonstrate a combined up regulated expression of ki 67/Topo IIa proliferation markers. Topo IIa protein provides a more accurate estimation of cell cycle activity than ki 67 due to strictly S/G2/M-phase expression.
Disclosure of Interest: No significant relationships.

P018
Papillary lesions diagnosed on breast core biopsies: is routine surgical excision necessary?

B. Ho[1]*, E.Y. Tan[2], B.K. Chong[3], P. Chan[2], W.M. Yap[1]. *[1]Pathology, Tan Tock Seng Hospital, Singapore, Singapore, [2]General Surgery, Tan Tock Seng Hospital, Singapore, Singapore, [3]Diagnostic Radiology, Tan Tock Seng Hospital, Singapore, Singapore*

Goals: It remains debatable whether all papillary lesions, particularly benign papillomas, diagnosed on needle core biopsies require routine surgical excision. The aim of this study was to determine the risk of upgrade to malignancy of core-biopsy detected papillary lesions on the subsequent surgical excision.
Methods: Following IRB approval, we searched the pathology database for all papillary lesions diagnosed on needle core biopsies over a nine-year period from June 2005 to June 2014. Malignant

papillary tumours diagnosed on needle biopsies were excluded. Histopathologic review was performed and the papillary lesions were categorized as benign, atypical or suspicious for malignancy. The core biopsy findings were correlated with the subsequent excision specimens (surgical excision was routinely offered for all papillary lesions in our practice) to determine any upgrade to DCIS and/or invasive carcinoma.

Results: A total of 273 papillary lesions were diagnosed on needle core biopsies in 245 patients, with a mean age of 56 years (range 23–92). A median of 5 cores of breast tissue per papillary lesion was received. Of these papillary lesions, 205 were benign, 56 were atypical and 12 were suspicious for malignancy. Overall, an excision rate of 77% was achieved. Among the 156 excised benign papillary lesions, the majority (79%) were benign or showed no residual lesion, while 17% disclosed the presence of atypical ductal hyperplasia (ADH) and/or lobular neoplasia. Malignancy was found in six cases (4%): all comprised DCIS (tumour sizes ranging from 2 mm to 55 mm), with one case associated with a 5 mm invasive component. Notably, the papillary lesions in these six cases were benign in both the initial biopsies and excision specimens, while the needle biopsies revealed epithelial atypia (ADH=3, flat epithelial atypia=2, apocrine atypia=1) in the breast parenchyma outside the papillomas. Among the 46 atypical papillary lesions excised, 18 (39%) were malignant (all showed in situ papillary carcinomas; 4 of these were associated with invasive carcinoma as well), 11 revealed ADH and/or lobular neoplasia and 17 were benign/showed no residual lesion. All seven excised papillary lesions suspicious for malignancy on needle core biopsies were confirmed malignant on excision.

Conclusion: Papillary lesions diagnosed as atypical or suspicious for malignancy on needle core biopsies should be completely excised in view of the high positive predictive value for malignancy. However, our data suggest that routine surgical excision may not be necessary for core biopsy diagnosed benign papillomas which are not associated with atypia.

Disclosure of Interest: No significant relationships.

P019

Histopathological features of operable breast cancer detected in women younger than 35 years

A. Hironaka[1] *, H. Tsuda[2], M. Yoshida[1], C. Shimizu[3], K. Tamura[3], Y. Fujiwara[3], T. Hojo[3], T. Kinoshita[3], A. Maeshima[1], N. Hiraoka[1].
[1]Pathology, National Cancer Center Hospital, Japan, Tokyo, Japan, [2]National Defense Medical College, Tokorozawa, Japan, [3]National Cancer Center Hospital, Japan, Tokyo, Japan

Goals: There is limited knowledge about histopathological features of breast cancer arising in very young women aged <35 years old. The aim of this study was to evaluate pathological features and expression of biomarkers in primary invasive breast cancer arising in very young women.

Methods: From consecutive 110 young (<35 years old) patients who received surgical therapy in National Cancer Center Hospital, Tokyo, between 1997 and 2013, 102 tumor samples were available for the analysis. Histopathological tumor characteristics, including histological grade (HG), tumor infiltrating lymphocytes (TIL), lymphatic invasion (ly), and necrosis were assessed. The expression of estrogen receptor (ER), progesterone receptor (PgR), androgen receptor (AR), p53, HER2, EGFR, cytokeratin 5/6 (CK5/6), and Ki-67 were also examined immunohistochemically using tissue microarrays. Comparisons were made between the group of very young patients and older premenopausal patients (40–44 years old) whose pathological stage was matched.

Results: There were significant differences in the positivity of ER, and AR expressions (p = 0.0016 and 0.0044, respectively) between very young and older patient groups. Triple-negative subtype tended to be more frequent (17%) in very young patients than in the older patients (6%). There were no significant differences in the prevalence of histopathological features examined or of other molecular expressions between two patient groups.

Conclusion: In the breast cancers detected in very young patients, hormone-receptor-negative tumors were more frequent than in those in older patients.

Disclosure of Interest: No significant relationships.

Table: Histological/biomarker characteristics

Parameter		Number of patients (%)		p value
		Very young	Older	
HG	1	8 (8)	12 (12)	0.62
	2	37 (36)	38 (37)	
	3	54 (53)	58 (57)	
	No assessment	3 (3)	2 (2)	
TIL	Low	36 (35)	25 (25)	0.093
	High	66 (65)	77 (75)	
ly	Negative	54 (53)	53 (52)	0.89
	Positive	48 (47)	49 (48)	
Necrosis	Negative	64 (63)	65 (64)	0.88
	Positive	38 (37)	37 (36)	
Subtype	Luminal A	17 (18)	22 (22)	0.097
	Luminal B	55 (60)	67 (68)	
	HER2	4 (4)	3 (3)	
	Triple-negative	16 (17)	6 (6)	
ER	Negative	26 (25)	9 (9)	0.0016
	Positive	76 (75)	93 (91)	
PgR	Negative	21 (21)	12 (12)	0.087
	Positive	81 (79)	90 (88)	
AR	Negative	21 (21)	7 (7)	0.0044
	Positive	81 (79)	95 (93)	
p53	Negative	50 (49)	46 (45)	0.57
	Positive	52 (51)	56 (55)	
HER2	Negative	84 (87)	90 (88)	0.73
	Positive	13 (13)	12 (12)	
EGFR	0	74 (72)	85 (83)	0.31
	1+	13 (13)	7 (7)	
	2+	5 (5)	3 (3)	
	3+	10 (10)	7 (7)	
CK5/6	Negative	80 (78)	89 (87)	0.095
	Positive	22 (22)	13 (13)	
Ki-67	High	83 (81)	80 (78)	0.60
	Low	19 (19)	22 (22)	

P020

Deficiency of neurofibromin and increased risk of relapse in triple negative breast cancer

Y. Yap[1] *, A.A. Thike[2], C. Lim[3], W.S. Yong[4], A.S. Lee[5], P.H. Tan[2].
[1]Medical Oncology, National Cancer Centre Singapore, Singapore, Singapore, [2]Pathology, Singapore General Hospital, Singapore, Singapore, [3]Clinical Trials and Epidemiology, National Cancer Centre Singapore, Singapore, Singapore, [4]Surgical Oncology, National Cancer Centre Singapore, Singapore, Singapore, [5]Medical Sciences, National Cancer Centre Singapore, Singapore, Singapore

Goals: NF1 (Neurofibromatosis type 1) is one of the significantly mutated genes in many cancers, including breast cancer. However, the clinical relevance of neurofibromin deficiency in sporadic breast cancer is unclear. We hypothesise that loss of neurofibromin, a tumour suppressor, will be associated with worse outcome. The objectives of the study are to evaluate the immunohistochemical expression of neurofibromin in breast cancer, and its association with clinocopathologic features and survival outcomes.

Methods: The expression of neurofibromin was evaluated through immunohistochemistry on microarrayed cores obtained from 314 stage 1–3 breast cancer specimens diagnosed between April 2000

and Dec 2002. Expression of neurofibromin in nuclei and cytoplasm was scored separately. Positive expression was defined as nuclear and cytoplasmic staining in 10% or more of tumour cells. Survival outcomes were estimated with the Kaplan–Meier method and compared between groups with log-rank statistics. Median follow-up was 132.2 months.

Results: Positive expression of neurofibromin, as defined above, was seen in 44.6% (140/314) of tumours. Staining for neurofibromin was observed in a median of 5% (0–95%) of cells for nuclear staining, and 40% (0–95%) of cells for cytoplasmic staining. Negative expression of neurofibromin was associated with high tumour grade ($p < 0.001$), hormone receptor negativity ($p < 0.001$), lymph node positivity ($p = 0.041$) and larger tumour size ($p = 0.031$). Negative expression of neurofibromin was also associated with increased risk of relapse (5-year relapse rate 29.2% vs 17.0%; hazard ratio 1.56, $p = 0.029$) and death (5-year death rate 21.7% vs 12.7%; hazard ratio 1.64, $p = 0.029$) on univariate analysis. On multivariate analysis, lack of neurofibromin was an independent predictor of relapse and death for triple negative cancers (hazard ratios 3.33, $p = 0.011$ and 2.94, $p = 0.026$ respectively), but not in the luminal and HER2 positive immunohistochemical subtypes.

Conclusion: In breast cancer, deficiency of neurofibromin is associated with adverse prognostic features, increased risk of relapse and inferior survivor outcomes in triple negative breast cancers. Elucidating the mechanisms of neurofibromin loss and its downstream effects will improve our understanding of the role of neurofibromin in breast cancer.

Disclosure of Interest: No significant relationships.

P021

Primary tissue culture in a bioreactor system: a new tool for personalized medicine?

S. Muenst[1] *, M.G. Muraro[2], G.C. Spagnoli[2], D. Oertli[2], W.P. Weber[2], S.D. Soysal[2]. *[1]Institute of Pathology, University Hospital Basel, Basel, Switzerland, [2]Surgery, University Hospital Basel, Basel, Switzerland*

Goals: The development of cancer treatment protocols has traditionally been based on studies in experimental animal models or taking advantage of human established tumor cell lines for in vitro and in vivo assays. Our aim is to develop a new and feasible method to culture primary breast cancer tissue in vitro by use of a 3D porous scaffold-based perfusion bioreactor system.

Methods: Freshly excised breast cancer specimens were fragmented and cultured in a 3D "sandwich-like format" between porous scaffolds under perfusion flow, with "on-line" monitoring of environmental condition. DMEM/F12, supplemented with 10% autologous human serum, was used as a culture medium in the presence or absence of estrogens in estrogen (ER)-receptor positive cancer. The ability of tumor cells in perfusion cultures to survive and infiltrate the scaffold as well as their ability to recapitulate features of the original breast cancer specimens was histologically assessed. In a second step anti-ER (Fulvestrant) treatment was added to the cultures.

Results: With this innovative method we were able to preserve viability and even expand breast cancer tissue with concomitant stromal and immune cells. Expanding cancer cells were viable after 21 days and recapitulating the initial histology with formation of glands. ER administration was associated with increased expansion of cancer tissue into the scaffold. Interestingly, ER expression was partly lost in the expanding cancer cells. Administration of anti-ER led to decreased survival of normal breast and breast cancer tissue.

Conclusion: The culture of breast cancer tissue in a 3D scaffold-bioreactor preserves malignant, interstitial and immunocompetent cells, thus allowing direct testing of basic cancer immunobiology research hypotheses in complex, human tumor microenvironments. Additionally, it allows a direct evaluation of the effects of various treatments on malignant and non-transformed cells. This engineered in vitro model could be extended beyond the context of our primary scientific interest, namely breast cancer, as a broader platform allowing animal-free testing of innovative approaches to treatment of human malignancies, possibly in the direction of personalized medicine.

Disclosure of Interest: No significant relationships.

P022

Associations of TOX3 RS3803662 polymorphisms and breast cancer in the Han nationality

H. Liu[1] *, Q. Chen[2], Y. He[2]. *[1]Breast Surgeon, Henan Province Tumor Hospital, Zhengzhou, China, [2]Henan Province Tumor Hospital, Zhengzhou, China*

Goals: To study the associations between sporadic breast cancers and single nucleotide polymorphism rs3803662 in TOX3 gene among the Han Nationality in Henan Province which has been identified in the European population and East Asian populations.

Methods: A case–control study was performed in 253 patients with breast cancer and 343 cases of benign breast lesions, the TOX3 rs3803662 genotype was detected by imLDR technique, using relevant statistical methods to analysis correlation between different alleles and breast cancer.

Results: The distribution of TOX3 rs3803662 allele between breast cancer and the control group were different. Compared with allele AA and GA, allele GG increased the risk of breast cancer in codominant inheritance (OR = 2.19, 95% CI: 1.19–4.02) and recessive genetic models (OR = 2.06, 95% CI: 1.15–3.70). Further stratifying analysis was conducted based on estrogen receptor status, TOX3 rs3803662 polymorphism increased the risk of both ER positive and negative breast cancer.

Conclusion: The single nucleotide polymorphism of TOX3rs3803662 gene may be the risk factors of breast cancer, in codominant and recessive genetic models, allele GG increased breast cancer risk in Han women in Henan area, and was associated with the pathogenesis of different ER status breast cancer.

Disclosure of Interest: No significant relationships.

P023

Morphobiological peculiarities of metaplastic breast cancer

S.S. Todorov *, E. Bosenko. *Pathology, Rostov Oncological Institute, Rostov-on-Don, Russian Federation*

Goals: Metaplastic breast cancer is a rare neoplasm. It's incidence varies between 0.5% and 1% of all histological variants of breast cancers. To understand the biological behavior of this type of neoplasia we decided to do the comparative morphological, immunohistochemical investigation and to estimate different variants of growth, production in these tumors.

Methods: We have studied metaplastic breast cancer for the period 2011–2014. The average age of women was 53 years. After performing sectoral resection was performed urgent histological examination of surgical specimens. Another part of the material separately carved in the form of plates no larger than 1 cm in length, embedded in buffered 10% formalin, fixed no more than 24 hours after posting routine embedded in paraffin. Thereafter, paraffin blocks were prepared with histological sections 3–4 micrometers in thickness on a microtome Accu-Cut SRM 200 from Sakura (Japan), which were stained with hematoxylin-eosin. Separately for immunohistochemical studies histological sections obtained highly adhesive coated on glass and dried in a vertical oven at a temperature of 55–56°C for 10 hours. Dewaxing reconstitution activity and antigenic immunohistochemical reaction steps have

performed in VENTANA BenchMark ULTRA by Roche (Switzerland). As a system for detecting the primary antibody was used "ultraView Universal DAB Detection", produced by Roche for VENTANA. We used antibodies to Ki-67, p53, Her-2, receptors to estrogen, progesteron, androgen, vimentin, pancytokeratin, topoisomerase-2a, cyclin D1, p63 to identify the tumor's growth and biological heterogenity.

Results: Grossly metaplastic breast cancer was presented tumor node dense consistency diameter not exceeding 3.5 cm, with whitish pearl surface on the cut. Metaplastic carcinoma histology differed variability of its components. Thus, along with the solid portions of the large dark cell tumor, small-scale tubular structures it for almost the entire mesenchymal components were represented as cartilaginous and osteoid-like tissue immersed in myxomatous connective tissue framework. The structure was represented by tumor epithelial and mesenchymal components. At higher magnification, it was obvious that the tumor was represented by small and large solid areas, small atypical tubules are localized in the edematous stroma. The structure of the tumor expressed CK5 6, vimentin, indicating different origin of the cancer. Besides the tumor's structures hav shown biological heterogenity with high capacity to proliferation in epithelial-like zones (high index Ki-67, cyclin D1, low index p53), absence of hormonal receptors in mesenchymal structures.

Conclusion: Metaplastic breast cancer has dimorphic development due to transdifferentiation epithelial to mesenchymal tissue.

Disclosure of Interest: No significant relationships.

P024

Navigating genomic landscape: PI3KSIGNALING algorithm for rational combination in precision medicine

N. Dey*, C. Williams, A. Krie, B. Solomon, Y. Sun, K. Williams, J. Klein, J.H. Carlson, P.K. De, B. Leyland-Jones. *Molecular & Experimental Medicine, Avera Research Institute, Sioux Falls, United States of America*

Goals: The characteristically abundant and diverse genetic alterations in BC lead to an upregulation of common group of oncogenic signal transduction pathways which have well-defined functional consequences on cell growth and thus may determine therapeutic sensitivity. A better therapeutic outcome can be designed by merging the (1) in-depth information about genetic alterations from the patient and (2) understanding of the associated cell signaling pathways pertaining to tumorigenesis. The systemic management of metastatic BC is mostly based on the presence/absence of ER/PR or HER2 status of the primary tumor. In our study we have enriched this conventional approach by including the major genetic alterations and proteomic changes in the individual patient towards the development of a better treatment rationale based on a signaling algorithm.

Methods: We retrospectively analyzed data from 75 consecutive BC patients those were seen in our center over 10 months from February through November 2014. Patients were re-biopsied after consultation and samples were characterized (IHC for ER, PR, and HER2; FFPE samples for genomic [Foundation Medicine] and proteomic analyses [Theranostics]).

Results: A total of 76 genes were altered in 48 ER+ BC patients. In 79% of ER+ BC patients PI3K pathway genes (PIK3CA, PIK3R1, AKT, PTEN, MDM2, MDM4, TSC1, mTOR, RICTOR) were altered. Analyzing the composite alterations in individual patients, we observed that within these 48 patients 25% had alterations in more than one node of the pathway. The most common combination (alterations) being the amplification/mutation of PIK3CA with the amplification of MDM2/4 genes. In contrast the percentage of patients belonging to other two subtypes of BC (HER2+ and TNBC) exhibiting a similar alterations in the PI3K pathway genes were significantly lower (~40%). Among these patients only a negligible % exhibited alterations of more than one node of the pathway. In cell line based models, a combination of the pan-PI3K pathway inhibitor, GDC-0941 or isoform-specific inhibitors along with AI, transtuzumab, or HRD inhibitors (PARP) blocked proliferative signals and enhanced apoptosis in ER+/PIK3CA mutated, HER2+/PIK3CA mutated or PTEN-null TNBC cells respectively.

Conclusion: Plotting the in-depth information about genetic alterations from the patient on the signaling landscape will eventually be useful in cracking the code for the improved treatment options.

Disclosure of Interest: No significant relationships.

P025

Immunological factors to predict disease progression during neoadjuvant chemotherapy

Y. Tanabe[1]*, H. Tsuda[2], M. Yoshida[3], T. Kinoshita[4], M. Kodaira[1], H. Yamamoto[1], K. Yonemori[1], C. Shimizu[1], Y. Fujiwara[1], K. Tamura[1]. *[1]Breast and Medical Oncology, National Cancer Center Hospital, Tokyo, Japan, [2]National Defense Medical College, Tokorozawa, Japan, [3]Pathology, National Cancer Center Hospital, Tokyo, Japan, [4]Breast Surgery, National Cancer Center Hospital, Tokyo, Japan*

Goals: Given the heterogeneous response to neoadjuvant chemotherapy (NAC) in triple negative breast cancer (TNBC), predictive biomarkers are required for subtype-specific characterization. Tumor infiltrating lymphocytes (TILs) are shown to be correlated with response of breast cancers to NAC. The high-mobility group box protein 1 (HMGB1) is a binding partner, inducer, and/or chaperone for many of proinflammatory molecules and is suggested to play a role in tumor progression through immune suppression. We performed a retrospective case–control study to identify histopathological and immunohistochemical predictive factors of clinically progressive disease (cPD) in patients with TNBC treated with NAC.

Methods: Twenty-two TNBCs that showed cPD during NAC and resected from the patients and 80 control TNBCs that were resected from patients without receiving NAC were collected. Tissue microarrays were constructed and histopathological examination on histological type, number of mitotic figures and TIL, and immunohistochemical studies on Ki-67 labeling index (LI) and HMGB1 expression were performed. The difference of these parameters was compared between cPD and control groups.

Results: Histologically, cPD group comprised 14 invasive ductal carcinomas (IDCs) (64%) and 8 metaplastic carcinomas (MPCs) (36%), whereas control group comprised 59 IDCs (74%), one MPC (1%), and 20 (25%) other types ($p < 0.001$). Compared with control group, cPD group showed a higher Ki-67 LI (39.0% vs 62.1%) and a higher mean number of mitotic figures (3.5 vs 6.1 per high-power-field). The percentage of cases with high TIL was lower in cPD group than in control group (23% vs 45%, $p = 0.040$). Cytoplasmic HMGB1 expression was more frequent in cPD group than in control group (86% vs 51%, $p = 0.0023$).

Conclusion: A larger number of mitotic figures, a higher Ki-67 LI, metaplastic phenotypes, cytoplasmic HMGB1 expression, and lack in TIL appeared predictors for cPD, during NAC in the patients with TNBC.

Disclosure of Interest: No significant relationships.

P026

Mechanical ventilation promotes lung metastasis in 4T1 breast cancer lung-metastasized models

Y. Huang[1] *, L. Pan[2], K. Helou[3], Q. Xia[2], T. Zhao[2], H.-Y. Li[2], B. Xu[2], J. Zhang[3], Z. Chen[2], H. Li[2]. *[1]Breast Cancer Department, Sodra Alvsborgs Sjukhus, Boras, Sweden, [2]China–Japan Friendship Hospital, Beijing, China, [3]Sahlgrenska Cancer Center, University of Gothenburg, Gothenburg, Sweden*

Goals: Recent evidence suggests that general anaesthesia and perioperative factors significantly increased risk of cancer recurrence compared to locoregional anaesthesia in patients undergoing surgery, however, their effects on behavior of cancer cells are not yet known. The endothelial cell and epithelial disruption was observed during mechanical ventilation, general anaesthesia in animal models. This study was to test the hypothesis that mechanical ventilation during cancer surgery induces lung stroma/tissue milieu changes, creating a favorable microenvironment for postoperative lung metastatic tumor establishment.

Methods: Female BALB/c mice were anesthetized by intraperitoneal pentobarbital administration and divided into a mechanical ventilation group [mice ventilated with low pressures and low tidal volumes, 60 min; n = 8) and a control group (no ventilation; n = 8). All the mice were subjected to intravenous injection of murine mammary adenocarcinoma 4T1-green fluorescent protein (GFP) 10^5 cells during anaesthesia. 24 hr later, sections from the lung tissue were examined and 4T1 celler were counted by direct GFP fluorescence observation, hematoxylin-eosin histology and Ep-CAM immunohistochemistry. To closely mimic human cancer surgical and anaesthetic manipulation, A clinically relevant animal model of spontaneous breast cancer lung metastasis with surgical resection of primary tumor was used to investigate the purified mechanical ventilation event that dictate lung metastasis post-operation. Female BALB/c mice were inoculated with metastatic murine mammary adenocarcinoma 4T1 cells in the mammary fat pad (3×10^5/mouse). After 14 day growth, mice were anesthetized by intraperitoneal pentobarbital administration and divided into a mechanical ventilation group [mice ventilated with low pressures and low tidal volumes, 60 min; n = 6) and a control group (no ventilation; n = 6). All the mice were subjected to flank tumor resection during anaesthesia. Two weeks later, Metastatic tumor burden was assessed by both macroscopic metastatic nodule count and hematoxylin-eosin histology.

Results: Mechanical ventilation was associated with increased circulating breast tumor cells arrest at microvasculature of lung ($P = 0.01$). The histology analysis data indicated that mechanical ventilation induced endothelial-epithelium abnormalities, inflammatory reaction and significantly upregulated the expression of epithelial adhesion molecules (Ep-CAM). Postoperative metastases exhibited significantly increase in mechanical ventilated groups in comparison with those in non-ventilated group ($P < 0.05$).

Conclusion: Mechanical ventilation led to a progressive phenotype of lung metastases that exhibited a microenvironment for cancer cell adhesion, invasion, survive and growth within lungs.

Disclosure of Interest: No significant relationships.

P027

The analysis of cytogenetic intra-tumoral heterogeneity in squamous cell carcinoma of the breast

M. Oikawa[1] *, A. Igawa[2], M. Ishida[1], Y. Nakamura[1], S. Nishimura[1], C. Koga[1], S. Akiyoshi[1], Y. Koi[1], K. Taguchi[2], S. Ohno[1]. *[1]Breast Oncology, National Kyushu Cancer Center, Fukuoka, Japan, [2]Pathology, National Kyushu Cancer Center, Fukuoka, Japan*

Goals: Squamous cell carcinoma (SCC) of the breast is rare and generally aggressive disease constituting less than 0.1% of all breast carcinomas. Albeit their distinctive morphological feature, the origin and cytogenetic profile of SCC are still not well understood. In this study, three cases of SCC of the breast which consists of SCC component and invasive or noninvasive ductal carcinoma of no special type (NST) component were analyzed to elucidate the cytogenetic intra-tumoral heterogeneity and the origin of SCC of the breast.

Methods: Among pathologigal database for 3,000 patients with breast cancer, five patients with SCC were determined. Their medical records were retrospectively reviewed to obtain clinicopathological, radiological, treatment and outcome information. Among them, three cases showed morphological intra-tumoral heterogeneity, thus components of SCC and invasive or noninvasive ductal carcinoma of NST were contained. Both components of each case were separately macro-dissected using five 10-μm-thick sections and tumor DNA was extracted using the QIAmp DNA Mini Kit (Qiagen), followed by array comparative genomic hybridization (aCGH) analysis using a high-density oligonucleotide microarray (Agilent® SurePrint G3 8×60k microarray). The cytogenetic profile of SCC component was compared with paired NST component in each case.

Results: Sufficient amounts of DNA were obtained with an average of 0.79 μg (0.54–1.04 μg). The quality of the aCGH was acceptable, as judged by the mean derivative log ratio spread (DLRSpread) of 0.475 (0.36–0.55), which estimates the log ratio noise by calculating the spread of log ratio differences between consecutive probes along all chromosomes. The cytogenetic profiles of SCC and NST component were almost identical in case 2 and case 3. However comparing with NST component, large number of copy number aberrant (CNA) region was detected in SCC component and all aberration in NST component were encompassed in SCC component in case 1. There is no common SCC component specific aberration in the three cases.

Conclusion: Our result showed diversity of cytogenetic intra-tumoral heterogeneity in SCC of breast. Comparison with cytogenetic profile in one case indicated that the SCC component originated from NST component.

Disclosure of Interest: No significant relationships.

P028

Characteristics of mucocele-like tumors

K. Takebe *, T. Arai. *Breast Surgery, Takebe Breast Cancer Care Clinic, Takamatsu, Japan*

Goals: Mucocele-like tumors (MLT) are mucus-producing benign lesions that have been proposed by Rosen. Since the malignant merger case exists, attention to diagnosis and treatment is needed. The purpose of this study is the elucidation of the pathological diagnosis and image diagnosis of MLT and the construction of the treatment strategy.

Methods: From 1997 to 2013, 70 cases of MLT were diagnosed in our facility. Excisional biopsy (or lumpectomy) accounted for 35 cases. In the 2008–2013 period, we examined 35 follow-up cases of MLT without ductal hyperplasia that were diagnosed by fine-needle aspiration cytology (FNAC) or core needle biopsy (CNB).

Results:
1. MLT discovered in MMG screening in our facility numbered 10 cases and the discovery rate was 0.05%. Approximately one-eighth of DCIS was found at the same time.
2. In the patients who underwent excisional biopsy, cases with DCIS or micro-invasive cancer were 29%, cases with ductal hyperplasia were 46%, and cases that did not involve ductal hyperplasia were 26%.
3. MMG findings showed that 83% were accompanied by calcification. Coarse calcification in the mucus lake (we advocated this calcification with graded coarse calcification) was observed in 63%.
4. Birads category of calcification was not possible to accurately diagnose with the malignant merger example of MLT.
5. In observation, 31% of the cases resulted in the loss of the lesions, 9% of the cases resulted in increased calcification. But there was no malignant merger in the increased cases.

Conclusion: MLT is not an extremely rare disease. After detecting a graded coarse calcification in MMG, it can be relatively easily diagnosed by detecting cystic lesions with ultrasonography. Although malignancies are also found in 29% of the cases, if there is no ductal hyperplasia collected by FNAC or CNB, immediate excisional biopsy is not necessary.

Disclosure of Interest: No significant relationships.

P029

The relationship between tumour lymphocyte infiltration and survival in early breast cancer patients

J. Huszno[1] *, E. Zembala Nożyńska[2], Z. Kolosza[3], E. Nowara[1]. *[1]Clinical and Experimental Oncology Department, Maria Skłodowska Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, Gliwice, Poland, [2]Tumor Pathology Department, Maria Skłodowska Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, Gliwice, Poland, [3]Department of Epidemiology and Silesia Cancer Registry, Maria Skłodowska Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, Gliwice, Poland*

Goals: Infiltration of breast tumors by tumor-infiltration lymphocytes (TILs) has been associated with improved outcome and sensitivity to anthracycline-based chemotherapy. The aim of this study was to evaluated the influence of TILs on progression free survival (PFS) and overall survival (OS) in primary operable breast cancer.

Methods: Paraffin sections were retrospectively evaluated in 60 cases in early stage breast cancer patients who received surgery and next systemic treatment (anthracycline based adjuvant chemotherapy and trastuzumab in patients with HER2 overexpression) between 2010 and 2013 in Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch in Poland. Lymphocytic infiltrations were classified as: absent (grade 0), little (grade 1), moderate (grade 2), and marked (grade 3). Statistical analysis was carried out using STATISTICA 7 software. Survival evaluation was performed using the Kaplan–Meier estimator with log rank test. Differences were considered as significant if the p value was ≤0.05.

Results: Tumor lymphocyte infiltration were present in 82% of patients. Marked grade infiltration (grade 3) was detected in 7% of them. There was observed no association between OS and lymphocyte infiltration (TILs) in whole group. In subgroups analysis, overall survival was significantly longer in tumors with absent or little TILs and without HER2 overexpression or amplification ($p = 0.030$). There was also detected no association between TILs and progression free survival (PFS) in the whole group. In subgroup with HER2 overexpression or amplification PFS was significantly longer in tumors with strong lymphocyte infiltration ($p = 0.012$). In logistic regression analysis HER2 overexpression (OR = 4.2, $p = 0.023$) and negative steroid receptor status (OR = 9.5, $p = 0.002$) were independent factors that increase the risk of occurrence of TILs.

Conclusion: TILs reduce the risk of disease progression in patients with HER2 overexpression. It also improved OS in HER2 negative early breast cancer patients. TILs was positively associated with negative steroid receptor status and HER2 overexpression. Further studies with the larger group of patients are necessary.

Disclosure of Interest: No significant relationships.

P030

Impact of different Ki67 assessment methods on St.Gallen subtyping of breast cancer

C.M. Focke*, D. Gläser, K. Finsterbusch, T. Decker. *Institut für Pathologie, Dietrich Bonhoeffer Klinikum, Neubrandenburg, Germany*

Goals: The Gallen Consensus recommended clinicopathological subtyping of breast cancer (BC). Besides histological special types, luminal A, B, HER2, and triple negative subtypes were defined by immunohistochemical detection of ER and PgR, detection of overexpression and/or amplification of HER2, and assessment of Ki-67 labelling index (Ki67-LI). These subtypes are generally accepted to guide therapy. Luminal A BCs are agreed to be less responsive to chemotherapy (CT) which is considered as less useful. In all ER positive and HER2 negative BCs which express PgR >20% luminal A and B BCs should be distinguished by Ki67-LI "low" or "high". The 2013 consensus agreed a threshold of ≥20% as indicative of 'high'. We investigated the influence of different Ki67 assessment methods on clinicopathological subtyping and on the rate of potential CT.

Methods: Subtyping was performed on 300 unifocal UICC stage I and II BCs according to the St. Gallen 2013 criteria. ER positive HER2 negative BCs which at the same time showed both, PgR ≥20% and Ki67-LI <20% were categorized as luminal A. Ki67-LI was assessed by counting any Ki67 nuclear staining of defined areas on whole slides of surgical specimens. We used three methods including the International Ki67 in Breast Cancer Working Group recommendations with different distinctly defined target areas: (1) 100 tumour cells within the hot spot (Ki67–100), (2) a total of 1020 tumour cells in 3 high power fields (HPF) in the tumour periphery including the hot spot (Ki67–1020periphery), and (3) a total of 1020 tumour cells in 3 HPF including hot spot, cold spot and an intermediate area (Ki67–1020spectrum). The quality of Ki67 staining and counting accuracy was tested as "excellent" by the circulation of the "German Quality Initiative in Pathology".

Results: Of 300 BCs, 241 (80%) were luminal, 3 (1%) HER2+ (non-luminal), 34 (11%) triple-negative, and (22) 8% special type, respectively. Depending on the different proliferation assessment methods the overall rates for luminal A-like vs. luminal B-like BCs came out with: Ki67–1020spectrum: 50% vs. 30% (149 vs. 93/300), Ki67–1020periphery: 36% vs. 44% (109 vs. 133/300), and Ki67–100: 16% vs. 64% (47 vs. 195/300), respectively.

Conclusion: Depending on the Ki67-LI assessment method the overall rate of "less CT responsive" luminal A-like BCs varies between 16% and 50%, respectively. That means that in up to 34% of all BC patients the decision about CT may result in over- or undertreatment caused by this strong variation of Ki67-LI.

Disclosure of Interest: No significant relationships.

P031

Correlation between CHEK2 mutation and clinicopathological factors in early breast cancer patients

J. Huszno[1]*, M. Budryk[2], Z. Kolosza[3], E. Nowara[1]. [1]*Clinical and Experimental Oncology Department, Maria Skłodowska Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, Gliwice, Poland,* [2]*Genetic Outpatient Clinic, Maria Skłodowska Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, Gliwice, Poland,* [3]*Department of Emidemiology and Silesia Cancer Registry, Maria Skłodowska Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, Gliwice, Poland*

Goals: CHEK2 encodes a checkpoint kinase, involved in response to DNA damage. A mutation in CHEK2 gene leads to decrease of DNA-repair and may cause an increase of susceptibility to cancer. The aim of this study was to evaluate the relationship between CHEK2 mutation and standard clinicopathological factors such as hormone status [oestrogen receptor (ER), progesterone receptor (PR)], human epidermal growth factor (HER2), Ki67, tumor size, the presence of lymph nodes metastases, patients age and menopausal status.
Methods: The analysis was conducted on the medical records of 34 patients who were treated with anthracycline/taxane-based chemotherapy, hormonotherapy and immunotherapy in years 2012–2014 in MSC Memorial Cancer Center in Gliwice. Hormone status, HER2 overexpression and Ki 67 were determined by routine immunohistochemical techniques. CHEK2 mutation was assessed by PCR technique. Statistical analysis was performed using STATISTICA 7 Stat Soft.
Results: The median age of Chek2 mutation carriers was 58 years (range from 25 to 74). There was detected association between postmenopausal period and the presence of Check2 mutation (62%). Luminal type B was the most frequently observed breast cancer type in Chek2 mutation carriers (88%). The large majority of tumors had positive estrogen (ER) and progesterone (PR) receptor status, 85% and 76% respectively. 18% of tumors have shown HER2 overexpression. In most of tumors Ki67% was lower then 40%. Triple negative breast cancer was not observed. Lymph node involvement was detected 32% of patients with Chek2 mutation. Chemotherapy was applied to 62% of patients. 59% of them received anthracycline based an 15% taxane based chemotherapy. 24 (70%) of them received adjuvant chemotherapy and 10 (30%) neoadjuvant treatment. Hormonotherapy was applied to 86% of patients. 56% of women received radiotherapy.
Conclusion: CHEK2 mutation was associated with lower TNM stage, lower Ki67%, positive steroid receptor status and luminal B type of cancer. Further studies with the larger group of patients are necessary. Patients are still recruited.
Disclosure of Interest: No significant relationships.

P032

Central lab HER2 testing by RT-PCR, IHC and FISH in locally HER2-Neg, ER+ IBC with in situ carcinoma

V. Tan*, R. Lu, A. Tharayanil, J. Anderson, A. Tsiatis, H. Bailey, M. Bonham, A. Pingitore, S. Shak, F. Baehner. *Pathology, Genomic Health Inc, Redwood City, United States of America*

Goals: Our HER2 QA program requires confirmatory testing with IHC and FISH at an outside central lab on all IBC samples with in situ carcinoma (IS) that are HER2-positive (HER2+) by central Oncotype DX (ODX) but are locally IHC/FISH HER2-negative (HER2-Neg), equivocal (EQ), or unknown (UNK). The objective of this QA program is to further assess the quality of HER2 testing by RT-PCR and to identify rare intratumoral differences in HER2 expression between IBC and IS.
Methods: From 12/1/10 to 8/26/14, RT-PCR HER2+ IBC cases with IS which were locally HER2-Neg, EQ, or UNK were sent to a central lab (Vitro Molecular Labs; Miami, FL) for IHC/FISH testing using HER2 SP3 IVD assay and PathVysion, respectively. HER2 status was determined before 10/13 by the 2007 ASCO-CAP guidelines, and after 10/13 by the 2013 revised ASCO-CAP HER2 guidelines. In cases of central IHC/FISH discordances (in <2% of cases), HER2 status was recorded as + if at least 1 method was +. RT-PCR for HER2 used ODX and the pre-defined HER2 cutoffs: + = ≥11.5 units, EQ = 10.7–11.4 units, and negative = <10.7 units, where each unit represents a 2-fold change in gene expression.
Results: See the table. 2,454 of 310,525 cases were RT-PCR HER2+. 327 IBC cases with IS that were HER2+ by RT-PCR and locally HER2-Neg, EQ, or UNK were sent for central lab IHC/FISH. 10 cases were excluded for inconclusive IHC/FISH due to preanalytic compromise. 317 IBC cases with IS were local HER2-Neg, EQ, or UNK in 212 (66.9%), 26 (8.2%), or 79 (24.9%) cases, respectively. 131 of 212 (61.8%) HER2-Neg cases by local sites were HER2+ by central IHC, FISH, and RT-PCR. 56 of 212 (26.4%) locally HER2-Neg cases were found to have differences between IBC and IS by central IHC/FISH. 22 of 212 (10.4%) of locally HER2-Neg cases were central IHC/FISH HER2-Neg.

	Local HER2-Neg, EQ or UNK (N = 317)	Local HER2-Neg (N = 212)
RT-PCR concordant w/ central IHC/FISH	**211 (66.6%)**	**131 (61.8%)**
RT-PCR+ vs. central EQ	**7 (2.2%)**	**3 (1.4%)**
RT-PCR discordant w/ central IHC/FISH	**99 (31.2%)**	**78 (36.8%)**
RT-PCR+ vs. Central−	30 (9.5%)	22 (10.4%)
RT-PCR+ vs. Central IBC−/IS+	69 (21.8%)	56 (26.4%)

Conclusion: RT-PCR testing has clinical utility in identifying pts who may be HER2+ by central FISH/IHC and therefore candidates for HER2 targeted therapy. The QA program identifies rare cases where IS is HER2+ and IBC is HER2-Neg.
Disclosure of Interest: All authors are Genomic Health employees.

P033

Mcl-1 confers protection of breast cancer cells exposed to hypoxia: therapeutic implications

M.H. Bashari[1]*, F. Fan[1], M. Arn[2], S. Vallet[1], J. Opferman[3], M.H. Cardone[2], A. Schneeweiss[1], D. Jäger[1], K. Podar[1]. [1]*Medical Oncology, National Center for Tumor Diseases (NCT), University of Heidelberg and German Cancer Research Center (DKFZ), Heidelberg, Germany, Heidelberg, Germany,* [2]*Eutropics Pharmaceuticals, Inc, Cambridge, United States of America,* [3]*St. Jude Children's Research Hospital, Memphis, United States of America*

Goals: Despite unprecedented advances in breast cancer (BC) therapy during the last two decades it remains the most common cause of cancer-related death in women. Molecular mechanisms, which lead to the adaptation of BC cells to hypoxia, e.g. modulation of cell proliferation, survival, metastasis, and chemo- and radiotherapy resistance are elusive. This study aims to delinate a previously unknown role of the anti-apoptotic Bcl2 family member myeloid cell leukemia 1 (Mcl-1) in the protection of HER2+ BC cells exposed to hypoxia; and to identify derived novel therapeutic strategies.
Methods: The molecular role of Mcl-1 in BC cells under hypoxic conditions was investigated by genetically as well as pharmacologically targeting Mcl-1 and HER2 not only in HER2+, but also in luminal A and triple negative (TN) BC cells versus non-malignant MCF-10A cells. Effects were analyzed by proliferation, survival, and spheroid forming assays as well as immunoprecipitation/blotting. Mcl-1$^{(\Delta/null)}$ Murine Embryonic Fibroblasts (MEFs) were used to verify mechanistic findings obtained in BC cells.
Results: Having identified the improved adaptation of HER2+ cells versus HER2− and non-malignant MCF-10A cells under hypoxic

conditions, we next delineated a functional correlation of Mcl-1 and HIF-1α in HER2+ BCs. Specifically, we observed rapid induction of Mcl-1 and HIF-1α in HER2+ cells, but not in HER2− cells. Genetic depletion of Mcl-1 in HER2+ cells downregulated HER2 and HIF-1α levels followed by inhibition of BC cell survival. Surprisingly, Mcl-1 protein levels did not decrease after HER2 depletion or pharmacological inhibition of HER2, indicating a regulatory role of Mcl-1 upstream of HER2. The functional interrelation of Mcl-1 and HER2 under hypoxic conditions was also supported by co-immunoprecipitation experiments with the specific Mcl-1 binding BH3 protein NOXA. Our results additionally demonstrate significant cell death of HER2+ cells resistant to HER2 inhibitors triggered by genetic Mcl-1 depletion compared to HER2 depletion (54.4% vs 7.4%, $p < 0.01$). The novel small molecule Mcl-1 inhibitor EU5346 induced apoptosis in Mcl-$1^{(wt/wt)}$, but not Mcl-$1^{(\Delta/null)}$ MEFs. It not only enhanced HER2+ cell sensitivity to trastuzumab via downregulation of HER2 and HIF-1α but also inhibited proliferation and survival of BC cells resistant to HER2 inhibitors, luminal A and TNBC cells.

Conclusion: The present study shows for the first time that Mcl1 plays a critical role in the survival of BC cells, in HER2+ cells in particular, under hypoxic conditions; and strongly support the therapeutic potential of targeting Mcl1 under hypoxic conditions.

Disclosure of Interest: MA and MHC are employees of Eutropics, Inc. The remaining authors declare no conflict of interest.

P034

Quantitative gene expression by RT-PCR in classic and variant lobular carcinoma in ER+ breast cancer

J.M. Anderson*, C. Yoshizawa, V. Tan, H. Bailey, A. Tsiatis, M. Bonham, A.P. Sing, S. Shak, F. Baehner. *Pathology, Genomic Health Inc., Redwood City, United States of America*

Goals: Classic lobular carcinoma is characterized by a distinctive morphology, loss of E-cadherin commonly due to mutation or deletion of CDH1 on chromosome 16q, and a variable clinical course (Pestalozzi JCO 2008 26: 3006). Variants (pleomorphic, solid and alveolar) with distinct morphologies and potential differences in outcome have been described (Rosen 2009). We provide a 9-year update of the patterns of quantitative gene expression as measured by the 21 gene Oncotype DX® assay for ductal NOS (DC) and classic and variant lobular carcinomas.

Methods: All tumors analyzed in the Genomic Health laboratory from 6/04–5/13 were included. Central path used WHO criteria for classification of classic lobular (CL), solid and alveolar lobular (SAL), and pleomorphic lobular (PL) carcinomas. Quantitative expression of 16 cancer related genes was measured on a scale from 2 to 15 (relative to reference genes) where a 1 unit increment is associated with an ~2-fold change in expression. Descriptive statistics for RS and individual genes [ER, PR, invasion gene group (IGG) and proliferation gene group (PGG)] among the different subtypes were obtained. Comparisons of means among the subtypes were adjusted to control the overall error rate under any complete or partial null hypothesis.

Histologic subtype	N	RS Group			ER+/PR−
		Low (<18)	Intermediate (18–30)	High (>31)	
Classic lobular (CL)	26,491	62.3%	34.9%	2.9%	14.7%
Pleomorphic lobular (PL)	2,260	51.8%	40.4%	7.7%	19.2%
Solid/alveolar lobular (SAL)	1,380	58.3%	31.3%	10.4%	24.6%
Ductal NOS (DS)	292,162	55.3%	32.8%	11.9%	13.8%

Results: DC accounted for 90.7% of 292,162 cases, CL 8.2%, SAL 0.4% and PL 0.7%. For all types a continuous range of RS was observed. DC had the greatest percentage of high risk RS followed by SAL, PL and CL. DC had the highest mean RS and PL and CL had the lowest RS. SAL had the highest mean ER expression and CL and PL had the lowest ER expression. These results may reflect a submission bias and are not population based. The proportion with ER+/PR− phenotype was slightly different among the subtypes: SAL (24.6%) and PL (19.2%) had a higher incidence compared to DC (13.8%) and CL (14.7%). SAL had the highest PGG expression; CL had the lowest. DC had the highest IGG; CL had the lowest.

Conclusion: Classic lobular carcinoma and variants are characterized by differential patterns of gene expression. Outlier cases are not infrequent within each of the subtypes in this large observational cohort. The variation in gene expression, noted by histologic subtype, will be presented in detail.

Disclosure of Interest: All the authors are Genomic Health employees.

P035

Quantitative RT-PCR gene expression in the special histologic subtypes of invasive breast cancer

V. Tan*, F. Baehner, C. Yoshizawa, J. Anderson, H. Bailey, A. Tsiatis, A.P. Sing, S. Shak. *Pathology, Genomic Health Inc., Redwood City, United States of America*

Goals: ER+ special histologic breast cancer subtypes are prognostically significant. Here we report the special histologic subtypes of ER+ breast carcinoma and associated patterns of observed gene expression as measured by the 21 gene OncotypeDX assay.

Methods: All tumors from 6/1/04–5/31/13 were included in analyses. Central path used WHO criteria. Ductal NOS (DC), tubular (TC), cribriform (CC), mucinous (MC) and papillary (PC) carcinomas were included. Quantitative expression of 16 cancer related genes was measured on a scale from 2 to 15 (relative to reference genes) where a 1 unit increment is associated with ~2-fold change in expression. Recurrence Score (RS) was calculated as published. Descriptive stats for the RS and individual genes [ER, PR, invasion gene group (IGG) and proliferation gene group (PGG)] were obtained. Comparisons of means were adjusted to control the overall error rate under any complete or partial null hypothesis.

Results: DC accounted for 95.1%, TC 0.7%, CC 0.4%, MC 3.1% and PC 0.7% of 307,175 cases. For all histological subtypes a wide continuous range of RS was noted. DC had the highest mean RS, followed in decreasing order by MC, TC, CC and PC. PC had the highest ER; PC and CC had the highest PR; TC had the lowest ER. ER was not different between CC and MC but PR was. The proportion with ER+/PR− phenotype was different among the subtypes: TC (8.2%) and CC (6.8%) had the lowest incidence whereas MC (12.7%) and PC (9.5%) were more similar to DC (13.8%). TC had lowest PGG expression. MC and PC had lower IGG expression compared to other subtypes.

Histologic subtype	N	% of cases	Mean age	ER+/PR−
Ductal carcinoma, NOS	292,162	95.1	58	13.8%
Tubular carcinoma	2,227	0.7	54	8.2%
Cribiform carcinoma (IBC)	1,098	0.4	56	6.8%
Mucinous carcinoma (IBC	9,644	3.1	59	12.7%
Papillary carcinoma (IBC)	2,044	0.7	62	9.5%

Conclusion: The special subtypes had a wide continuous range of RS: DC had the highest mean RS, followed in decreasing order by MC, TC, CC and PC. PC had the highest ER; PC and CC had the highest PR; TC had the lowest ER (may reflect submission bias). ER was not different between CC and MC but PR was. The proportion with ER+/PR− phenotype was different among the subtypes: TC and CC

had the lowest incidence, MC and PC were more similar to DC. TC had the lowest PGG expression. MC and PC had lower IGG expression.
Disclosure of Interest: All the authors are Genomic Health employees.

P036
Effects of estriol on growth, gene expression and ERE activation in human breast cancer cell lines

C. Lattrich*, M. Diller, S. Schüler, S. Buchholz, O. Treeck, O. Ortmann. *Department of Gynecology and Obstetrics, University Medical Center Regensburg, Regensburg, Germany*

Goals: Local application of estradiol (E2) to treat vulvovaginal atrophy in postmenopausal breast cancer patients receiving aromatase inhibitors is known to elevate serum estradiol levels and thereby might counteract breast cancer therapy. Thus, vaginal application of estriol (E3) has been recommended for these patients. However, it is unclear to what extent E3 stimulates breast cancer cell growth. In this study, we examined the effect of E3 on growth and gene expression of two human breast cancer cell lines.
Methods: We used an established in vitro cell culture assay and compared the effect of E2 and E3 on growth of the estrogen receptor alpha-positive breast cancer cell lines MCF-7 and T-47D testing a wide range of hormone concentrations of 10^{-12}–10^{-7}M. E3 effects on gene expression were examined by means of reporter gene assays, RT-qPCR and Western blot analysis.
Results: E3 acted as a potent estrogen and exerted a mitogenic effect on T-47D and MCF-7 cells at concentrations of 10^{-9}M (288 pg/ml) and higher. With regard to activation of an estrogen response element (ERE) in breast cancer cells, effects of E3 were visible at 10^{-10}M. The same concentrations of E3 activated expression of the estrogen-responsive gene PR and of the proliferation genes cyclin A2, cyclin B1, Ki-67, c-myc and b-myb, providing molecular mechanisms underlying the observed growth increase.
Conclusion: Like E2, low levels of E3 were able to trigger a robust estrogenic response in breast cancer cells. Thus, our data suggest caution regarding use of E3 by breast cancer survivors.
Disclosure of Interest: No significant relationships.

P037
Ki67 assessment using a 5-grade scale revealed high reproducibility for luminal type breast cancer

K. Aogi[1]*, A. Hida[2], Y. Oshiro[2], H. Inoue[3], H. Kawaguchi[3], N. Yamashita[4], T. Moriya[5]. *[1]Department of Breast Oncology, NHO Shikoku Cancer Center, Matsuyama, Japan, [2]Department of Pathology, Matsuyama Red Cross Hospital, Matsuyama, Japan, [3]Department of Breast Surgery, Matsuyama Red Cross Hospital, Matsuyama, Japan, [4]Department of Clinical Research, NHO Shikoku Cancer Center, Matsuyama, Japan, [5]Pathology 2, Kawasaki Medical School, Kurashiki, Japan*

Goals: The distinction between luminal A and B type breast cancer depends on the proliferative marker, i.e. Ki67 expression, but the standard method has not yet determined. We aimed to establish an easy and practical method to measure Ki67 expression.
Methods: Resected tissues of 347 invasive ductal carcinomas were stained with ER, HER2 and Ki67. A hot spot with Ki67 positive cells was identified in a low-power field (×40). Three independent areas were selected to calculate the labeling index (LI) in a high-power field (×400). Alternatively, one pathologist assessed Ki67 expression by applying a 5-grade scale (eye-5) using some cut-points with ratios of positive/negative cells: 1/9 (10%), 1/6 (14.3%), 1/2 (33.3%) and 1/1 (50%). Finally, 10 pathologists used eye-5 to assess 100 samples with hot spots to evaluate the inter-observer variability.
Results: The average number of counted cancer cells was 1088 (median Ki67 LI: 22.5%). All 43 cases scored as 1 had LI lower than 20%, and all 111 cases with score 4–5 had LI higher than 20%. Plotting eye-5 scale on X-axis and LI on Y-axis showed a good correlation (R^2=0.84, $P < 0.0001$). Inter-observer variability of eye-5 among 10 pathologists was very low (weighted $\kappa = 0.83$) for assessment of 100 samples. Cases of score 1–2 showed significantly better relapse-free survival than those of score 3–5 ($P = 0.029$). The average number of counted cancer cells was 1088 (median Ki67 LI: 22.5%). All 43 cases scored as 1 had LI lower than 20%, and all 111 cases with score 4–5 had LI higher than 20%. Plotting eye-5 scale on X-axis and LI on Y-axis showed a good correlation (R^2=0.84, $P < 0.0001$). Inter-observer variability of eye-5 among 10 pathologists was very low (weighted $\kappa = 0.83$) for assessment of 100 samples. Cases of score 1–2 showed significantly better relapse-free survival than those of score 3–5 ($P = 0.029$).
Conclusion: Eye-5 is an easy and fast assessment method, which would be a candidate as a standard method to evaluate Ki67 expression.
Disclosure of Interest: No significant relationships.

P038
Copy number alteration and genomic instability in breast cancer

F. Taira*. *Divisionofmoloecularpathology, The Institute of Medical Science, The University of Tokyo, Tokyo, Japan*

Goals: Identify CNAs showing somatic alterations in breast cancer DNA in comparison with non-cancerous DNA from the same patients by CNV Microarray, which is designed to detect highly polymorphic CNVs preferentially. Clarify the clinical significance of each CNA in breast cancer.
Methods: Somatic alterations at the sites of CNV were examined as somatic copy number alterations (CNAs) in 20 cases with invasive carcinoma of the breast using array CGH specifically designed to detect changes at these sites. Tumor DNA was extracted from surgically resected fresh-frozen tissue samples, while control DNA was extracted from peripheral blood lymphocytes of the same patient.
Results: Somatic CN changes were detected in 39.9% of probes. A high CNA rate correlated significantly with high nuclear grade. Alterations of fragments exceeding 10Mb caused by chromosomal instability correlated significantly with nuclear grade and high Ki-67 status. CNAs correlated significantly with clinicopathological features, and many of the genes located in these CNA regions are known to have cancer-related functions.
Conclusion: A number of CNAs showing significant correlations with clinicopathological features were detected, including several genes with functions known to be related to cancer. A high CNA rate correlates significantly with high nuclear grade, and longer CNA regions show significant correlations with greater numbers of clinicopathological factors. Analysis of CNAs in cancer might be a novel tool for identifying oncogenes, tumor suppressor genes and other cancer-related genes involved in the development or progression of malignancies.
Disclosure of Interest: No significant relationships.

P039

Triple negative breast cancer (TNBC): clinical utility of immunohistochemical classification

M. Perez-Lopez[1]*, M. Arias[2], M. Penin[2], J. Garcia-Mata[1], T. Garcia-Caballero[3]. *[1]Medical Oncology, C.H. Ourense, Ourense, Spain, [2]Pathology, C.H. Ourense, Ourense, Spain, [3]Pathology, C.H. and University of Santiago de Compostela, Santiago de Compostela, Spain*

Goals: To determine differences in TNBC between expression of cytokeratins 5 and 6 (CK 5/6) and their prognosis.
Methods: Data from 888 consecutive female patients with invasive breast cancer but without metastatic disease, who had undergone surgery and were registered between 1 January 1997 and 31 December 2004 in the Tumour Registry of the University Hospital of Ourense (CHUO), Galicia, Spain, were collated and analysed. 100 of them were triple negative breast cancer. IHC was then performed on archived biopsies from the patients, who were thus classified by breast cancer subtype. First, a descriptive analysis of the study population was performed. Qualitative variables were analysed as absolute percentages and relative frequencies, and quantitative variables in terms of central tendency values, i.e. mean.
Statistical analyses were then performed, using statistical tests appropriate to each type of variable, i.e. Chi-square test or Fisher's exact test. Global survival and disease-free survival, using Cox regressions and Kaplan–Meier estimates, were calculated for classical prognostic variables (included age, tumour size and grade, node involvement). We present the results of triple negative breast cancer cases, which were divided in "basal like" and "no basal like" by CK 5/6 expression. SPSS version 17.0 (SPSS Inc., Chicago, IL) was used for all statistical analyses. Results were considered significant when $p < 0.05$.
Results: One hundred triple negative (11.26%) cases among a total of 888 breast cancers were identified: 48 basal like (48%), 45 (45%) no basal like and 7 of them unclassified, because it was not possible to find histological samples. The basal like subtype showed CK 5/6 expression and no basal like absence of this expression. The relapse happened in 28% of TNBC. 42% of the relapses were visceral metastasis, 10% in nervous central system (CNS) and 7% in bones. There was more recurrences in CNS in basal-like than no basal like subtype (11 versus 7%) There was much more mortality-related breast cancer in basal like than in patients with the no basal like subtype (23% versus 18%) and much higher non-cancer-related mortality in patients with no basal like subtype. Patients without node involvement (N0) and basal like subtype had more relapses than no basal like subtype (22 versus 12.5%). None of the no basal like subtype patients died. Nevertheless, 22% of patients of basal like subtype died.
Conclusion: TNBC is a bad prognostic factor in multivariate analyses, independent of size, nodal involvement and grading. By immunohistochemical expression of CK 5/6 we classified TNBC in basal like and no basal like subtypes, founded prognostic differences. Even though patients with no basal like tumors relapse, it seems that they have a lesser aggressive behavior. In contrast, basal like subtype tumors have a threatening prognosis with a short time between relapse and death. This evidence must make us think about the consideration of more intense adjuvant therapy in basal like TNBC to decrease relapse and death.
Disclosure of Interest: No significant relationships.

P040

Role of cooling in the uptake in human keratinocytes of drugs causing chemotherapy-induced alopecia

O. Hussain*, W. Al-Tameemi, C. Dunnill, A. Collett, N. Georgopoulos. *School of Applied Sciences, University of Huddersfield, Huddersfield, United Kingdom*

Goals: Chemotherapy induced alopecia (CIA) is the most common and distressing side effect of cancer chemotherapy. Head cooling using advanced medical devices such as the Paxman scalp cooling system offer the only promising solution against CIA. We have previously shown by in vitro studies using human keratinocyte cell models that cooling protects cells against chemotherapy drug-induced cytotoxicity. One explanation for this cytoprotective role could be that cooling may affect the amount of chemotherapy drug present in these cells via regulating (reducing) drug uptake. To determine the effect of temperature on the uptake of chemotherapy drugs on human keratinocytes in vitro.
Methods: HaCaT and adapted HaCaT cells cultured in serum free conditions (HaCaTa) were exposed to three commonly used chemotherapy drugs, doxorubicin, docetaxel or the active metabolite of cyclophosphamide, 4-hydroperoxy-cyclophosphamide (4-OH-CP). Drug uptake was determined at physiological temperature (37°C) and cooling conditions (18°C) following 1 hour of drug exposure using high-performance liquid chromatography (HPLC).
Results: We show that cooling can modulate the concentration of chemotherapy drug present in the target cells. We will present data demonstrating that uptake of both doxorubicin and docetaxel was significantly affected by temperature conditions. Interestingly, we found that the concentration of these two drugs inside cells was greater at 18°C compared with 37°C. By contrast, temperature did not affect the uptake of 4-OH-CP.
Conclusion: We have shown that cooling affects the concentration of chemotherapy drugs in human keratinocytes in an unexpected manner, as higher levels of chemotherapy drug are present under cooling conditions in comparison to physiological temperature. Our results imply that cooling may modulate drug efflux rather than drug uptake and have raised questions not only with regards to the mechanisms of cooling-mediated cytoprotection but also as to how overall the process of chemotherapy drug uptake is regulated.
Disclosure of Interest: No significant relationships.

P041

Serum and tissue expression of tumor suppressors miR-195 and let-7A in breast cancer

R.A.C. Vieira[1]*, A.F. Evangelista[1], T. Macedo[1], C. Scapulatempo Neto[1], R.M. Reis[1], A. Carvalho[1], I.D.C. Guerreiro[2], M.M.C. Marques[1]. *[1]Molecular Oncology Research Center, Barretos Cancer Hospital, Barretos, Brazil, [2]Federal University of São Paulo, Sao Paulo, Brazil*

Goals: Evaluate the expression of tumor suppressors microRNAs miR-195 and let-7a in breast cancer.
Methods: A total of 200 individuals were grouped as 32% controls, 28% with no neoplastic alteration after biopsy and 32% as malignant breast cancer from different clinical staging. Serum samples were collected for all patients but tissue samples were only available for benign group and malignant neoplasia. Further, miR-195 and let-7a expression levels were measured by real-time PCR and biomarkers were analyzed alone and in combination, including the estimation of sensitivity and specificity in ROC curves.
Results: It was observed downregulation of both microRNAs in malignant compared to benign groups in serum and tissue. The expression combined in serum of malignant compared to the control groups has showed improved results. The combination of biomarkers in benign group compared with malignant one has showed good sensitivity and specificity in tissue and serum with AUC of 0.77 and 0.72, respectively. In serum, biomarkers combination in control group compared with malignant one has showed improved sensitivity and specificity compared with the comparison with benign group.
Conclusion: These findings support the evidence that combination of both tumor suppressors miRNAs can be used as candidates of non-invasive biomarkers for detection of breast cancer progression.
Disclosure of Interest: No significant relationships.

P042

Antibody titres to heat shock protein 27 are elevated in patients with breast cancer

F. Homaeishandiz[1] *, M. Ghayour Mobarhan[2], H. Hassan Rooki[2], M. Tasbandi[1], M.M. Kianisharif[1]. *[1]Radiation Oncology, Mashhad University of Medical Sciences, Mashhad, Iran, [2]Nutrition, Mashhad University of Medical Sciences, Mashhad, Iran*

Goals: The aim of this study was to compare anti-HSP27 antibody levels in patients with breast cancer and cancer-free controls to assess whether serum anti-Hsp27 antibody levels are associated with two-year disease-free survival.
Methods: The study was performed by analyzing sera from 97 patients with breast cancer (74.4% with early stage tumor), and 65 healthy subjects. Anti-HSP27 antibody was measured using an in-house enzyme-linked immunosorbent assay. Moreover spectroscopic methods were used to measure an oxidant-antioxidant balance.
Results: The results showed that anti-HSP27 antibody levels were significantly ($p < 0.001$) higher in patients with breast cancer than in the normal group, but no relationship was found with the two-year disease free survival, histological grade and number of lymph nodes ($p > 0.6$, 0.16 and 0.91 respectively). However, evaluation of the oxidant-antioxidant balance showed a significant increased level of oxidants in patients ($p < 0.001$) and accordingly the increased risk of relapse ($p < 0.001$).
Conclusion: Anti-HSP27 antibody levels are enhanced in patients with breast cancer and do not appears to be linked with two-year disease free survival in node-negative or positive patients.
Disclosure of Interest: No significant relationships.

P043

Bevacizumab/paclitaxel as first line therapy for metastatic breast cancer: new schedule in real life

K. Cannita *, S. Paradisi, V. Cocciolone, L. Rinaldi, P. Lanfiuti-Baldi, A. Irelli, A. Cortellini, G. Bruera, E. Ricevuto, C. Ficorella. *Medical Oncology, S. Salvatore Hospital, University of L'Aquila, L'Aquila, Italy*

Goals: Angiogenesis plays an essential role in the growth and progression of breast cancer (BC). Taxanes inhibit the proliferation of endothelial progenitor cells, obtaining an antiangiogenic effect at lower doses than those needed to inhibit cancer cells. Bevacizumab enhances the anti-angiogenic effect of chemotherapy, providing the rationale for combination therapies. We conducted an observational study to evaluate activity, efficacy and tolerability of bevacizumab/paclitaxel combination as first line treatment of unselected, HER2-negative, metastatic BC (MBC) patients (pts) in "clinical practice", in a new weekly schedule in real life.
Methods: Thirty-five pts with HER2-negative MBC were enrolled, median age 56 years (range 40–81). Pts received paclitaxel (70 mg/m^2) on days 1, 8, 15 q21 (60 mg/m^2 if age ≥65 years or secondary Cumulative Illness Rating Scale) plus Bevacizumab (10 mg/kg) every 2 weeks. Twenty-two pts had ≥2 metastatic sites; 43% visceral disease. Eleven pts (31%) had triple-negative BC (TNBC).
Results: Objective Responses: clinical complete response (cCR), 6 (17%), after a median of 7 cycles; partial response (PR), 22 (63%); stable disease (SD), 6 (17%); progressive disease (PD), 1 (3%), after 4 cycles; clinical response rate 97%. TNBC pts reported: cCR, 1 (9%); PR, 8 (73%); SD, 2 (18%); any patient had PD. At a median follow-up of 13 months (range 1–79), median PFS was 10 months, median OS was not reached (24+ months). Treatment was delivered for a median of 6 cycles, with a median paclitaxel received dose-intensity (rDI) of 66.95 mg/m^2/week. Eighteen pts continued maintenance therapy with bevacizumab, associated to endocrine therapy in case of hormone receptor positive disease. No Grade 4 adverse events. Grade 3 toxicities were: neutropenia 4/35 (11.4%), hypertension 2/35 (5.7%), fatigue 1/35 (2.8%), stomatitis 1/35 (2.8%), diarrhea 1/35 (2.8%); vomiting 1/35 (2.8%), alopecia 100% of pts. The most common G2 adverse events were: hypertension 14/35 (40%); neuropathy 4/35 (11.4%) and fatigue 2/35 (5.7%).
Conclusion: Paclitaxel (70 mg/m^2) on days 1, 8, 15 q21 plus Bevacizumab (10 mg/kg) every 2 weeks produced higher activity results and similar efficacy data than previously reported schedules, with a comparable rDI and a good toxicity profile.
Disclosure of Interest: No significant relationships.

P044

Interlaboratory variability of Ki67-labelling index in breast cancer tissue microarrays

C.M. Focke[1] *, H. Bürger[2], E. Korsching[3], D. Gläser[1], K. Finsterbusch[1], M.O.T. German Breast Screening Pathology Initiative[4], T. Decker[1]. *[1]Institut für Pathologie, Dietrich Bonhoeffer Klinikum, Neubrandenburg, Germany, [2]Institut für Pathologie, Paderborn-Höxter, Germany, [3]Institut für Bioinformatik, Universität Münster, Münster, Germany, [4]Referenzzentrum Mammographie Münster und Berlin, Berlin-Münster, Germany*

Goals: Assessment of tumour proliferation using the Ki67-labelling index (Ki67-LI) is increasingly recommended for prognostication and (neo)adjuvant chemotherapy decisions in breast cancer. Our aim was to investigate interlaboratory variability of Ki67-LI results using TMA and centralized assessment to exclude preanalytic influences and postanalytic variance.
Methods: 25 pathology laboratories (19 German, 3 Austrian, 1 Dutch, 1 Hungarian and 1 Swiss) performed Ki67 staining of a TMA slide according to their routine in house protocol (including internal and external quality assurance). 38 samples per lab were centrally analysed. The Ki67-LI was calculated after counting first all tumour cells and subsequently all Ki67 positive tumour cells of each sample regardless of staining intensity. For each tissue sample we evaluated the range of Ki67-LIs between different labs.
Results: The range of Ki67-LIs between the labs was: <5% in 1 (3%), 5–10% in 5 (13%), 10–15% in 2 (5%), 16–20% in 5 (13%), 20–25% in 4 (10%), 25–30% in 6 (16%), 30–35% in 1 (3%), 35–40% in 3 (8%), 40–45% in 2 (5%), 45–50 in 1 (3%) and >50% in 8 samples (21%), respectively. Thus, in 55% of results of the 25 labs (21 of the 38 TMA specimens) the Ki67-LI differed by more than 25%. The analysis of variance (ANOVA) came out with $F = 4.24$ which is much larger than the critical F value of 1.97 for these study results ($p = 7.74902 \times 10^{-5}$). This means that the observed interlaboratory variance of 4.24 is systematic and not due to sampling error. The respective standard deviation is 33.4%.
Conclusion: Even in a setting strictly standardised in terms of preanalytic influences by using TMA and postanalytic variance by centralised quantification, Ki67-LI seems to be heavily influenced by laboratory-specific analytic variables. Taking this into consideration, there may be a risk of prognostic or predictive misclassification in some breast cancer patients in daily practice.
Disclosure of Interest: No significant relationships.

P045

Risk of discordant Ki-67 level between biopsy and surgical specimens in breast cancers

H.S. Kim[1] *, S. Park[1], J.S. Koo[2], J. Ryu[1], S. Kim[1], J.Y. Kim[1], H.S. Park[1], S.I. Kim[1]. *[1]Department of Surgery, Yonsei University College of Medicine, Seoul, Korea, [2]Department of Pathology, Yonsei University College of Medicine, Seoul, Korea*

Goals: The Ki-67 labelling index is significant for the management of breast cancer. However, the concordance of Ki-67 expression between preoperative biopsy and postoperative surgical specimens has not been well evaluated. This study aimed to find the correlation

of Ki-67 expression between biopsy and surgical specimens and to determine the clinicopathological risk factor of discordantly distributed value.

Methods: Ki-67 levels were immunohistochemically measured using paired biopsy and surgical specimens in 310 breast cancer patients from January 2008 to December 2013. Staining of Ki-67 was scored by counting the number of positively stained nuclei and was expressed as a percentage of total tumor cells. ΔKi-67 was calculated by postoperative Ki-67 minus preoperative level. The outlier of ΔKi-67 was defined as less than Q1 − {1.5 × [interquartile range (IQR)]} or more than Q3 + (1.5 × IQR). Patients receiving neoadjuvant chemotherapy were excluded. Correlation and logistic regression models were used for the analysis.

Results: Median of preoperative and postoperative Ki-67 level was 10 (IQR, 15) and 10 (IQR, 25), respectively. Correlation of Ki-67 expression between biopsy and surgical specimens indicated a moderately positive linear relationship (correlation coefficient = 0.676, $p < 0.001$). Of 310 patients, 44 (14.2%) were the outlier of ΔKi-67 that was determined as ≤−20 or ≥28. These patients were significantly associated with age ≤35 years, tumor size >1 cm, grade III tumor, ER or PR-negative expression. Multivariate analysis determined that significant risk factors for the outlier of ΔKi-67 were age ≤35, size >1 cm, grade III and PR-negative expression. Among 171 patients with hormone receptor-positive and HER2-negative tumors, the breast cancer subtype according to preoperative or postoperative Ki-67 levels had discordantly changed in 46 (26.9%) patients and a significant proportion of patients with discordant subtype had ≥1 risk factor.

Conclusion: Ki-67 expression obtained a substantial concordance between biopsy and surgical specimens. Discordantly different Ki-67 levels were associated with younger age, larger size, high grade and PR-negative expression. In patients with luminal HER2-negative tumor, determination of Ki-67 value should be cautious considering type of specimens or clinicopathological risk factors.

Disclosure of Interest: No significant relationships.

P046

Subtype specific DNA methylation in circulating DNA of metastatic breast cancer patients

N. Uehiro[1] *, F. Sato[1], S. Saji[2], M. Toi[1]. [1]*Department of Breast Surgery, Kyoto University Guraduate School of Medicine, Kyoto City, Japan,* [2]*Department of Medical Oncology, Fukushima Medical University, Fukushima City, Japan*

Goals: Elevation of circulating DNA (cDNA) concentration in the blood of cancer patient has been reported. Some reports showed cDNA reflect copy number alterations or mutations of primary cancer and cDNA became an active area of research as biomarker of cancer detection and treatment. DNA methylation is one of epigenetic regulation of gene expression. DNA methylation seems to be a promising marker for cancer detection, because it is stable chemical modification of DNA. Breast cancer has five subtypes according to clinicopathologic features. One of clinical challenge for triple negative breast cancer (TNBC) is early detection because of its rapid growth and worse prognosis. Whereas, luminal breast cancer (LBC) grows slowly and late recurrence is critical issue. Since DNA methylation pattern is different among these subtypes, we tried to find subtype specific methylation markers which can work in cDNA of breast cancer patients. Purpose of this study is to identify subtype specific methylation pattern in cDNA of breast cancer patients, leading to early detection of TNBC and risk estimation of late recurrence of LBC.

Methods: DNA was extracted from breast cancer cell lines, micro-dissected cancer cells and normal/benign mammary epitheliums from FFPE tissues and blood of healthy volunteers (HVs). Methylation analysis was done using Illumina Infinium Human Methylation 450 Beads chip. We selected four specific methylation markers for each of LBC and TNBC, and four common markers for breast cancer. We also designed four internal control primer sets to estimate cDNA amount. CDNA was extracted from 1 ml of plasma from 30 metastatic breast cancer (MBC) patients and 26 HVs. Methylation status of each marker in cDNA was estimated using droplet digital PCR. Amount of cDNA was calculated by mean of 4 internal control amount. Cut off of each marker was set by ROC curve analysis and sum of detected copy amount was used as Methylation Marker Index (MMI).

Results: CDNA amount of MBC patients was significantly higher than HVs. Sensitivity of MMI was 0.77 and specificity was 0.85. Area under the ROC curve was 0.82. The dominant subtype of positive subtype specific markers was correspond to subtype of primary cancer in three LBC patients and one TNBC patient. Other patients had mixed pattern of subtype specific markers.

Conclusion: Subtype specific methylation pattern was detected in cDNA of some MBC patients. These markers have potential to be applied to subtype specific detection or management of breast cancer. Since mixed pattern of methylation markers may reflect heterogeneity or phenotypic change of metastatic sites, further investigation is needed.

Disclosure of Interest: No significant relationships.

P047

Characterizing prostaglandin E receptor on epithelial–mesenchymal transition and metastasis in TNBC

M. Siu, J. Ho, I. Chuek, J. Chen, A. Kwong*, V. Shin. *Surgery, The University of Hong Kong, Hong Kong, Hong Kong*

Goals: Metastatic breast cancer is characterised by uncontrolled cell proliferation, epithelial–mesenchymal transition (EMT), and escape from apoptosis. Prostaglandin E receptors have been reported to play a role in breast cancer carcinogenesis, however, its contribution to EMT reversal is largely unknown. Specifically, prostaglandin E2 (PGE2)-induced prostaglandin E (EP) receptors have been reported to be associated with human cancer carcinogenesis. This study aims to evaluate the role of EP2 receptor in metastatic xenograft model and delineate the mechanistic pathway involving EMT in TNBC.

Methods: We used a metastatic xenograft model of human breast cancer to study the role of EP receptor during cancer progression. In addition, construction of stable EP2-expression MB-231 cells was used to study tumorigenesis and characterization of EP2 receptor. The functional role of EP2 receptor on cell proliferation, migration, invasion and EMT gene expression were examined in EP2-overexpressing and EP2 siRNA transfected cells. The xenografts were immunostained to examine the expression of Ki67 and CD31 in xenografts and the localization of EMT markers was assessed by immunofluorescence.

Results: Expression of EP2 receptor was induced during tumor progression and was found to be highly expressed in primary breast tumor tissues. The MB-231-EP2 clone developed a more aggressive tumor with larger tumor size, promoted metastasis, and resulted in a poorer survival. Cell proliferation (Ki-67) and angiogenesis (CD31) were more prominent in the metastatic than local xenografts. In addition, loss of E-cadherin and increase Twist expression were seen in the metastatic xenograft. In vitro study showed that MB-231-EP2 clone was more resistance to staurosporine-induced apoptosis than parental MB-231 cells. EP2 receptor promoted cell migration, and invasion were increased through modulation of EMT markers (E-cadherin, TWIST, ZEB1, MMP2). Immunofluorescence study demonstrated that E-cadherin was restored and Twist translocation was blocked in EP2 siRNA transfected cells, implicating silencing of EP2 receptor could reduce metastatic potential of the cells. Moreover, Twist expression level was higher in plasma of breast cancer patients than healthy controls.

Conclusion: These novel findings suggest that EP2 receptor plays an important role in metastatic breast cancer though EMT. Targeting EP2 receptor could be a potential therapeutic strategy to improve survival in breast cancer patients.
Disclosure of Interest: No significant relationships.

P048
Absorption of glucose by MCF-7 cells under the influence of herceptin

T. Nikolaienko*, L. Garmanchuk, V. Nikulina, I. Saraieva, N. Petruk, Y. Stupak, O. Dzhus. *Biochemistry, Educational and Scientific Centre "Institute of Biology" of Taras Shevchenko National University of Kyiv, Kyiv, Ukraine*

Goals: Cellular transformation is associated with the reprogramming of cellular pathways that control proliferation, survival, and metabolism. Although many of the metabolic alterations are largely similar to those in normal proliferating cells, they are aberrantly driven in cancer by a combination of genetic lesions and nongenetic factors such as the tumor microenvironment. Among the metabolic changes exhibited by tumor cells is an increase in glucose metabolism and glucose dependence. The purpose of the research was to study absorption of glucose by MCF-7 cells under the influence of Herceptin.
Methods: Herceptin is humanized antibody to EGFR II type and used in target therapy of breast cancer. MCF-7 cells were incubated in DMEM medium, 2mM L-glutamine and 40 mg/ml gentamicin. Cell lines were cultured at the standard conditions at 37°C in humidified atmosphere with 5% CO_2. Two variants culture media were used: complete (with 10% FBS), and incomplete (without serum). Glucose absorption was tested by typical glucosooxidase method.
Results: Absorption of glucose by MCF-7 cells differ significantly in complete culture medium and serum free medium. It has been shown that Herceptin increased level of glucose by $38\pm1.3\%$ ($p < 0.05$) in serum free medium conditions compared to the respective control during 48 hours of incubation. But with continued incubation time to 72 hours is observed the converse effect in the reduction this indicator by $36\pm1.8\%$ ($p < 0.05$). Level of glucose under the influence of Herceptin in complete culture conditions were not significantly change. While Herceptin caused reduction of MCF-7 cell proliferation by $16\pm0.5\%$ ($p < 0.05$) compared with control.
Conclusion: The result demonstrate controversial effect of Herceptin in relation to glucose, but inhibition of glucose uptake by MCF-7 tumor cells may serve perspective target in the treatment of breast cancer.
Disclosure of Interest: No significant relationships.

P049
Genomic landscape of the PI3K pathway and cell-cycle pathway in ER+ BC: a treatment strategy

P.K. De*, C. Williams, A. Krie, B. Solomon, Y. Sun, K. Williams, J. Klein, J.H. Carlson, N. Dey, B. Leyland-Jones. *Molecular and Experimental Medicine, Avera Cancer Institute, Sioux Falls, United States of America*

Goals: Since alterations of genes belonging to the CDK4–cyclin D1 cell-cycle pathway are common in BC including ER+ cancers, targeting this pathway using CDK4/6i (palbociclib, LEE011 and LY2835219) and anti-hormonal drugs are clinically effective (NCT00721409, NCT01958021). In a phase II trial, frontline therapy with palbociclib and letrozole caused a significant improvement in PFS. Activation of the PI3K pathway occurs frequently in BC and PIK3CA mutations are observed in over 40% in ER+BC. Based on our examination of genomic alterations in ER+BC patients at Avera Cancer Institute, SD, we tested anti-tumor effect of combination of inhibitors of PI3K and CDK4–cyclin D1 pathways in the context of concurrent alterations of pathway specific genes.
Methods: Retrospectively data from 75 consecutive BC patients (February through November, 2014) were analyzed. Patients were re-biopsied after consultation and samples were characterized (ER, PR, and HER2 by IHC; FFPE samples for genomic [Foundation Medicine] and proteomic analyses [Theranostics]).
Results: Total 76 genes were altered in 48 ER+BC patients, out of which PI3K pathway-genes (PIK3CA, PIK3R1, AKT, PTEN, MDM2, MDM4, TSC1, mTOR, RICTOR) were altered in 79% of patients. Analyzing the composite alterations in individual ER+BC patient, we observed that 25% of patients had alterations in more than one nodes of the PI3K pathway while MYC amplification was observed in 27% of patients. Genes of the cell-cycle pathway (CCND1, CDK4, CDKN1B, CDKN2A/B, RB) were altered in 34% of ER+BC patients. Interestingly, all of the ER+BC patients (41%) of who showed concurrent alterations of the above two pathways had wt RB. Hence we tested the anti-tumor efficacy of the combination of BKM120 and LEE011 using cell line (PIK3CA mutated T47D, PTEN-null MDA-MB415 cells) based model. Data show a synergistic effect of PI3Ki and CDK4/6i as determined from the changes in proliferative and apoptotic signals as well as cell cycle arrests.
Conclusion: Since a persistent expression of the CDK4–cyclin D1 pathway activation enables tumor cells survival even in the presence of PI3K inhibitor (Cancer Cell 2014), results of our study demonstrated the anti-tumor effect of PI3Ki and CDK4/6i indicating that such a combinatorial strategy may be beneficial in RBwt ER+BC patients with a concurrent genetic alterations of these pathways.
Disclosure of Interest: No significant relationships.

P050
Contribution of estrone sulfate to cell proliferation in aromatase-inhibitor resistant breast cancer

T. Higuchi[1]*, M. Endo[2], T. Hanamura[3], T. Gohno[2], T. Niwa[2], Y. Yamaguchi[4], J. Horiguchi[1], I. Takeyoshi[1], S. Hayashi[2]. *[1]Department of Visceral and Thoracic Organ Surgery, Graduate School of Medicine, Gunma University, Maebashi, Japan, [2]Department of Molecular and Functional Dynamics, Graduate School of Medicine, Tohoku University, Senddai, Japan, [3]Department of Surgery, School of Medicine, Shinshu University, Matsumoto, Japan, [4]Research Institute for Clinical Oncology, Saitama Cancer Center, Saitama, Japan*

Goals: Aromatase Inhibitors (AIs) are first-choice drugs for estrogen-receptor (ER) positive postmenopausal breast cancer patients, and their efficacies are validated by some big trials, but some patients do not respond to AIs and experience recurrence. Several AI-resistant mechanisms has been reported by our laboratory and other researchers, but the whole mechanism remains to be solved. In this study, we now present another AI-resistant mechanism.
Methods: We introduced plasmids carrying aromatase gene to MCF-7 cells whose ER activity could be visually monitored by expression of green fluorescent protein (GFP). These candidate-cell lines were cultured in estrogen-depleted medium including testosterone and letrozole for three months, visually monitoring ER activity using GFP system. We finally established ER-positive Letrozole-Resistant cell lines (LR cell lines), and analyzed the AI-resistant mechanism of LR cell lines.
Results: In LR cell lines, mRNA expression of steroid sulfatase (STS) and four organic anion transporter peptides (OATPs) which were involved in metabolism of estrone sulfate (E1S) were induced, but there was no change in mRNA expressions of efflux drug transporters, aromatase-catabolic enzyme, enzymes related with production for estrogenic androgen, androgen receptor and its target genes. It was suggested that E1S–STS pathway probably was associated with AI-resistance of LR cell lines rather than AR activity, estrogenic-androgen, efflux transporter and catabolic enzyme related with AI.

Furthermore, LR cell lines proliferated by E1S in dose-dependent manner more than their parental cells, but there was no difference of proliferation when estrone and estradiol treated. STS inhibitor administered with letrozole was inhibitory to proliferation of LR cells. LR cells were also inhibited by SERM and SERD. In mRNA analysis of clinical primary tissues of postmenopausal patients, expression of STS mRNA significantly correlated with those of three OATPs which were induced in LR cell lines.

Conclusion: In this study, we first demonstrated that the contribution of E1S to ER-positive breast cancer in the context of AI resistance. Targeting therapy to E1S–STS pathway could present a new choice of treatments to AI-resistant breast cancer patients, especially by combination with AI.

Disclosure of Interest: No significant relationships.

P051

Photoacoustic imaging of breast cancer and histological markers of angiogenesis

E. Fakhrejahani[1]*, M. Torii[1], I. Yamaga[1], Y. Asao[1], T. Kitai[2], M. Kataoka[3], S. Kanao[3], M. Takada[1], T. Shiina[4], M. Toi[1]. *[1]Department of Breast Surgery, Kyoto University, Kyoto, Japan, [2]Department of Surgery, Kishiwada City Hospital, Osaka, Japan, [3]Department of Diagnostic Radiology, Kyoto University, Kyoto, Japan, [4]Department of Human Heath Scinece, Kyoto University, Kyoto, Japan*

Goals: Photoacoustic mammography (PAM) non-invasively can visualize breast cancer vasculature and provide information about the hemoglobin oxygenation level (SO_2) in breast lesions. We presented clinical study of the first prototype PAM-01 (CK project) during San Antonio Breast Cancer Symposium 2014 and reported that in almost 3 out of four cases, lesion associated signals were detectable. The correlation between microvessel perimeter as well as carbonic anhydrase IX (CAIX) expression with SO_2 was also reported. In order to better understand the tumor microvessel characteristics which might have an impact on PAM signals, we analyzed microvessel maturity of central area of all lesions.

Methods: Histological sections from the widest area of the lesions were evaluated post-excisional by immunohistochemistry using anti-smooth muscle actin (SMA) as pericyte marker. Histological slides were scanned (Hamamatsu Inc. Japan). A 3.36×3.36 mm area from the central part of each tumor (excluding possible necrosis) was extracted and divided into 100 smaller squares using a 10×10 grid. Squares with minimum one vessel positive for SMA were counted and the total count/100 squares was considered as central tumor vessel maturity index (TVMI).

Results: The median of TVMI in total cases was 61.5% (15–91%). There was no difference between TVMI of visible and non-visible cases (63% vs. 60%). TVMI showed no correlation to size, grade and Ki67 index of the tumors. Invasive cancer positive for CAIX showed higher total vascular perimeter in comparison with CAIX negative cancers (8.51 vs. 4.44, p-value 0.027, Mann–Whitney U test) while TVMI was the same (62.5% vs. 61.5%). History of neoadjuvant treatment did not show any effect on TVMI (60% for cases without vs. 61% for cases with treatment). SO_2 did not show difference between cases with low vs. high TVMI (72.7% vs. 68.3%, p = 0.8, Mann–Whitney U test).

Conclusion: Although vessel maturity did not show any correlation to visibility or measured SO_2, the second generation PAM (PAM-02) which is now under a clinical evaluation study and has higher resolution and a built-in ultrasound will be able to provide more accurate information on breast cancer functional imaging. At the same time, further study on tumor vasculature shape is necessary to better understand the correlation between histology and oxygenation data of breast cancers.

Disclosure of Interest: Yasufumi Asao is an employee of Canon Inc.

P052

Identification and targeting of Wnt-driven breast cancers

V. Arndt*, E. Meuser, J. Waak, K. Ross, F. Agerer, A. Friebe, J. Vollmer. *Late Discovery, Nexigen GmbH, Cologne, Germany*

Goals: Targeted inhibition of oncogenic Wnt signaling holds great promise for the treatment of various cancers. For instance, dysregulation of the Wnt pathway has been associated with several aggressive breast cancer subtypes. In breast cancer, pathway activation has been shown to play a critical role in tumor growth, metastasis and chemoresistance, indicating that Wnt inhibitors could have therapeutic benefit for breast cancer patients. Targeting of the Wnt pathway, however, has been difficult in practice due to the lack of druggable targets and a defined susceptible patient population. Using our proprietary next generation peptide screening platform, we have previously identified a cell-permeable Wnt peptide inhibitor that effectively inhibits tumor growth and metastasis in different in vitro and in vivo models of triple-negative breast cancer. In the present study, we aimed to better define breast cancer tumors that can be targeted by our peptide inhibitor.

Methods: For this purpose, we analyzed the expression of Wnt pathway components by Western Blot in a representative panel of breast cancer cell lines. Autocrine and paracrine Wnt pathway activation was assessed through β-catenin stabilization and target gene expression. Different Wnt inhibitors were used to study the effect of Wnt pathway blockage on tumor growth and metastasis in several cell-based assays.

Results: In contrast to colorectal cancer, oncogenic activation of the Wnt pathway in breast cancer is rather based on alterations in expression level and/or autocrine/paracrine stimulation of the pathway than genetic mutations. Analysis of the expression levels indeed showed significant differences in the expression of Wnt pathway components between the different breast cancer cell lines. In accordance with this finding, assessment of autocrine and paracrine pathway activation revealed a set of Wnt-responsive cell lines. Treatment with different Wnt pathway inhibitors or knock-down of β-catenin in these cell lines resulted in decreased cell proliferation, migration and tumorsphere formation, indicating that some breast cancers could benefit from therapeutic inhibition of Wnt signaling.

Conclusion: In summary, our Wnt pathway peptide inhibitor could be a promising new drug candidate to be interrogated for the treatment of breast cancer stem cells and a defined subset of breast cancer tumors.

Disclosure of Interest: All contributors are employees of Nexigen GmbH. A. Friebe and J. Vollmer additionally are shareholders of Nexigen GmbH.

P053

Serum HER2 extracellular domain before surgery compared with HER2 in breast cancer

J. Zidan[1]*, R. Mzalbat[2], A. Sharabi[2]. *[1]Oncology, Oncology Institute. Ziv Medical Center, Safed, Israel, [2]Ziv Medical Center, Safed, Israel*

Goals: Human epidermal growth factor receptor 2 (HER2) is an important prognostic and predictive factor in breast cancer (BC). The importance HER2 extracellular domain (ECD) in serum is not yet determined. The aim of this study was to explore the correlation between serum ECD and tissue HER2 expression, clinical and pathological features in primary BC.

Methods: In this prospective study only patients with stage I–III BC were included. Serum ECD levels were measured by ADVIA Centaur automated assays before surgical resection of the tumor. Serum ECD >15 ng/ml was considered to be positive.

Results: Eighty patients with breast tumors were included. Stage I–III BC was diagnosed in 64 patients, Ductal carcinoma in situ in 9 and

benign tumors in 7 patients. HER2 overexpression was observed in 8 of 64 patients (16.4%). Mean value of serum ECD was 10.9 ng/ml (range: 6.7 to 21.5). Four (6.2%) of the 64 patients had high ECD levels and in 60 (93.8%) patients lower levels of ECD were found. No significant relationship was found between ECD levels and tissue HER2 overexpression. ECD was higher in women aged >40 than in women <40. ECD was higher in Arab than in Jewish patients. No significant relation was found between ECD and all clinical and pathological features.
Conclusion: The sensitivity of HER2 ECD for the diagnosis of HER2 overexpression in primary breast cancer is poor. No significant correlation was found between ECD levels and tissue HER2 expression, clinical and pathological characteristics of primary BC.
Disclosure of Interest: No significant relationships.

P054
Embryonic stem cells and BR CA risk & prognosis in a North Indian cohort: multi-analytical study

G. Agarwal[1] *, S. Tulsiyan[2], P. Lal[3], B. Mittal[2]. [1]*Endocrine & Breast Surgery, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India,* [2]*Genetics, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India,* [3]*Radiation Oncology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India*

Goals: Variations in surface biomarkers (CD44) and regulatory genes (OCT4, SOX2, NANOG, LIN28) of Embryonic Stem Cells (ESCs) may lead to breast cancer cell growth, differentiation and metastasis. We studied the role of ESCs gene polymorphisms in breast cancer risk and prognosis using multi-analytical strategies in a North Indian breast cancer patient cohort and healthy controls.
Methods: Polymorphisms in CD44 (rs353639, rs13347), OCT4 (rs3130932), NANOG (rs11055786), LIN28 (rs4274112) and SOX2 (rs11915160) genes were evaluated in 258 females North Indian breast cancer patients and 205 healthy controls. Response to neo-adjuvant chemotherapy (NACT) was evaluated per RECIST criteria in 114 patients. Taqman allelic discrimination assays were used for genotyping. Statistical analysis was performed using SPSS and GMDR. Online browser F-SNP was used for in-silico analysis for prediction of functional effects.
Results: Comparing the OCT4 gene polymorphism in breast cancer patients and healthy controls, a protective effect of genotypes AC [P = 0.016, OR = 0.64 (0.44–0.92)] and AC+CC [P = 0.019, OR = 0.62 (0.42–0.92)] was apparent. In SOX2 rs11915160, AC [P = 0.017, OR = 2.93 (1.21–7.09)] and AC+CC [P = 0.011, OR = 3.09 (1.28–7.43)] genotypes were found associated with breast cancer risk. No association of CD44, NANOG, and LIN28 gene polymorphisms were found with breast cancer risk. For CD44 rs353639 polymorphism, AC+CC genotype [P = 0.017, OR = 4.29 (1.30–14.11)] and C allele [P = 0.025, OR = 3.34 (1.16–9.59)] were significantly correlated with tumour size. However, no association was seen with CD44 rs13347. Significant association of AG+GG genotype [P = 0.021, OR = 6.08 (1.83–20.15)] and G allele [P = 0.021, OR = 3.07 (1.21–7.77)] of LIN28 rs4274112 polymorphism were seen with lymph node metastases. For OCT4 rs3130932, significant association of allele C was seen with hormone receptor negative status [S_r = 0.021, OR = 0.51 (0.29–0.90)]. None of the studied polymorphisms individually were found correlated with response to NACT. On GMDR analysis, we found combination of SNPs OCT4 rs3130932, NANOG rs11055786 to be the best interaction model for predicting breast cancer risk [CVC = 8/10] and OCT4 rs3130932, LIN28 rs4274112 for response to NACT [CVC = 9/10]. In-silico analysis using F-SNP, showed altered transcriptional regulation for rs353639, rs13347, rs11915160 and rs4274112 polymorphism. However, rs3130932 showed change in protein coding mechanism and rs11055786 in splicing regulation.
Conclusion: Combination of genetic variants in ESC genes may have influence in both breast cancer susceptibility and poor response to NACT in north Indian breast cancer patients.
Disclosure of Interest: No significant relationships.

P055
Clinical dilemma of contradictory HER2 results in breast cancer resolved by microarrays

M.J. Kotze[1] *, E. Murray[2], H.K. Lukhoff[1], K. Grant[1]. [1]*Pathology, Stellenbosch University, Cape Town, South Africa,* [2]*Private Oncology Practice, Cape Town, South Africa*

Goals: The study was performed at the interface between the laboratory and oncology practice in an attempt to address the clinical dilemma presented by equivocal and contradictory results for human epidermal growth factor receptor-2 (HER2) status frequently obtained in patients with early-stage breast cancer. The aim was to evaluate whether microarray gene profiling might provide additional benefit under these circumstances. The high false-negative rate of HER2 status reported with use of Oncotype DX cautions against the use of reverse transcriptase polymerase chain reaction (RT-PCR) technology for selection of breast cancer patients for HER2 targeted treatment.
Methods: Microarray analysis was performed using RNA extracted from 41 fresh tumour biopsies and 119 formalin-fixed paraffin embedded (FFPE) tissue specimens. Three lines of genomic information based on MammaPrint, TargetPrint and BluePrint were obtained over and above standard immunohistochemistry/fluorescence in situ hybridisation (IHC/FISH) to help guide treatment decisions.
Results: We demonstrated 100% agreement of HER2 status following IHC/FISH reflex testing in all five discordant cases identified (Grant et al. in press). In a further patient suffering from idiopathic thrombocytopenic purpura and who presented with contradictory IHC/FISH findings, the following results were obtained that support a low risk for distant recurrence: 1) MammaPrint (70 genes): Low-risk profile, despite HER2 copy number of 6.5 compatible with HER2-positive status according to the ASCO/CAP guidelines. 2) TargetPrint (3 genes): HER2-negative, in accordance with the HER2/CEP17 ratio of 1.5 considered compatible with HER2-negative status according to local guidelines for HER2 assessment (modified in November 2014 partly as a result of this comparative study) 3) BluePrint (80-genes): Luminal A subtype, which is associated with HER2-negative status (excluded the HER2-enriched and Luminal B subtypes mostly associated with HER2-positive status).
Conclusion: Determination of HER2 status across three assay platforms facilitated improved quality assurance and led to a higher level of confidence on which treatment decisions were based. Equivocal and contradictory IHC/FISH results and borderline HER2 cases have become important considerations when either Oncotype DX or the MammaPrint microarray is requested in South African patients. Breast cancer patients with rare categories of HER2 status not adequately covered by existing guidelines may also benefit from objective microarray gene profiling.
Disclosure of Interest: Prof MJ Kotze is a shareholder and director of Gknowmix (Pty) Ltd.

P056

High-density lipoprotein (HDL) subfractions and progesterone receptor in breast cancer patients

V.G. Flote[1]*, R. Vettukattil[2], T. Egeland[3], A. Mctiernan[4], H. Frydenberg[1], A. Husøy[1], J. Lømo[5], E.A. Wist[1], T.F. Bathen[2], I. Thune[1]. *[1]Oslo University Hospital, The Cancer Center, Oslo, Norway, [2]Department of Circulation and Medical Imaging, Norwegian University of Science and Technology (NTNU), Trondheim, Norway, [3]Norwegian University of Life Sciences, Aas, Norway, [4]Fred Hutchinson Cancer Research Center, Public Health Sciences Division, Seattle, United States of America, [5]Oslo University Hospital, Department of Pathology, Oslo, Norway*

Goals: High-Density Lipoprotein (HDL) is responsible for cholesterol excretion. Low HDL-C has been associated with increased inflammation and breast cancer development, and 27-hydroxycholesterol may induce breast cancer cell proliferation and metastasis. Negative Progesterone receptor (PgR) status is associated with poor breast cancer prognosis. However, whether HDL subfractions are associated with PgR status is less known.
Methods: Women with newly diagnosed invasive breast cancer stage I/II, aged 35–75 years were invited to participate in a pilot study. Before surgery, body mass index (BMI, kg/m^2), overnight fasting serum concentrations of lipids, and lipoproteins were assessed. All breast tumors were histologically and immunohistochemically examined in surgical specimen. Serum metabolomic profiles of HDL subfractions (HDL, HDL_{1-4}) and their contents of cholesterol, free cholesterol, phospholipids, apolipoprotein A1 and A2 were assessed, using nuclear magnetic resonance (NMR), to study whether subfractions were associated with different breast cancer tumor characteristics. Principal component analysis (PCA), partial least square analysis (PLS), uni- and multivariable linear regression models were performed.
Results: Altogether 56 breast cancer patients were included with following means: age at diagnosis, 55.1 years; BMI, 25.1 kg/m^2; serum total cholesterol, 5.74 mmol/L; HDL-Cholesterol, 1.78 mmol/L; LDL-Cholesterol, 3.45 mmol/L; and triglycerides, 1.18 mmol/L. The tumor size was on average 16.4 mm, and the mean Ki67 hotspot index was 26.5%. Most (93%) of the patients had estrogen receptor (ER) positive tumors (≥1% ER+), and 82% had progesterone receptor (PgR) positive tumors (>10% PgR+). Several HDL subfraction contents were postively and strongly associated with progesterone receptor (%) in the breast tumors: HDL cholesterol (β-coefficient 0.81, 95% CI 0.33–1.29, p = 0.001), HDL free cholesterol (β 2.48, CI 0.75–4.20, p = 0.006), HDL phospholipids (β 0.62, CI 0.24–1.00, p = 0.002), HDL ApoA1 (β 0.46, CI 0.17–0.75, p = 0.003). No association was observed between HDL and ER.
Conclusion: Our findings hypothesize a positive association between different HDL subfractions and their lipid contents with PgR receptor in breast cancer. These findings may have clinical implications, and HDL-C subfractions and lipid metabolomics should be focused in larger breast cancer studies including PgR status.
Disclosure of Interest: No significant relationships.

P057

Breast cancer-specific signatures in saliva metabolites for early diagnosis

H. Jinno[1]*, T. Murata[2], M. Sunamura[3], M. Sugimoto[4], Y. Kitagawa[1]. *[1]Department of Surgery, Keio University School of Medicine, Tokyo, Japan, [2]Saitama Municipal Hospital, Saitama, Japan, [3]Tohoku University, Miyagi, Japan, [4]Institute for Advanced Biosciences, Keio University, Yamagata, Japan*

Goals: Saliva is an easily accessible and informative biological fluid which has high potential for the early diagnosis of various diseases. Saliva-based diagnostics, particularly those based on metabolomics technology, offer a promising clinical strategy by characterizing the association between salivary analysts and a particular disease. The aim of this study is to identify breast cancer-specific signatures in saliva metabolites to facilitate the early diagnosis of breast cancer.
Methods: Comprehensive metabolite analysis of saliva was conducted using capillary electrophoresis time-of-flight mass spectrometry. Saliva samples were obtained from 20 healthy controls and 90 breast cancer patients including 85 invasive ductal carcinoma, 2 invasive lobular carcinoma and 3 ductal carcinoma in situ (DCIS). Thirty-three patients were treated with neoadjuvant chemotherapy. Statistical analyses were performed by using a nonparametric Mann–Whitney U test, multiple logistic regression and the receiver operating characteristics (ROC) to evaluate the predictive power of biomarkers.
Results: After removing the concomitantly observed and noise peaks, an average of 205 peaks were identified from the salivary metabolites. Among these peaks, 62 salivary biomarkers demonstrated significantly higher concentrations in breast cancer patients comparing with healthy individuals ($p < 0.05$). Known markers such as N1-acetylspermidine, spermine, putrescine and N8-acetylspermidine were included in these 62 markers. In 5 salivary biomarkers demonstrating significant differences with p value <0.00001, the area under the ROC curves (AUCs) were 0.765 for substance A, 0.716 for substance B, 0.809 for substance C, 0.819 for substance D and 0.850 for substance E. These 5 potential markers did not show any significant correlations with age and tumor size. The concentrations of 5 potential markers of patients with DCIS is between the patients with IDC and healthy individuals.
Conclusion: These data suggested that quantitative information for salivary metabolites and their combinations could be promising biomarkers for the early diagnosis of breast cancer.
Disclosure of Interest: No significant relationships.

P058

Comparison of EndoPredict and MammaPrint in hormone receptor positive, HER2 negative breast cancer

A. Bösl[1]*, A. Spitzmueller[2], A. Haid[3], Z. Jasarevic[1], K. Baruschke[1], S. Jaeger[1], F. Offner[1]. *[1]Institute of Pathology/Molecular Diagnostics, Academic Teaching Hospital, Feldkirch, Austria, [2]Department of Genome Oriented Bioinformatics, TU Munich, Freising, Germany, [3]Institute of Surgery, Academic Teaching Hospital, Feldkirch, Austria*

Goals: The assessment of the risk of distant metastasis in patients with breast cancer is critically important for the choice of adjuvant treatment.
Methods: In the present study 48 breast cancer samples [grade 1: 4.2% (2/48), grade 2: 45.8% (22/48), grade 3: 50% (24/48)] were analysed to compare the quantitative reverse transcription polymerase chain reaction (RT-qPCR)-based multigene assay EndoPredict and the multigenomic assay MammaPrint.
Results: Based on the molecular EP-Score of the EndoPredict test 18.2% (8/44) of the tumours were assigned to the low risk group and 81.8% (36/44) to the high risk group. The EPclin-Score of the EndoPredict test integrates the molecular data as well as tumour diameter and nodal status. Based on the EPclin-Score 38.64% (15/41) of the tumours were classified as low risk and 61.36% (27/41) as high risk. There was a significant correlation between the EP-Score and EPclin-Score (Fisher's Exact Test $p < 0.001$). However, there was no significant correlation between the EndoPredict test results and the MammaPrint (Spearman's rho: EP-Score: $\rho < 0.212$; EPclin-Score: $p < 0.284$). There was a correlation between the tumour cell proliferation detected by Ki-67 and the EP-Score (Spearman's $\rho = 0.345$) as well as the MammaPrint (Fisher's Exact Test $p = 0.499 \times 10^{-2}$). No correlation was found between the Ki-67 index and EPclin-Score. In a virtual tumour board the choice of therapy based on classic clinical-pathologic prognostic markers

and on the EndoPredict as well as on the MammaPrint test results were compared. In comparison to the clinical-pathological prognostic markers the EndoPredict would lead to a change of therapy in 36.4% (16/44).
Conclusion: It was noticeable that the amount of recommendations for chemotherapy grew by one-third, which is in contrast to all studies published so far. One reason could be a selection bias of the sample cohort because of the high amount of tumours with a grading of 3. If the choice of therapy would base on the MammaPrint result the EndoPredict would lead to a change of therapy in 37.5% (15/40). Both tests lead to different risk classification in 34.2% of patients. Our results shed doubt on the reliability of the current gene expression tests. Follow-up of our patients for extended time periods will be necessary to properly assess the value of the assays.
Disclosure of Interest: No significant relationships.

P059
Ranolazine administered after trastuzumab treatment prevents cardiotoxicity in mice

C. Coppola[1], G. Piscopo[1], F. Galletta[1], C. Maurea[1], D. Rea[2], C. Arra[2], N. Maurea[1]*. [1]*Divion of Cardiology, National Cancer Institute Pascale Foundation, Naples, Italy,* [2]*Animal Facility, National Cancer Institute Pascale Foundation, Naples, Italy*

Goals: Trastuzumab (TRAS), an anti-ErbB2 inhibitor, is the foundation of care for patients with HER2-positive breast cancer. Cardiovascular complications due to TRAS are a growing problem in clinical practice that may frustrate modern oncological outcome of therapy (asymptomatic left ventricular dysfunction and heart failure). The mechanisms of cardiotoxicity of TRAS have not been fully elucidated and can include changes in Ca2+ regulation related to blockade of ErbB2 and PI3K–Akt and MAPK pathways. Here, we aim at assessing whether Ranolazine (RAN), administered after TRAS treatment, blunts TRAS cardiotoxicity in vivo.
Methods: To evaluate cardiac function in vivo, fractional shortening (FS) and ejection fraction (EF) were measured by M/B mode echocardiography and radial and longitudinal strain (RS and LS) were measured using 2D speckle-tracking echocardiography, in C57/BL6 mice, 2–4 mo old, at day 0, and after 2 and 7 days of daily administration of TRAS (2.25 mg/kg/day, ip). These measurements were repeated after 5 days of RAN treatment (305 mg/Kg/day, gavage, dose comparable with that used in humans of 750 mg twice) initiated at the end of TRAS treatment.
Results: To evaluate cardiac function in vivo, fractional shortening (FS) and ejection fraction (EF) were measured by M/B mode echocardiography and radial and longitudinal strain (RS and LS) were measured using 2D speckle-tracking echocardiography, in C57/BL6 mice, 2–4 mo old, at day 0, and after 2 and 7 days of daily administration of TRAS (2.25 mg/kg/day, ip). These measurements were repeated after 5 days of RAN treatment (305 mg/Kg/day, gavage, dose comparable with that used in humans of 750 mg twice) initiated at the end of TRAS treatment.
Conclusion: RAN post-treatment blunts cardiotoxic effects due to TRAS, as demonstrated by the normalization of the values of FS, EF and RS. The explanation for the persistent abnormalities of LS could be that the subendocardial fibers, responsible for the alteration of LS, are the first to impair and may be the last to recover.
Disclosure of Interest: No significant relationships.

P060
Incidence of other previously diagnosed primary malignant tumors in breast cancer patients

A. Kovács[1]*, T. Parris[2], I. Várkonyi[1], E. Werner Rönnerman[1], G. Mohammad[1], E. Holmberg[3], K. Helou[4]. [1]*Dept of Pathology, Sahlgrenska University Hospital, Göteborg, Sweden,* [2]*Sahlgrenska Cancer Center, Sahlgrenska Academy at the University of Gothenburg, Göteborg, Sweden,* [3]*Department of Oncology, Institute of Clinical Sciences, Sahlgrenska Academy at University of Göteborg, Göteborg, Sweden,* [4]*Sahlgrenska Cancer Center, Sahlgrenska Academy at the University of Gothenburg, Göteborg, Sweden*

Goals: The aim of this study was to analyze primary diagnosed breast cancer patients who had already been diagnosed with another primary malignancy in our biopsy material during a five year period, between 2010 and 2014.
Methods: Using our own database at the Dept. of Pathology, we performed a retrospective search for other primary malignancies in about 3000 breast cancer patients with primary invasive and/or in situ.
Results: The incidence of other previously diagnosed primary malignant tumors in patients now diagnosed with breast cancer increased from 3% to almost 10% during this five year period. The most striking increase was found among the gynecological tumors (endometrium and ovarian adenocarcinomas) and malignant melanoma. The number of lymphoma/leukemia cases, urothelial/renal cell carcinomas, soft tissue malignant tumors did not show a significant increase, while cancers in the head and neck region, thyroid gland carcinomas, lung cancer showed only a slight increase. The number of gastrointestinal malignancies showed an irregular incidence during this time period. We even found 10 patients with three different malignant tumors and two patients with five different malignancies. While evaluating our data, we took into consideration the patient age, breast cancer pathological characteristics, as well as the time interval between the occurrence of the two malignancies.
Conclusion: Second primary malignancies in breast cancer patients are becoming an issue of concern worldwide. It is a well-known fact that breast cancer patients have an elevated risk for a second malignancy after hormone therapy (gynecological malignancies), chemotherapy (leukemia) and irradiation (lung cancer and sarcoma). However, in the present study we reflect over the opposite situation, where breast cancer is the second primary malignant tumor. In cases of previous gynecological cancers, BRCA1/2 mutations may explain the metachronous appearance of these two (gynecological and mammary) tumors. Patients after radiotherapy for Hodgkin's lymphoma have strongly elevated risk for breast cancer. Second malignancies that occur in long-term survivors may be due to sporadic cancers that would have occurred anyway, when environmental, genetic and lifestyle (smoking, alcohol consumption and body mass index) factors may also play role.
Disclosure of Interest: No significant relationships.

P061
Effect of cooling on cytotoxicity by monotherapy versus combinatorial chemotherapy in keratinocytes

O. Hussain*, W. Al-Tameemi, C. Dunnill, A. Collett, N. Georgopoulos. *School of Applied Sciences, University of Huddersfield, Huddersfield, United Kingdom*

Goals: Head cooling using medical devices such as the Paxman scalp cooling system offers the only promising solution against chemotherapy-induced alopecia (CIA). We have shown using human keratinocyte in vitro models that cooling can protect cells effectively against cytotoxicity induced by individual chemotherapy drugs [doxorubicin, docetaxel and the active metabolite of cyclophosphamide, 4-hydroperoxy-cyclophosphamide

(4-OH-CP)]. Combinatorial therapies such as TAC (docetaxel, doxorubicin and cyclophosphamide), FAC [5-fluorouracil (5-FU), doxorubicin and cyclophosphamide] and FEC (5-FU, epirubicin and cyclophosphamide) are commonly used clinically and such therapies cause CIA to a greater extent when compared to monotherapies. Clinical findings suggest that scalp cooling shows differential capacity to protect from CIA depending on the specific drug combination used. To use in vitro keratinocyte models to study the effect of TAC, FAC and FEC on cell viability and determine whether cooling can protect from combinatorial drug-induced cytotoxicity.

Methods: HaCaT cells cultured in serum free conditions (HaCaTa) were treated with a range of concentrations of 5-fluorouracil, epirubicin and paclitaxel; for combinatorial treatments TAC, FEC and FAC we employed our previously reported methodologies. Drug-induced cytotoxicity following treatment at physiological temperature (37°C) and cooling conditions (max 22°C) was determined at 72 hours post-treatment.

Results: Our findings show that combinatorial drug treatments TAC, FEC and FAC are more cytotoxic in comparison to individual chemotherapy drugs. Moreover, cooling demonstrated the ability to protect very well from individual drug-induced cytotoxicity (e.g. 5-FU associated toxicity), whilst showing differential ability to protect from combinatorial drug-induced cytotoxicity. For instance, cooling was significantly better at reducing FAC-mediated than TAC-mediated cytotoxicity. Importantly our in vitro observations are in direct agreement with available clinical observations for TAC, FEC and FAC.

Conclusion: The similarity of our in vitro data with clinical observations provides biological support for the cytoprotective role of scalp cooling as well as evidence that, despite their reductive nature, our in vitro models are biologically relevant. Our aim is to use these models to better understand the role of cooling in rescuing from drug cytotoxicity and thus help in the design of scalp cooling-based protocols with improved efficiency for both monotherapy and particularly CIA-inducing combinational therapy in breast cancer patients.

Disclosure of Interest: No significant relationships.

P062

The balance on a knife's edge: factors influencing diagnostic accuracy of frozen section analysis

C. Kornauth[1]*, F. Rössler[2], E. Langthaler[1], J. Pammer[1], H. Wiener[1], F. Fitzal[3], P. Dubsky[4], R. Horvat[1], M. Rudas[1], Z. Bago-Horvath[1].
[1]Clinical Institute for Pathology, Medical University of Vienna, Vienna, Austria, [2]Universitätsspital Zürich, Zürich, Switzerland, [3]Hospital of Sisters of Mercy, Linz, Austria, [4]Medical University of Vienna, Vienna, Austria

Goals: The herald of oncoplastic surgical techniques increased the need for improved intraoperative assessment of surgical resection margins (RM) in breast cancer patients. In the present study, we investigated how patient- and tumor-related factors influenced diagnostic accuracy of frozen section analysis.

Methods: 215 patients with invasive breast cancer who underwent surgical resection at the Breast Cancer Centre of the Medical University of Vienna were included in our study. Invasive breast cancer was confirmed in all patients by core needle biopsy. Factors analysed included age and menopausal status of patients, as well as tumor size, multifocality, histological tumor grade, lymph node status, presence of in situ tumor component and/or lymphovascular invasion, BIRADS category of radiological anomaly, and immunohistochemically defined intrinsic subtype. Association of these patient- and tumor-related characteristics with RM status and presence of residual tumor in subsequent extended resection specimens was analysed by Chi square test.

Results: 175 of 215 cases (81.4%) were submitted to frozen section analysis, with RM being positive for tumor cell clusters in 49 cases (28.0%). In 99 cases (46%), additional tissue was resected, of which 38 (38.8%) contained residual invasive or in situ carcinoma. Frozen section was more often requested in cases radiologically classified as BIRADS 4 compared to BIRADS 5 (93.0% vs. 74.4% $p < 0.001$) and in multifocal/multicentric disease (89.0% vs. 52.2%, $p < 0.001$). Histological tumor size ($p < 0.01$) and intrinsic subtype were also statistically significantly associated with request for intraoperative assessment. Resection margins were significantly more frequently positive for tumor cells in premenopausal patients ($p = 0.015$), in larger ($p = 0.001$) and multifocal ($p = 0.001$) primary tumors. In subsequent resection specimens, only immunohistochemically determined intrinsic subtype ($p = 0.021$) was associated with the presence of residual invasive or in situ carcinoma, which was found in all cases of HER2-enriched and triple negative breast cancers and was more frequent in luminal B disease.

Conclusion: We conclude that intrinsic subtype of breast cancer significantly influences diagnostic accuracy of frozen section analysis. Further studies are needed to confirm our results in larger patient cohorts to improve surgical outcome and patient survival.

Disclosure of Interest: No significant relationships.

P063

Ultra deep panel-based NGS of cancer-relevant genes as treatment decision support

D. Döcker*, M. Menzel, S. Armeanu-Ebinger, A. Rinckleb, S. Biskup.
Diagnostics, CeGaT GmbH, Tübingen, Germany

Goals: Panel-based next generation sequencing of somatic mutations in tumors has dramatically extended our molecular understanding of cancers, thereby revealing new insights into optimizing cancer treatment. The time has come to transfer individual molecular information into beneficial individualized patient care.

Methods: We have developed a complete pipeline to sequence more than 550 cancer-relevant genes in parallel using next generation sequencing of FFPE or frozen tumor tissue. DNA is extracted from tumor material and the patient's blood. Enrichment for cancer-related genes is performed using whole exome or a specially designed custom enrichment kit, and the samples are sequenced with extremely high coverage (up to 2000×). Somatic mutations are detected by the HiSeq2500 by comparison of sequencing data from the tumor and the blood sample. Clinical interpretation of mutations is performed by a team of scientists and medical doctors. A medical report is generated, listing actionable mutations, potentially beneficial drugs and contraindications, as well as clinical trials the patient may be suitable to participate in.

Results: We are able to detect somatic mutations (often present only in a subset of cells) with a very high sensitivity and specificity in virtually all tumor samples, even if the tumor content is as low as 10%. Especially when analyzing probes with low tumor content, panel sequencing has a major advantage compared to whole exome sequencing, as the average coverage of relevant genes is significantly higher. In a majority of cases, personalizing the cancer treatment options becomes applicable, e.g. by predicting resistance to currently prescribed drugs and/or depicting unexpected targetable genes. In addition, based on the individual mutation spectrum, our panel allows the classification of cancers of unknown primary (CUP) as metastases of specific tumor entities.

Conclusion: Comprehensive molecular profiling using ultra deep panel-based next generation sequencing in cancer patients exhibits great potential in modern health care. Our approach enables so-far unexpected treatment options ranging from the adjustment of chemotherapy to the implementation of individualized therapies, including tumor vaccination strategies.

Disclosure of Interest: All authors are employees of CeGaT GmbH, Tuebingen, Germany.

P064

Expression of tumor initiating markers in metaplastic carcinoma of the breast

N. Riaz[1]*, Z. Naqvi[2], R. Idress[2], S.M. Khan[2], A.A. Siddiqui[1], E. Lalani[1]. *[1]Surgery, Aga Khan University, Karachi, Pakistan, [2]Research, Aga Khan University, Karachi, Pakistan*

Goals: Metaplastic carcinoma is distinct albeit, rare and aggressive form of invasive breast cancer. Histologically, these tumors exemplify enrichment of tumor initiating markers such as CD44 and ALDH1 along with low expression of CD24. Our aim was to review clinico-pathological and outcome data of patients diagnosed with metaplastic carcinoma at Aga Khan University and to correlate immunohiostochemical expression of CD44, CD24 and ALDH1 with overall survival.
Methods: Cases were identified through breast cancer registry from 2000–2013. Immunohistochemical staining for CD44, CD24 and ALDH1 was performed on 5 um serial sections of archival tumor blocks. Data was analyzed on SPSS 19 and overall survival was estimated by Kaplan–Meier.
Results: Metaplastic carcinoma was diagnosed in 25 female patients with mean age of 54.6 years. Eighty-eight percent (22/25) cases had grade III tumors. ER and PR expression was observed in 52% and 36% cases, respectively. HER-2/neu overexpression and amplification was identified in 4% (1/25) and 13.3% (2/15) patients, respectively. Stage I disease was found in 4% (1/25) patients, 52% (13/25) had stage II, 36% (9/25) had stage III and 8% (2/25) patients had stage IV disease. Mean duration of follow-up was 23 months. Systemic recurrence developed in 24% (6/25) patients. Overall death rate was 28% (7/25). Membranous expression of CD44 was seen in 94% tumors whereas cytoplasmic expression of CD24 and ALDH1 was observed in 63% and 26.3% tumors, respectively. Six cases revealed $CD44^+$/ALDH1−/CD24− expression. Two patients in this subgroup expired due to systemic metastasis, whereas the remaining 4 patients remained event free. $ALDH^+/CD44^+/CD24^+$ pattern of expression was observed in 4 patients and 1 patient in this subgroup expired due to systemic progression of stage IV disease. No significant difference was identified in median survival between $CD44^+$/CD24−, ALDH1−/$CD24^+$ and $CD44^+/ALDH^+$ groups.
Conclusion: In this study, prevalence of metaplastic carcinoma was 1.17%. Majority of patients presented with stage II disease and hormone receptor positivity. CD44 expression was detected in all except one tumor. ALDH1−/$CD24^+$ subgroup was associated with lower median overall survival however this was not statistically significant.
Disclosure of Interest: No significant relationships.

P065

Luminal A vs luminal B: impact of different St.Gallen Ki67 and PgR cut points in the TEAM study

J. Felipe Lima[1]*, C.L. Brookes[2], J. Bayani[1], D. Dion[1], B. Smith[1], J.M.S. Bartlett[1]. *[1]Transformative Pathology, OICR, Toronto, Canada, [2]Cancer Research UK Clinical Trials Unit, University of Birmingham, Birmingham, United Kingdom*

Goals: The purpose of this study is to analyse retrospectively 3,679 ER positive breast carcinomas from the TEAM cohort, to explore the impact of subdividing luminal cancers into A and B subcategories when applying different Ki67 and PgR cut points. The intended outcome will illustrate the impact of grouping cancers into each subcategory using different cut points discussed and recommended at the St. Gallen Consensus Meetings of 2011 and 2013.
Methods: Pathology blocks from 4,781 TEAM patients randomly assigned to exemestane versus tamoxifen followed by exemestane for 5 years of total therapy were collected centrally, and tissue microarrays were constructed from 4,598 patients. Quantitative analysis of hormone receptors (ER and PgR) and Ki67 were performed by using image analysis and immunohistochemistry. From the total, 3,679 cases were successfully analysed in this study.
Results: The TEAM cohort showed that depending on different Ki67 cut points, there is an important variation in the number of cases called luminal A and luminal B. Dividing Ki67 cut points, as defined by St. Gallen in 2013 (using 14% 20% 25%), the percentage of "luminal A" cases ranged from 3 to 58%, and of "luminal B" from 42 to 97%. Integrating PgR expression into the classification of "luminal A" versus "luminal B" tumours identified further subgroupings. The impact of these subgroupings on survival will be further discussed.
Conclusion: Luminal tumours express a significant range of ER, PgR and Ki67. The established literature suggests that expression of these molecular factors identifies a spectrum of risk, which may differ by 100 fold or more across the luminal breast cancer population. Artificial dichotomisation of these cancers into "luminal A" and "luminal B" may be convenient, but may serve many patients poorly, particularly in the light of variation between centres for pivotal IHC markers. The choice of cut point can have important repercussions for patient management on the individual but also on the population level. Whilst improvements in categorical grouping of luminal cancers may be possible, these should always be interpreted in the knowledge that there are often marginal differences between so called "luminal A" and "luminal B" cancers.
Disclosure of Interest: No significant relationships.

P066

OSNA predicts axillary status in breast cancer patients: possible intra-operative implications

L. Di Tommaso[1]*, T. Abbate[1], A. Sciarra[1], C. Garcia Etienne[2], W. Gatzemeir[2], A. Testori[2], G. Masci[3], L. Santarpia[4], C. Tinterri[2], M. Roncalli[1]. *[1]Department of Medical Biotechnology and Translational Medicine and Unit of Pathology, University of Milan, Milan, Italy; Humanitas Cancer Center, Rozzano, Italy, [2]Senology Unit, Humanitas Cancer Center, Rozzano, Italy, [3]Oncology, Humanitas Cancer Center, Rozzano, Italy, [4]Laboratory of Oncology Experimental Therapies, Humanitas Cancer Center, Rozzano, Italy*

Goals: After ACOSG-Z0011 study, axillary dissection in patients with overtly metastatic sentinel lymph node (SLN) has been a math of strong debate. We aimed to investigate if a molecular, rather than morphological, approach to SLN may help to recognize patients who may really benefit of the dissection.
Methods: Among 1000 breast cancer patients who have received SLN examination at our Institution since 2012, the molecular method OSNA recognized a metastatic fingerprint (i.e. CK19 mRNA copies) in 267 cases (27%). After the following axillary dissection, 180 (67%) patients had no further involvement, 56 (21%) had 1 or 2 additional metastatic nodes, and 31 (12%) had ≥3 positive nodes. The last group of patients were considered "high risk" as opposed to patients with 0, 1 or 2 additional metastatic nodes ("low risk"). Clinical, pathological and molecular features of the primary tumor and SLN involvement were then compared to risk categories to elucidate any possible relationship.
Results: At univariate analysis the "high risk" (≥3 positive nodes at dissection) group was related to: size of tumor as evaluated preoperatively (>2 cm; p: 0.01); grade (G3; p: 0.01), molecular type (luminal B, her2 rich: p: 0.01) and proliferative activity (p: 0.02) of the tumor, as evaluated by histopathological examination; and to the total amount of CK19 mRNA copies, as evaluated by OSNA during the intra-operative examination of SLN ($p < 0.001$). The multivariate analysis confirmed that clinical size and intra-operative amount of CK19 mRNA copies might be used during the surgery to evaluated the risk of additional nodal metastasis. Size and mRNA copies, like in a metro ticket, impact on the cost for the patients: the greater the values, the higher the price to be paid. Thus, patients at "high risk",

might be suitable for an "expensive" procedure such as complete axillary dissection.
Conclusion: Clinical size of primary tumor and the total amount of CK19 mRNA copies in the SLN strongly impact on the risk of developing additional nodal metastasis in patients affected by breast cancer and a positive SLN. In this large unicentric study we have shown that these data, available during intra-operative time using a molecular approach to SLN examination, might help to select patients to be addressed to complete nodal dissection.
Disclosure of Interest: No significant relationships.

P067
Arsenic trioxide increases paclitaxel-induced apoptosis in resistant breast cancer cells

T. Oghabi Bakhshaiesh[1], M. Armat[2], S. Sharifi[3], M.S. Hejazi[3], N. Samadi[4]*. [1]*Faculty of Advanced Medical Sciences, Tabriz University of Medical Sciences, Department of Medical Biotechnology, Tabriz, Iran,* [2]*Faculty of Advanced Medical Sciences, Tabriz University of Medical Sciences, Tabriz, Iran,* [3]*Department of Pharmaceutical Biotechnology, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran,* [4]*Department of Biochemistry, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran*

Goals: A partial response or resistance to chemotherapuetic agents is considered as a main obstacle in treatment of patients with cancer including breast cancer. Refining taxan based treatment procedures using adjuvant or combination treatment is a novel strategy to increase the efficacy of chemotherapy. In this study, we examined the effects of arsenic trioxide on changing paclitaxel-induced apoptosis in paclitaxel-resistant MCF-7 cells.
Methods: Resistant cells were developed from the parent MCF-7 cell by applying increasing doses of paclitaxel. MTT assay was used to determine of the rate of cell survival. Fluorescent microscopic technique using DAPI staining was applied to study apoptotic bodies. To investigate PPM1D mRNA level, real-time RT-PCR analysis was applied.
Results: Our results revealed that combination of arsenic trioxide and paclitaxel has synergetic effect on reducing cell survival in MCF-7/PAC resistant cells by reducing the IC50 value from 500 to 250 nM ($p < 0.05$).
Conclusion: Our finding suggests that arsenic trioxide in combination with paclitaxel along with down regulation of PPM1D signaling can be considered as a novel strategy to improve the impact of paclitaxel in induction of apoptosis in resistant breast cancer cells.
Disclosure of Interest: No significant relationships.

P068
Sequencing to identify potential targets of resistance to primary therapy

C. Williams*, P.K. De, N. Dey, K. Williams, J. Klein, B. Young, S. Willis, B. Solomon, A. Krie, B. Leyland-Jones. *Department of Molecular and Experimental Medicine, Avera Cancer Institute, Sioux Falls, United States of America*

Goals: The optimal combination, sequence, and schedule for neoadjuvant chemotherapy has not been established. We hypothesized that genomic and proteomic profiling of tumors from women with newly diagnosed breast cancer that are scheduled to receive either neoadjuvant or adjuvant therapy would allow us to identify aberrations that may lead to treatment failure.
Methods: This is a single center prospective analysis of 8 consecutive patients with newly diagnosed breast cancer seen from September 2014 to December 2014. All samples were collected at the same center and sent for standard immunohistochemistry and FISH when appropriate. All samples were also sent to Foundation Medicine for genomic profiling using the FoundationOne test and to Theranostics for reverse-phase protein microarray analyis. Patients were referred by their oncologist for sequencing and then went on to receive standard treatments. Once any results were obtained from the proteomic and genomic analysis, the oncologist was sent the treatment recommendations by the Genomic Oncology Service. The oncologist and the Genomic Oncology Consult Service worked together to determine the best course of treatment for the patient.
Results: Sequencing results are available for all 8 patients. Actionable targets were found in 7/8 patients from the Foundation Medicine analysis. Only three patients overall had targets based upon the proteomic analysis, and 2 were HER2 positive, and the other was a patient with triple negative breast cancer. The most common actionable mutation found was PIK3CA, which was seen in 3 patients (38%), followed by FGFR1, EGFR, and PTEN loss in 1 patient each. To date, one patient receiving neoadjuvant therapy for metaplastic breast cancer received the recommended therapy based upon the sequencing (cetuximab added to standard docetaxel and carboplatin) and achieved a pathologic complete response. An additional 3 patients are due to receive therapy that was guided or directed by the results of the analysis. Results presented at the meeting will be updated as they become available.
Conclusion: Our very preliminary results suggest that genomic and proteomic profiling in women with newly diagnosed breast cancer is a useful strategy to identify potential targets of resistance to primary therapy. We identified possible actionable targets in 88% of patients tested and plan to move ahead with a large randomized trial in newly diagnosed women that are due to receive neoadjuvant therapy.
Disclosure of Interest: No significant relationships.

P069
Na^+,HCO_3^- cotransport mediates upregulated acid extrusion during human breast carcinogenesis

M. Mele[1]*, S. Lee[2], P. Vahl[3], P.M. Christiansen[1], V.E.D. Jensen[3], E. Boedtkjer[2]. [1]*Breast Surgery Department, Aarhus University Hospital, Aarhus, Denmark,* [2]*Biomedicine, Aarhus University Hospital, Aarhus, Denmark,* [3]*Pathology, Aarhus University Hospital, Aarhus, Denmark*

Goals: Metabolic and biochemical changes in breast carcinogenesis accelerate cellular acid production. Extrusion of this acid load from the cancer cells raises intracellular pH while it decreases extracellular pH. This acid-base compartmentalization has been proposed to favor cancer development and progression by promoting cell metabolism, proliferation, migration and invasion. Na^+,HCO_3^--cotransporter NBCn1 (SLC4A7) has been linked to breast cancer susceptibility in genome-wide association studies covering women of multiple ethnicities. Here, we investigated the effects of breast carcinogenesis on the mechanisms of intracellular pH control.
Methods: We investigated multicellular epithelial organoids freshly isolated from human primary breast carcinomas and matched normal breast tissue. Intracellular pH was measured by fluorescence microscopy while protein expression was investigated by immunofluorescence imaging and immunoblotting.
Results: We demonstrate that cellular net acid extrusion increased during human breast carcinogenesis due to enhanced Na^+,HCO_3^- cotransport. Compared to normal breast tissue, the augmented CO_2/HCO_3^--dependent acid extrusion in human primary breast carcinomas created an alkaline shift (~0.3 units magnitude) in steady-state intracellular pH. Na^+/H^+-exchange activity and steady-state intracellular pH in the absence of CO_2/HCO_3^- were virtually unaffected by breast carcinogenesis. The prominent dependency on Na^+,HCO_3^- cotransport was evident under both acidic (pH 6.8, representative of the tumor micro-environment) and physiological (pH 7.4) extracellular conditions. Protein expression of NBCn1 was

2-fold higher in human breast carcinomas compared to matched normal breast tissue. Protein expression of the Na^+/H^+-exchanger NHE1 (SLC9A1) was markedly less affected.
Conclusion: We demonstrate that upregulation of Na^+,HCO_3^- co-transport during human breast carcinogenesis contributes to the characteristic acid distribution within human breast carcinomas and propose that NBCn1 is a new possible target for early breast cancer therapy.
Disclosure of Interest: No significant relationships.

P070
Recurrence pattern of breast cancer according to the molecular subtype

H. Lee[1] *, I.S. Park[1], H.J. Cho[1], G. Gwak[1], S. Han[2]. [1]*Surgery, Inje University Sanggye Paik Hospital, Seoul, Korea,* [2]*Surgery, Ajou University Hospital, Suwon, Korea*

Goals: Currently, the molecular classification of breast cancer has been one of th most powerful prognostic and predictivce indicator and inform us to help determine therapeutics We performed this study to find out recurrence patterns of classical four breast cancer subtypes according to the expression of estrogen receptor (ER), progesterone receptor (PR), HER-2 in the era befor the introduction of anti-HER2 therapy.
Methods: We collected the medical records and pathologic reports of total 278 patients who diagnosed as primary breast cancer and underwent radical operation from January 2004 to December 2007. We classified total 278 patients into four subgroups such as luminal A, luminal B, HER2-enriched, triple negative bresat cancer with using the expression of ER, PR, HER2, and proportion of Ki67. We analyzed the recurrence rate, pattern of resurrance (first metastatic sites), disease free survivals, and overall survivals according to molecular subtypes.
Results: The median age of whole patients were 49 years old and median follow up period was 98 months. Luminal A subtype was 95 (34.2%), luminal B 110 (39.6%), HER2-enriched 35 (12.6%), triple negative 38 (13.7%). There were 59 loco-regional and distant recurrences in breast, axilla, bone, lung, liver, brain and total recurrence rate was 21.2%. The recurrence rate of each subtype was luminal A 10 (10.5%), luminal B 34 (30.9%), HER2-enriched 9 (25.7%), triple negative 6 (15.8%), respectively ($p = 0.003$). Bone metastasis developed total 30 out of total 59 recurred patients and among them, luminal B was most common subtype of bone metastasis as 18 cases (60.0%). Lung metastasis occurred in 18 cases and 12 cases (66.7%) was also luminal B and 5 (27.8%) was luminal A. Brain metastasis occurred in 14 cases and liver metastasis occurred in 20 cases. Disease free survival also was worst in luminal B subtype with 99 months ($p = 0.0016$). Overall survival was worst in HER2-enriched subtype with 110 months ($p = 0.0004$).
Conclusion: There was statistically significant differences in recurrence pattern between four molecular subgroups. Luminal B and HER2-enriched subtype showed the worst prognosis in the era before introduction of anti-HER2 therapy in breast cancer treatment.
Disclosure of Interest: No significant relationships.

P071
Fenugreek as a possible preventive agent of breast cancer

V.V. Bentrad[1] *, S.P. Zaletok[2]. [1]*Department of Tumor Growth Biochemistry, RE Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology, Kyiv, Ukraine,* [2]*Of Tumor Growth Biochemistry, RE Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology, Kyiv, Ukraine*

Goals: Numerous studies shown antitumor effect of fenugreek (Trigonella foenum graecum L.) in vitro and scarce articles in vivo. Unfortunatelly, the possible prevention role and antitumor mechanisms of fenugreek activity are not clear. Goals: to study fenugreek's antitumor effect on the spontaneous and grafted mammary carcinoma and its possible role as a preventive agent of mammary cancer.
Methods: Experiments were carried out on the C3H/Sn female mice with spontaneous mammary tumors and mature C57Bl/6 female mice with subcutaneously grafted Ca755 mammary carcinoma. The C3H/Sn female mice obtained the fenugreek seed powder (0.2 or 2.0 mg/kg of body mass) and standard mash during 19 months, and then they were administered standard mash up to their death (totally 28 months). The animals with Ca755 obtained the fenugreek seed powder (250 mg/kg of body mass) and standard mash from the day of tumor grafting up to sacrifice (17 and 23 days in total). Antioxidant activity was evaluated by the level of malone dialdehyde (MDA) and generation of superoxide anion-radicals in organs of animals. The level of global DNA methylation in the tumor tissue was evaluated by ELISA and high pressure liquid chromatography (HPLC), PA content – HPLC. All experiments were carried out according to the rules of local Ethic Committee.
Results: It was shown that the fenugreek consumption decreased the spontaneous mammary tumors yield in C3H/Sn mice to 30% (0.2 mg/kg) and to 15% (2.0 mg/kg), versus 60% in control animals; inhibited of Ca755 tumor growth by 38–48%. The consumption of fenugreek increased C3H/Sn mice lifetime by 11% (0.2 mg/kg), by 24% (2.0 mg/kg) and Ca755 mice by 18% versus with control group. Fenugreek decreased level of MDA (37%) and generation of superoxide anion-radicals (11–23%) in organs of animals; improved hematological parameters [especially, increased the erythrocytes (30%) and hemoglobin level (37%)]; increased the level of global DNA methylation in tumor tissue. Also, fenugreek decreased the level of main polyamines, these data are in a good agreement with the tumor growth retardation.
Conclusion: Thus, obtaining results show that fenugreek has antitumor and antioxidant properties improving hematological parameters and can be prospective for practical oncology. We found that fenugreek play good role for the cancer prevention of mammary carcinoma and may be useful agent for the primary therapy of breast cancer.
Disclosure of Interest: No significant relationships.

P072
Clinical importance of E-cadherin and vimentin expression in invasive breast cancer

N. Yamashita[1] *, E. Tokunaga[2], Y. Inoue[1], K. Tanaka[1], Y. Nakashima[1], K. Ando[1], K. Ohgaki[1], H. Saeki[1], E. Oki[1], Y. Maehara[1]. [1]*Surgery and Science, Kyushu University, Fukuoka, Japan,* [2]*Comprehensive Clinical Oncology, Kyushu University, Fukuoka, Japan*

Goals: The aim of this study is to reveal the clinical importance of the expression of E-cadherin and vimentin in breast cancer tissues.
Methods: The E-cadherin and vimentin protein expression levels were evaluated by immunohistochemistry (IHC) in 177 invasive breast cancer samples. In addition, the E-cadherin and vimentin protein levels were also evaluated in the set of primary breast cancer tissue and metastatic lymph nodes acquired from 65 cases.
Results: The positive vimentin expression was highly correlated with poor DFS and OS ($p = 0.019$ and $p = 0.0044$), however, the E-cadherin expression alone did not correlate with prognosis. Interestingly, E-cadherin positive/vimentin positive tumor had worst DFS and OS among all breast cancer ($p = 0.0184$ and $p < 0.0001$), while E-cadherin positive/vimentin negative tumor had better prognosis. E-cadherin expression in metastatic lymph node metastasis was not associated with that in primary tumor, although vimentin expression was highly correlated between the primary breast cancer tissue and the metastatic lymph nodes. E-cadherin positive/vimentin positive

expression in the metastatic lymph node had worst DFS and OS ($p = 0.15$ and $p = 0.03$).
Conclusion: E-cadherin positive/vimentin positive breast cancer seems to have most aggressive phenotype, and positive E-cadherin expression may not always suggest positive role for tumor suppression.
Disclosure of Interest: No significant relationships.

P073
Anti-cancer and phytochemical screening of *Asparagus africanus* extracts

O.D. Okkolie*, S. Mashele, I. Manduna. *Health Science, Central University of Technology, Bloemfontein, South Africa*

Goals: Data collection and analysis, literature reviews, and drafting of a proposal. Currently, I am also completing a research project on Anti-Cancer screening using *Asparagus africanus* (South Africa Medicinal plant) I have thoroughly enjoyed this process of collecting, analysing samples and also data reporting using statistical analysis and I am excited to continue in this line of work after I graduate with my Masters in March, 2015 officially. I hope to combine this knowledge with my research skills to make a meaningful contribution to the innovative research team in the Republic Of South Africa Health and Pharmaceutical companies to improve the drug efficacy and good academic strength. I am very excited about this opportunity and I am confident that my skills and experiences are a good match for the conference about to apply for. Thanks for your anticipated support.
Methods: In this study, methanol and dichloromethane extracts from the roots of Asparagus africanus Lam. were tested against breast (MCF7), colon (HCT116) and prostate (PC3) cancer cell lines. Etoposide was used as a positive control. Total growth inhibition (TGI) of the cancer cells using the sulforhodamine B assay.
Results: Sulforhodamine B assay was determined to classify the extracts as inactive, weak, moderate or potent. And also the phytochemical properties of this plant were examined using quantitative method. The plant possesses some phytochemical constituents that show positive result, which give more questions to this research work. *A. africanus* extracts were inactive (TGI > 50 μg/ml) against all the cell lines.
Conclusion: The phytochemical screening of this plant shows positive result, which thereby raise questions for this plant to be tested with other type of cancer cell lines. However these results were inconclusive because the positive control was also inactive. More screening of the extracts with other cell lines and other positive standards may produce different results.
Disclosure of Interest: No significant relationships.

P074
Use of a probiotic for breast cancer treatment in female dogs

S.D. Iulian*. *C.S.V. Targoviste, C.M.V. Santa Dan Iulian, Targoviste, Romania*

Goals: The purpose was to find some microorganisms to "feed" on tumor cells. The first part consists of a few theoretical data on cancer: what is cancer, how it occurs, its 8 important characteristics and mode of action against it. It describes the way a tumor cell avoids the normal division, growth and cell death cycle (apoptosis), the modification of telomeres and of the cell metabolism. Part 2 describes the initial way of the author to heal a neoplastic disorder in female dogs. A probiotic was chosen which was made of the following bacterial strains: *Bifidobacterium bifidum*, *Lactobacillus casei* and *Lactobacillus acidophilus*, the product REFLOR FORTE, manufactured by Harmonium International Company – Canada.
Methods: The probiotic displays the 3 bacterial cultures absorbed on solid base. The bacteria were re-suspended in sterile deionized water (1 ml for each tablet). The so obtained solution was inoculated in the tumor in 3 distinct sites. An application schedule was followed using 3 probiotic tablets of 250 mg. 13 female dogs were studied.
Results: At the end of the treatment the tumor resolved until completely subsiding in 10 cases and in the other two cases its size was remarkably reduced and the health status was clearly improved.
Conclusion: This study is the basis of a more thorough research providing further details on the mode of action of the probiotic.
Disclosure of Interest: No significant relationships.

Adjuvant systemic therapy

P080
The relation between body mass index (BMI), diabetes and outcome in a cohort of early breast cancer patients

N.A. Ahmed[1]*, M.I. Shahin[1], O.A. Abdelsalam[2], R.R.A. Malak[1]. [1]*Oncology Department, Kasr Alainy Hospital, Cairo, Egypt*, [2]*Oncology Department, Ain Shams University, Cairo, Egypt*

Goals: Diabetes and cancer are two commonly coexisting conditions with many epidemiological studies suggesting potentially causal association between type 2 diabetes and three of the five leading causes of cancer mortality. A potential explanation lays in the fact that obesity and hyperglycemia may lead to increased oxidative stress which may contribute to increase cancer risk in diabetic patients. Our current analysis aims to investigate whether Adjuvant breast cancer women with diabetes and BMI body mass index (BMI) >30 kg/m^2 have statistically increased risk for relapse.
Methods: Breast cancer patients treated at a clinical oncology department in a governmental hospital, (Cairo, Egypt) in the period 2005–2010 were reviewed. The study population consisted of patients with early breast cancer patients. We investigated the correlation between diabetes, obesity and both DFS (disease free survival) and OS (overall survival) in this cohort of patients.
Results: A total of 431 early breast cancer patients were included fulfilling inclusion criteria. Median age was 54 years old. The patients were divided in 2 groups based on body mass index calculation: 154 Non obese with BMI < 30, and 182 obese with BMI > 30 while BMI calculation was not applicable for the rest of the group (95 patients). For both DFS and OS analyses, we found no significant differences between the 2 groups (obese vs. non obese) (P value 0.089 and $P = 0.0657$ respectively). When classifying the same group of patient according to diabetic status, 82 patients were found to have diabetes Mellitus while 349 patients were non diabetics; the P value for DFS was also non significant ($p = 0.635$). When further analyzing the diabetic group according to BMI, patients with diabetes and BMI higher than 30 were found to have a significantly shorter DFS and higher risk of relapse ($P = 0.041$).
Conclusion: According to our data, diabetic breast cancer patients with higher BMI have a higher risk of relapse compared to other subsets of patients. Further research into the underlying molecular pathogenetic events as well as personalized targeted therapies is highly recommended for this high risk cohort of patients.
Disclosure of Interest: No significant relationships.

P081
Do standard heart failure medications prevent fall in LVEF in patients on trastuzumab?

S. O'Connor[1], H. Majeed[2]*, M. Valdes[3], P. Andrew[3]. [1]*City University, London, United Kingdom*, [2]*Internal Medicine, University of Ottawa, Ottawa, Canada*, [3]*Medical Oncology, University of Ottawa, Ottawa, Canada*

Goals: β-blockers and angiotensin modulators form the cornerstone of heart failure (HF) management in the general population. The benefit of these agents is ill-defined in HER2-positive breast

cancer patients with known cardiac-related comorbidities given trastuzumab. We sought to determine if being on these medications when given trastuzumab prevents decline in LVEF in patients with known cardiac-related comorbidities.

Methods: Adhered to the PRISMA statement for pooled-analysis. Selection criteria: Clinical trials involving patient cohorts already on cardioprotective medications when treated with trastuzumab. Search strategy: PubMed, the Cochrane Library, Google Scholar, Web of Science, and Scopus databases from 1998 to 2013, plus www.asco.org and www.clinicaltrials.gov. Outcome measure: Decline in LVEF >10% of baseline per ECHO or MUGA while on β-blocker +/− ACEi or ARB, plus trastuzumab. Statistical analysis: Dedicated pooled-analysis statistical software (BioStat Inc., NJ, USA).

Results: From 218 articles, 6 clinical trials (n = 329) were selected with extractable data. Patients on β-blocker +/− ACEi or ARB tended to be older and heavily pretreated with chemotherapy. Being on cardioprotective medications during trastuzumab therapy was beneficial for stability of LVEF in patients at above-average risk for cardiotoxicity [mean odds ratio (OR): 0.664, 95% CI 0.44 to 1.01; random effects model p = 0.05 versus fixed effect model p = 0.004]. Statistical analyses revealed robustness of our analysis for comorbidity index ($p < 0.05$).

Conclusion: This hypothesis-generating analysis suggests that use of β-blocker +/− ACEi or ARB during trastuzumab therapy prevents decline in LVEF in breast cancer patients with known cardiac risk factors or co-morbidities.

Disclosure of Interest: No significant relationships.

P082

CBCSG-10, the addition of capecitabine to adjuvant chemotherapy in triple-negative breast cancer

J. Li[1], Z. Shao[1]*, S. Yang[2], J. Jiang[3], C. Wang[4], Y. Liu[5], P. Fu[6], D. Pang[7], Y. Sheng[8]. *[1]Breast Surgery, Shanghai Cancer Center, Fudan University, Shanghai, China, [2]Gansu Cancer Hospital, Lanzhou Gansu, China, [3]South West Hospital, Chongqing, China, [4]Jinlin Cancer Hospital & Institute, Changchun, Jilin, China, [5]The Fourth Clinical Medical College of Hebei Medical University, Shijiazhuang, Hebei, China, [6]Zhejiang First Hospital, Hangzhou, Zhejiang, China, [7]The Third Affiliated Hospital of Harbin Medical University, Harbin, Heilongjiang, China, [8]Changhai Hospital of Shanghai, Shanghai, China*

Goals: The optimal adjuvant chemotherapy regimen has not been determined for triple-negative breast cancer (TNBC). We aimed to assess the efficacy and safety of adding capecitabine (Xeloda, X) to the standard adjuvant treatment of TNBC.

Methods: In this prospective randomized, multi-center phase 3 trial, we recruited women with early TNBC after surgery. Eligible patients were randomly assigned (1:1) using a central patient screening and randomization system to sequential 3 cycles docetaxel (75 mg/m^2) followed by 3 cycles 5-FU (500 mg/m^2)/epirubicin (75 mg/m^2)/CTX (500 mg/m^2) (FEC) or to sequential 3 cycles docetaxel (75 mg/m^2) and X (1000 mg/m^2) followed by 3 cycles X (1000 mg/m^2)/epirubicin (75 mg/m^2)/CTX (500 mg/m^2) (XEC) as adjuvant chemotherapy regimen. The primary endpoint was 5-year disease free survival; the secondary endpoints were safety, life quality, 5-year relapse free survival, distant disease free survival and overall survival. We report the first analysis of safety and life quality; other survival follow-ups are still in progress. This trial is registered with ClinicalTrials.gov, number NCT01642771.

Results: Between Jun, 2012, and Nov, 2013, 561 patients were randomly assigned to X (n = 273) or control (n = 288). The clinical and pathological features were well balanced in two groups. 87.15% patients in the X group and 89.75% patients in the control group completed 6 cycles of chemotherapy. Analyzed by Fact-B questionnaire, no differences of life quality were found between two groups. The proportion of patients had dose reduction in the case group were 1.75% with docetaxel and 5.36% with epirubicin; in the control group were 1.83% with docetaxel and 5.79% with epirubicin. Totally 38.89% patients had X dose reduction. The most common grade 3–4 adverse events were hand–foot syndrome (13 [4.51%] patients in the X group vs 0 [0%] patient in the control group), leucopenia (58 [20.14%] vs 57 [20.88%]) and neutropenia (84 [29.17%] vs 70 [25.64%]). Serious adverse events were reported in 10 (3.47%) patients in the X group and 5 (1.83%) in the control group; no on-treatment deaths occurred in each group.

Conclusion: The addition of capecitabine to standard adjuvant chemotherapy was safe and tolerable in the treatment of TNBC. The clinical benefit of capecitabine in the adjuvant setting needs further follow-up.

Disclosure of Interest: No significant relationships.

P083

Anti-tumor and anti-cancer stem cell activities of eribulin and anti-estrogens in breast cancer cells

J. Kurebayashi[1]*, N. Kanomata[2], T. Yamashita[1], T. Shimo[1], T. Moriya[2]. *[1]Breast and Thyroid Surgery, Kawasaki Medical School, Kurashiki, Japan, [2]Pathology 2, Kawasaki Medical School, Kurashiki, Japan*

Goals: Eribulin mesylate (eribulin), a non-taxane microtubule dynamic inhibitor, has been widely used in the treatment of patients with advanced or metastatic breast cancer. The combined antitumor and anti-cancer stem cell (CSC) activities of eribulin with endocrine therapeutic agents have not yet been examined in breast cancer cells. We herein investigated the combined effects of eribulin and antiestrogens.

Methods: A panel of eight breast cancer cell lines, including five estrogen receptor (ER)-positive and three ER-negative cell lines, were used. These cells were treated with eribulin and/or the antiestrogen, 4-hydroxytamoxifen or fulvestrant. Their growth inhibitory activities and effects on cell cycle progression, apoptosis, and the CSC population were investigated. CSCs were detected using the CD44/CD24/EpCAM, Aldefluor, and mammosphere assays.

Results: The 50%-growth inhibitory concentrations of eribulin were 0.38–2.64 nM for the eight cell lines tested. Eribulin exhibited significant antitumor activity under estrogen-supplemented conditions in ER-positive breast cancer cells. The combined antitumor activity of eribulin with an antiestrogen was evaluated using the combination index. The combination index was 0.43–1.46 for ER-positive cell lines. The additive antitumor effect of eribulin with 4-OHT was only significant in MCF-7 cells. Eribulin induced the accumulation of G2/M and apoptosis, while antiestrogens induced the retardation of G1-S and apoptosis, respectively. Estrogen markedly increased the proportion of CSCs, whereas antiestrogens inhibited increases in ER-positive cell lines. Moreover, eribulin decreased the proportion of CSCs in either ER-positive or ER-negative cell lines. The combined treatment of eribulin with an antiestrogen did not additively decrease the proportion of CSCs in ER-positive cell lines.

Conclusion: The results of the present study demonstrated that eribulin had potent antitumor effects on estrogen-stimulated ER-positive breast cancer cells and the combined treatment of eribulin with an antiestrogen resulted in a weakly additive antitumor effect. We herein suggested for the first time that eribulin exhibited potent anti-CSC effects on either ER-positive or ER-negative breast cancer cells.

Disclosure of Interest: J. Kurebayashi received a research grant from Esai Co. The other authors declare that they have no conflict of interest.

P084

Feasibility study to examine underlying mechanisms for "Chemo Fog"

V. Jenkins[1]*, H. Harder[1], M. Cercingani[2], H. Whiteley-Jones[2], R. Thwaites[3], L. Mullen[3], N. Harrison[2], K. Davies[3], C. Zammit[4], S. Sacre[3]. *[1]SHORE-C Brighton & Sussex Medical School, University of Sussex, Brighton, United Kingdom, [2]CISC Brighton & Sussex Medical School, University of Sussex, Brighton, United Kingdom, [3]Brighton & Sussex Medical School, University of Sussex, Brighton, United Kingdom, [4]Breast Surgery, Brighton & Sussex University Hospitals, Brighton, United Kingdom*

Goals: To investigate the mechanisms underlying cognitive impairments reported by women treated for early stage breast cancer (EBC), specifically whether changes in peripheral cytokines following chemotherapy impact brain structure/function and are associated with objective and/or subjective cognitive functioning. Also to examine the association between patients' reported cognitive impairments and fatigue.

Methods: Women with (EBC) cancer were recruited to the study. Objective and subjective cognitive performance, quality of life, level of fatigue and cytokine blood levels were assessed at 3 time points, T1 (pre surgery), T2 (post-surgery) and T3 (6 months later). Brain imaging was conducted at T1 and T3 and included a volumetric scan for voxel-based morphometry (VBM), diffusion tensor imaging (DTI), resting-state fMRI and quantitative Magnetization Transfer (qMT).

Results: 14/52 (27%) women approached participated in the pilot study. 8 received chemotherapy, 6 did not. There were minimal objective cognitive changes across time but at T3 women who had chemotherapy reported more fatigue, problems with cognition and had lower scores on measures of quality of life. Levels of fatigue correlated with perceived cognitive impairment. There were increases in soluble Tumour Necrosing Factor receptor II (sTNFRII), interleukin-6 (IL-6), IL-10 and vascular endothelial growth factor (VEGF) in the chemotherapy group at T3. Brain imaging showed a larger reduction in grey matter volume in the subgenual and dorsal anterior cingulate, and the inferior temporal gyrus (ITG) in these patients. Across the whole group, levels of sTNFRII were inversely correlated with grey matter volume of the right posterior insula.

Conclusion: The pilot study confirmed that patient reports of fatigue following chemotherapy are associated with biological changes in the blood and this can be correlated with changes observed in brain imaging. In addition patient reported fatigue was strongly associated with reports of cognitive impairment. Although recruiting women pre surgery was difficult we can be confident that post-surgery assessments can act as a reasonable baseline for future prospective studies as there were no significant changes in pro inflammatory blood factors, or in cognitive assessments.

Disclosure of Interest: No significant relationships.

P085

Acupuncture for musculoskeletal symptoms induced by aromatase inhibitors: a single centre experience

G.P. Giardina[1]*, S. Gozzo[2], S. Barzaghi[1], R. Gueli[1], L. Bascialla[1], I. Marcon[1], I. Vallini[1], G. Pinotti[1]. *[1]Medical Oncology, Ospedale di Circolo e Fondazione Macchi, Varese, Italy, [2]Anaesthesiology, Ospedale di Circolo e Fondazione Macchi, Varese, Italy*

Goals: Aromatase Inhibitors (AIs) are recommended as part of the adjuvant treatment of hormone-sensitive early breast cancer. However, a consistent proportion of patients may experience musculoskeletal symptoms that can lead to discontinuation of this effective therapy or to a reduction of quality of life. The purpose of our study was to evaluate the efficacy of acupuncture for AIs-symptoms management.

Methods: Women with early breast cancer who reported musculoskeletal pain related to adjuvant AIs therapy were enrolled to receive Yamamoto New Scalp Acupuncture (YNSA) twice weekly for 3 weeks and once a week for one week. Outcome measures included Brief Pain Inventory-Short Form (BPI-SF), Functional Assessment of Cancer Therapy-General (FACT-G) quality of life measure, Visual Analog Scale (VAS) stiffness and Health Assessment Questionnaire (HAQ), obtained at baseline and at 3 and 6 weeks.

Results: Of 17 women enrolled, 16 were valuable for response. Median age was 62 yrs (range 49–78). From baseline to the end of treatment, patients reported improvement in the mean BPI-SF worst pain score (7.0 vs 4.6 vs 3.5, $p = 0.01$), in the mean FACT-G well-being score (20 vs 22.8 vs 23.6, $p = 0.03$), in the mean VAS score (72.4 vs 40.6 vs 28.9, $p = 0.01$) and in the mean HAQ score (11 vs 6.7 vs 5.6, $p = 0.03$). No significant side effects were reported.

Conclusion: All patients had a significant improvement of musculoskeletal AIs-related pain and our study suggests that acupuncture may be a promising modality for relieving AIs-related musculoskeletal side effects.

Disclosure of Interest: No significant relationships.

P086

Does an oral agent teaching tool in early stage breast cancer improve self-efficacy and adherence?

M.A. Rubba[1]*, M. Nematollahi[2], J. Petrushewsky[1]. *[1]Medical Oncology, Stronach Regional Cancer Centre, Newmarket, Canada, [2]Education, Stronach Regional Cancer Centre, Newmarket, Canada*

Goals: Treatment adherence is defined by the World Health Organization (WHO) (2003) as "the extent to which a person's behavior – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider". Adherence is crucial to obtain optimal treatment outcomes. Non-adherence to oral chemotherapy and/or hormonal therapy has been shown to negatively affect cancer outcomes, such as higher recurrence rates and shorter survival. The study aims are:

1. To evaluate the feasibility of using the MOATT (MASCC oral agent teaching tool) in face-to-face education with early breast cancer patients to support patients' self-reported medication adherence and self-reported medication understanding.
2. To examine the efficacy and usefulness of the MASCC Oral Agent Teaching Tool (MOATT) in early breast cancer patients.

Methods: This is a descriptive open label study. Participants will be assessed at baseline (prior to the intervention), within 72 hours through a nurse-initiated phone call, after the first cycle of oral cancer treatment and after the 2nd cycle of oral cancer treatment. In this feasibility study, all the breast cancer nurses will be trained by co-investigators on the use of MOATT. In the Stronach Regional Cancer Center at Southlake Regional Health Centre, each physician works with an assigned nurse in a clinical team to meet the needs of the cancer patients. This nurse works with the same physician for all the shifts, and sees all the cancer patients of this particular physician. Therefore, we have chosen to allocate specialized oncology nurses who are trained on the use of MOATT.

Sample and Settings: We plan to recruit 30 newly diagnosed early breast cancer patients. Stronach Regional Cancer Center at Southlake Regional Health Centre is located in Newmarket, Ontario, Canada. This is a large comprehensive cancer center that offers all treatment modalities and is a tertiary cancer treatment centre for all patients in the region, each year over 3000 patients are seen. Data analysis and interpretation: Repeated measures ANOVA will be used to examine if the intervention was effective in improving medication adherence and self-efficacy.

Results: Will be shared at the time of presentation.

Conclusion: It is hoped that this study demonstrates the feasibility of a nurse-initiated educational and monitoring protocol for early

breast cancer patients who are starting an oral cancer treatment agent, and reveal improvement in adherence.
Disclosure of Interest: No significant relationships.

P087
Endocrine sensitivity is decisive for patient outcome in small PN0 breast cancers (PT1A,b)

T. Kolben[1], R. Wuerstlein[1]*, N. Harbeck[1], G. Schubert-Fritschle[2], I. Bauerfeind[3], S. Schrodi[2], J. Engel[2]. *[1]Breast Center, University Hospital Munich – Grosshadern, Munich, Germany, [2]Medical Informatics, Biometry and Epidemiology, Munich Cancer Registry of the Munich Cancer Center, Munich, Germany, [3]Head of The Project Group "breast Cancer" of The Munich Tumorcenter, Klinikum Landshut, Germany, Landshut, Germany*

Goals: In clinical routine, adjuvant systemic therapy (ADST) in small node-negative (N0) breast cancers is controversial, in particular in HER2-positive disease. We aimed to define the patient subgroups with tumors <1 cm which would benefit from ADST based on their risk of BC-recurrence and survival using population-based cancer registry data.
Methods: From 2002–2009 (median follow-up 6 years), 9,707 primary breast cancer patients with N0 tumors <2 cm (pTis, pT1N0M0) were reported to the Munich Cancer Registry (MCR). Patients with pTis tumors (n = 1870) served as internal control. Time to progression, observed (OS) and relative survival rates (Kaplan–Meier estimates) are presented. Cox regression analysis was used to assess the influence of tumor size, age, HR−, and HER2-status.
Results: 10-year-OS in HR-positive tumors was 91.9% in pT1a, 90.6% in pT1b, and 86.8% in pT1c. In HR-negative tumors, rates were 91.7%, 86.8%, and 86.8%. In HER2-positive, it was 81.2% for pT1a, 88.1% for pT1b, and 86.7% for pT1c, in HER2-negative tumors it was 93.1%, 90.6%, and 86.0%, respectively. In the multivariate model, age, tumor size, and HR-status showed a significant impact on OS, while HER2-status was not an independent prognostic factor. (tumor size >1 cm vs. pTis: hazard ratio 1.94, p < 0.0001 (95% CI; 1.47–2.56). (HR− vs. HR+: hazard ratio 1.42, p = 0.011 (95% CI; 1.09–1.87). In this epidemiological registry, patients between 60 and 69 y – compared to patients aged 50 to 59 y – are at a 1.66 fold higher risk of dying (p = 0.0003; 95% CI 1.26–2.18), risk for patients aged 70–79 y was 3.99 fold (p < 0.0001; 95% CI 3.03–5.27) and for patients 80 y and older it was 15.38 fold higher (p ≤ 0.0001; CI 11.45–20.66). However, hazard ratio for death at ages <50 y was 0.88; this was not statistically significant (p = 0.457; 95% CI 0.62–1.24). Even young age <40 y by itself did not turn out to be a significant risk factor.
Conclusion: Prognosis of pN0 tumors <1 cm is excellent, especially if they are HR-positive, even in HER2-positive cases. Weighing potential benefits vs. side-effects, there seems to be no need for chemotherapy in tumors <0.5 cm. In pT1b tumors, chemotherapy may be considered, if tumors are triple negative or HER2-positive and HR-negative. In pT1c guideline-based adjuvant therapy using all therapeutic options seems to be warranted.
Disclosure of Interest: No significant relationships.

P088
Early menopause and comorbidities among Chinese breast cancer women after adjuvant chemotherapy

G.S. Liem[1], E. Pang[1], J.J. Suen[2], F.K. Mo[1], C.H. Yip[1], K.M. Lee[2], W.M. Ho[2], V.T. Chan[2], J. Koh[1], W. Yeo[1]*. *[1]Clinical Oncology, Chinese University of Hong Kong, Hong Kong, Hong Kong, [2]Clinical Oncology, Prince of Wales Hospital, Hong Kong, Hong Kong*

Goals: For young premenopausal Chinese breast cancer women who had received adjuvant chemotherapy with or without other adjuvant therapies, to determine the rate of chemotherapy-induced early menopause and incidence of cardiovascular risk factors including abnormal Body Mass Index (BMI) and hypertension.
Methods: 280 premenopausal Chinese breast cancer patients were recruited into this cross-sectional study. Eligibility criteria included breast cancer of stage I–III, age ≤45 years at breast cancer diagnosis and having received adjuvant chemotherapy. At the time of this study, patients should be within 3–10 years of their breast cancer diagnosis. Patients' background demographics including menstrual history at the time of breast cancer diagnosis, together with tumour characteristics and anti-cancer treatments were collected. At the time of study entry, the menopausal status based on menstrual history as well as information on BMI and blood pressure were collected.
Results: Of the 280 patients recruited, 41 were ≤35 years, 82 were aged 36–40 and 157 were aged 41–45 at the time of breast cancer diagnosis. At study entry, 8 were ≤35 years, 26 were aged 36–40, 76 were aged 41–45, 157 were aged 46–50 and 24 were aged >50. 88 had Stage I, 165 had stage II and 26 had Stage III breast cancer. Adjuvant chemotherapy regimens included CMF chemotherapy (5.5%), anthracycline-containing (64.6%), both anthracycline- and taxane-containing (24.3%) and others (5.7%). 256 patients (91.4%) patients stopped their menstruation within the first year of completing adjuvant chemotherapy. Of these, 67.2% regained menstruation thereafter. At the time of study entry, 47.5% had become postmenopausal at the age ≤45 years. When assessing BMI at diagnosis vs. at study entry, more patients were overweight (13.9% vs. 24.6%, p = 0.01) and obese (2.5% vs 5.4%, p = 0.08) at study entry. After adjuvant therapy, more patients with higher BMI developed hypertension when compared with those of normal BMI (46.5% and 28.5%, p = 0.0196).
Conclusion: After adjuvant chemotherapy, almost half of young Chinese breast cancer patients became postmenopausal at the age ≤45 years. This was associated with increased incidence of overweight and obese statuses, as well as higher incidence of hypertension.
Disclosure of Interest: No significant relationships. Acknowledgement: This study was supported in part by Hong Kong Cancer Fund.

P089
Have children an impact on compliance to adjuvant therapy in young breast cancer patients?

U. Güth[1]*, J. Alder[2], A. Schötzau[3], R. Moffat[4]. *[1]Gynecology & Obstetrics; Breast Center Senosuisse, Cantonal Hospital Winterthur, Winterthur, Switzerland, [2]Psychology, University of Basel, Basel, Switzerland, [3]Eudox Institut for Biomathematics, Basel, Switzerland, [4]Gynecology & Obstetrics, University Hospital Basel, Basel, Switzerland*

Goals: Children may affect the motivation for therapy in young breast cancer patients in two ways. One could hypothesize that the fact that young patients having a child might have a positive impact on compliance with oncological therapies because these women feel a high level of responsibility towards their children and want to do everything possible to gain victory over cancer. We analyzed whether the parity status, i.e. the fact of having children, influenced the patient's compliance and persistence to adjuvant therapies in young BC patients.
Methods: Based on the Basel Breast Cancer Database, we analyzed all patients who were ≤40 years at initial BC diagnosis (date of diagnosis 1990–2007, stage I–III, n = 95).
Results: Fifty-seven patients (60.0%) had children at the time of diagnosis (mean number of children: 1.03).
Out of the 69 patients to whom radiotherapy was suggested, only three (4.3%) refused the recommended therapy. Due to the low number of patients who did not follow the recommendations for

adjuvant radiation, we omitted an analysis regarding the impact of parity status on non-compliance.
Out of the 63 patients for whom chemotherapy (CT) was proposed, eight (12.7%) did not follow this recommendation (non-compliance, n = 5) or choose to stop the therapy prematurely (non-persistence, n = 3). Whether the patients had children or not was not a significant factor for compliance and persistence to CT (p=1.00).
Out of the 43 patients to whom endocrine therapy (ET) was recommended, seventeen women (39.5%) refused this therapy (non-compliance, n = 9) or chose to end ET prematurely (non-persistence, n = 8). Patients who had children were more likely to be compliant and persistent to therapy (p = 0.021). Out of the 17 patients who were non-compliant or non-persistent to ET, seven patients (41.2%) rejected or discontinued the therapy with the explicit intention to get pregnant in the near future.
Conclusion: Children might affect the motivation for therapy in two ways. For ET, present children were not the deciding factor for choosing therapy, but rather the unborn children the reason for declining therapy. These patients were fully aware of the impact of their decision on the outcome of a potentially life-threatening disease. This clearly highlights the enormous pressure that many young women face in this situation.
Disclosure of Interest: No significant relationships.

P090
Benefits and tolerability of adjuvant chemotherapy in geriatric breast cancer

M. Peng[1] *, C. Chen[2], Y. Lin[1], H. Chang[1]. *[1]Hematology and Oncology, Chang Gung Memorial Hospital, Taoyuan County, Taiwan, [2]General Surgery, Chang Gung Memorial Hospital, Taoyuan County, Taiwan*

Goals: Adjuvant chemotherapy might offer survival benefits for elderly patients above 70, but there were limited lieterature focused on these vulnerable patients. In this retrospective study, we analyze the benefits and tolerability of adjuvant chemotherapy in elderly breast cancer patients.
Methods: A total of 426 female patients aged above 70 were indicated for adjuvant chemotherapy for primary breast cancer between 1990 and 2009 in Chang Gung Memorial Hospital, Taiwan. Regimens of adjuvant chemotherapy included CMF, CEF and CEF plus taxane.

Univariate analysis	No. with CT	No. w/o CT	Hazard ratio	95% CI	P value
Nodal status					
N0	21	211	1.05	0.316–3.469	0.940
N1	33	87	0.67	0.283–1.573	0.355
N2	22	58	0.56	0.154–1.999	0.368
N3	52	199	1.72	0.814–3.648	0.155
Status of HR					
Positive HR	47	208	2.28	1.276–4.068	0.005
Negative HR	33	87	0.75	0.351–1.581	0.444
Status of HER2					
Positive HER2	22	58	1.42	0.607–3.317	1.432
Negative HER2	52	199	1.43	0.773–2.671	0.252
TNBC	14	48	0.43	0.141–1.282	0.129
Histologic grade					
Grade 1	11	79	2.48	0.498–12.400	0.267
Grade 2	41	139	0.96	0.433–1.946	0.913
Grade 3	22	58	1.91	0.943–3.883	0.072

Results: The median age was 75 (70–94) and the age distribution was 47.7% (70–74), 33.1% (75–79) and 19.2% (≥80). Of the 426 patients, only 103 patients (24.2%) had adjuvant chemotherapy and 88 patient (20.7%) completed it. The disease-free survival (DFS) and breast cancers-specific survival (BCS) were better in patients without chemotherapy. However, patients without chemotherapy were significantly younger and had less advanced nodal status, histologic grade and higher portion of positive hormone receptor (HR) than the others. In subgroup analysis, only patients with TNBC (n = 62), N1 (n = 103) or N2 (n = 48) status showed a trend of survival benefits toward adjuvant chemotherapy. Patients with positive HR (n = 255) had a even worse outcome after chemotherapy (P = 0.006). Of the 103 patients receiving adjuvant chemotherapy, 88 patients (85.4%) could complete the whole course while 12 patients (11.6%) withdraw chemotherapy prematurely due to treatment associated adverse events or unknown reasons. Thirty-one of the 419 cycles of CMF (7.4%) were delayed and 77.4% of the delayed cycles were attributed to neutropenia/leukopenia. Eighteen of the 214 cycles of CEF (8.4%) were delayed. Hematologic side effects accounted for 38.9% of them and non-hematologic events were 28.8%. None of patients died of chemotherapy-related adverse events. There was not significant difference in the completion of treatment course, the delayed cycles between CMF and CEF regimen (P = 0.254).
Conclusion: Adjuvant chemotherapy is tolerable and safe in elderly patients above 70. Patients with N1, N2 or TNBC would get benefits from adjuvant chemotherapy but it is not recommended on elderly patients with positive HR.
Disclosure of Interest: No significant relationships.

P091
Severe colitis associated with docetaxel use in breast cancer: a report of four cases

S. Gilani *. *Oncology, University Hospital of North Midlands, Stoke on Trent, United Kingdom*

Goals: Use of taxanes has increased significantly especially in node positive early breast cancer, locally advanced breast cancer and metastatic breast cancer. Several studies have shown promising response rates. Most common side effects are neutropenis, vomiting. Skin rash, alopecia, and edema. Bowel toxicity is not commonly seen. However, severe colitis with or without neutropenia has been reported in patients treated with docetaxel. We present four cases of severe colitis in patients undergoing treatment with docetaxel chemotherapy for breast cancer.
Methods: Retrospectively MedOnc electronic notes were studied for breast cancer patients undergoing docetaxel chemotherapy for severe bowel toxicity between January 2013 to December 2013 in Cancer centre University hospital of North Midlands UK..
Results: One patient presented with total colonic necrosis, two had bowel perforation. Fourth patient had findings of colitis. Apart from colitis, we describe patients presenting with neutropenic colitis as well as ischeamic colitis after docetaxel use in breast cancer patients. These patients are individually detailed with presenting symptoms, investigations, management and outcome.
Conclusion: They provide insight into the spectrum and varied clinical presentation of severe colitis associated with docetaxel use in breast cancer patients. Clinician are urged to be aware of these rare but potentially fatal side effects of docetaxel.
Disclosure of Interest: No significant relationships.

P092
QOL score changes in breast cancer patients: 2-year vs. 3-or-more-year administration of leuprorelin

Y. Ohashi[1] *, E. Shiba[2], T. Toyama[3], J. Kurebayashi[4], S. Noguchi[5], H. Iwase[6]. *[1]Department of Integrated Science and Engineering for Sustainable Society, Chuo University, Tokyo, Japan, [2]Osaka Breast Clinic, Osaka, Japan, [3]Nagoya City University Hospital, Aichi, Japan, [4]Kawasaki Medical School, Kurashiki, Japan, [5]Osaka University Graduate School of Medicine, Osaka, Japan, [6]Kumamoto University, Kumamoto, Japan*

Goals: To examine the appropriate administration period of LH-RH agonist in premenopausal patients with hormone receptor-positive

breast cancer, we conducted a pilot randomized trial of leuprorelin acetate sustained-release formulation (TAP-144-SR[3M]).

Methods: TAP-144-SR(3M) was administered postsurgically every 3 months for 2 years (y) (96 weeks [w]) or 3-or-more-y (up to 5 y, 240 w) both along with 5-y tamoxifen administration. The quality of life (QOL) was measured using 3 questionnaires (QOL Questionnaire for Cancer Patients Treated with Anticancer Drugs [QOL-ACD], QOL-ACD-Breast [QOL-ACD-B], and Functional Assessment of Cancer Therapy-Endocrine Symptoms [FACT-ES] subscale), at 96 (2 y), 120, 144, 192, and 240 w. The two groups were compared using a mixed-effects model for repeated measures, and exploratory regression analysis was conducted to explore the relationship between QOL and patients' conditions including menopausal status.

Results: A total of 222 patients were registered from July 2006 to July 2008. We compared 112 patients in the 2-y group (2YG) (age: mean 42.7; SD 5.81) and 110 patients (42.7; 5.71) in the ≥3-y group (3YG). The 3 questionnaires' scores showed similar time profiles between the 2 treatment groups during the study period. Mean changes in QOL scores from 96 w were stable at visits up to 240 w in the 3YG. Significantly greater improved score changes from 96 w, however, were found in the 2YG than in the 3YG: the QOL-ACD-B score (items 1–18) at 192 w (Cohen's d [effect size], 0.43), that at 240 w (0.36), and the FACT-ES subscale score (except the score of joint pain) at 192 w (0.35) (See Table). Symptoms associated with menopause such as hot flashes and sweating contributed to the significant results. Regarding the resumption of menses in the 2YG, 52 patients had menstruation at 192 w and 46 patients at 240 w. In the 3YG, 3 and 7 patients had menstruation at 192 and 240 w, respectively. Multiple regression analysis showed that the presence or absence of menstruation at the QOL evaluation contributed to the differences in QOL-ACD-B and FACT-ES scores between the two treatment groups.

Table: Changes from 96 w in QOL-ACD-B and FACT-ES subscale scores, and significant items: Cohen's d (2YG vs. 3YG)

Item	Cohen's d (effect size)		
	144 w	192 w	240 w
QOL-ACD-B			
Subscale score (Total score of items 1–18)	0.08	0.43	0.36
1. Did you have any pain or numbness in your breast, armpit or arm on the side of illness?	0.07	0.39	0.17
2. Did you have any bloating in your arm on the side of the illness?	0.19	0.19	0.49
13. Were you bothered by hot flashes or sweating on your body or forehead?	0.34	0.71	0.58
FACT-ES			
Subscale Score (Except for BM1)	0.05	0.35	−0.03
ES1. I have hot flashes.	0.27	0.92	0.49
ES8. I have pain or discomfort with intercourse.	0.31	0.37	0.38
ES10. I have gained weight.	−0.08	0.19	0.01

Conclusion: Discontinuation of LH-RH agonist administration yields resumed menses and improved menopause-associated symptoms and QOL.

Disclosure of Interest: Y. Ohashi, J. Kurebayashi, S. Noguchi and H. Iwase: Consulting fees and research funding from Takeda E. Shiba: Consulting fees from Takeda T. Toyama: Research funding from Takeda.

P094

Four cycles of TC regimen might not be suitable for triple negative early stage breast cancer

F. Hara*, E. Torigoe, S. Kiyoto, M. Takahashi, S. Takashima, K. Aogi, S. Ohsumi. *Department of Breast Oncology, Shikoku Cancer Center, Matsuyama Ehime, Japan*

Goals: TC (docetaxel/cyclophosphamide) is one of non-anthracycline regimens and has been widely and rapidly spread as a standard regimen for patients with early breast cancer (EBC). TC regimen is applicable for various subtypes, such as high risk luminal, low risk triple negative, and low risk HER2 subtype. We actively use TC regimen for EBC patients since Dr. Jones demonstrated positive results of US oncology 9735 study. The goal of this study is to evaluate the prognosis of patients who received TC regimen at Shikoku Cancer Center.

Methods: All patients with EBC treated with TC between June 2007 and December 2012 at the Shikoku Cancer Center were included. Demographic, adverse events and survival events were extracted from medical records. TC regimen: Four cycles of Docetaxel 75 mg/m^2, Cyclophosphamide 600 mg/m^2 in every 3 weeks. If patients with HER2 positive tumor, trastuzumab is administered with TC concurrently and then, trastuzumab alone continues until 1 year.

Results: Four hundred forty-one patients were involved in this retrospective cohort study. Median age was 52 years (range: 21–76). Of them 58.1% had pT1, 60% had negative nodes, 68% was hormone receptor positive and 21% was HER2 overexpressed. TC was completed in 98%. After median follow-up of 52.8 months, there were 20 (4.5%) disease relapses and 3-year disease free survival (DFS) rate was 97.4%. According to intrinsic subtype, 3-year DFS rate was 98.1% in luminal type, 97.8% in luminal-HER2 type, 100% in HER2 enriched type, and 92.3% in triple negative (TN) type. Median 3-year DFS rate in TN was statistically significant worse than non-TN ($p = 0.0466$). In hematological toxicities, grade 3/4 leukopenia was 57.8%/28.9% and neutropenia was 25.6%/68.9%. Febrile neutropenia was 37.8%. Arthralgia (58%), nausea (54%), fatigue (51%), and skin rash (49%) were the most common non-hematological toxicities and almost of all were less than grade2. No treatment related death occurred.

Conclusion: Four cycles of TC (docetaxel 75 mg/m^2 and cyclophosphamide 600 mg/m^2 in every 3 weeks) regimen was effective, although some patients with TN breast cancer may not be suitable for TC. TC is well tolerated other than myelotoxic in Japanese patients with EBC. It is warranted to identify subset in TN where TC is not ineffective.

Disclosure of Interest: No significant relationships.

P095

Contraception in young breast cancer patients – considered important but not reliably monitored?

U. Güth[1]*, D.J. Huang[2], J. Bitzer[2], C. De Geyter[2], R. Moffat[2]. [1]*Breast Center, Cantonal Hospital Winterthur, Winterthur, Switzerland,* [2]*Gynecology & Obstetrics, University Hospital Basel, Basel, Switzerland*

Goals: The majority of premenopausal breast cancer (BC) patients are in their late reproductive years; even in the group of BC patients ≤40 years of age, the median age is with 36–37 years, at least from the perspective of reproductive medicine, comparatively high. Contraceptive methods utilized by this population are very heterogeneous and tend to be insufficient, resulting in a substantially increased risk for unwanted pregnancy. To make matters worse, hormonal contraception is usually contraindicated and therefore discontinued in women with BC. Today, oncologists are increasingly offering counseling for fertility preservation to their young BC

patients. However, does this newly developed attitude eclipse the fact that pregnancy must be effectively prevented after diagnosis and during adjuvant therapy? In a self-report questionnaire, we surveyed oncologists in Switzerland, Austria and Germany with the aim of evaluating attitudes towards the issue "contraception in young breast cancer patients" and how patients are being counseled in the practical clinical setting.

Methods: We conducted a cross-sectional survey. The survey instrument (poster Table 1), specifically created for this study, included four multiple-choice questions on the oncologists' attitude regarding contraception in young BC patients and how they addressed this issue in daily practice. A total of 120 colleagues were invited to participate in the survey. 101 colleagues (84.2%) agreed to participate and completed the questionnaire.

Results: Almost all respondents (99%) stated that the issue of contraception is an important aspect in the surveillance of young BC patients (Table 1, Question 1). For the vast majority of the respondents (90%), this item was not only theoretically considered important but was part of the standard discussion with young BC patients before starting adjuvant therapy (Question 2). Once the therapy had started, only 30% of the respondents reported that they actively ask whether the patients actually use contraceptive measures (Question 3). The majority of the respondents admitted that they do not regularly address the question of contraceptive use during ongoing adjuvant therapy ("rarely": 45%; "never": 10%). Only 20% of the respondents reported that they (a) inform the patients that reliable contraception is necessary before starting adjuvant therapy, (b) ask whether contraceptive methods are used during ongoing therapy, and (c) regularly refer their patients to specialist counseling by a gynecologist (Question 4).

Conclusion: Oncologists should be aware that the use of reliable contraceptive methods should not only be discussed before starting adjuvant therapy, but also during ongoing therapy. Oncologists should consider actively referring young BC patients to gynecologists to ensure proper contraceptive counseling.

Disclosure of Interest: No significant relationships.

P096

Comparison of adjuvant TAC vs. FEC-D in women <50 with node positive, HER2 negative breast cancer

R.E. Lester[1] *, D. Tilley[2], X. Kostaras[2], J.W. Henning[1], A. Joy[3], S. Lupichuk[1]. *[1]Medical Oncology, Tom Baker Cancer Centre, Calgary, Canada, [2]Guideline Utilization Resource Unit, Calgary, Canada, [3]Cross Cancer Institute, Edmonton, Canada*

Goals: A retrospective cohort study to compare TAC (taxotere, adriamycin and cyclophosphamide) and FEC-D (5-fluorouracil, epirubicin and cyclophosphamide followed by docetaxel) in terms of disease free survival (DFS), overall survival (OS), Granulocyte-colony stimulating factor (G-CSF) use, and adverse events.

Methods: Women under the age of 50 with node positive, HER2 negative breast cancer (BC) diagnosed from 2008 through 2012 were identified from the Alberta Cancer Registry (ACR). Chart review was undertaken to confirm chemotherapy (CT) regimen. Patients who did not receive CT, had neoadjuvant CT, or had a regimen other than TAC or FEC-D, were excluded. Patient and tumour characteristics, type of surgery, radiation, G-CSF use, adverse events, recurrence, and death were also recorded. Statistical analysis included: t-tests and chi-square tests where appropriate to compare baseline characteristics between cohorts; G-CSF use and adverse events; Kaplan–Meier technique for plotting DFS and OS; and, log-rank tests for comparing DFS and OS.

Results: From 2008 through 2012, there were 780 women under the age of 50 diagnosed with node positive, HER2 negative BC, and of these, 496 received either TAC (198) or FEC-D (274). Demographic variables, tumour characteristics, and other treatments were similar for the TAC and FEC-D cohorts. With median follow up of 49.6 months, DFS was 91.4% for TAC and 92% for FEC-D, HR 1.105 ($p = 0.76$; 95% CI 0.590–2.071). OS was 96% for TAC and 95.3% for FEC-D, HR 0.923 ($p = 0.86$; 95% CI 0.382–2.231). There were no differences in terms of incidence of dose reduction and grade 3–4 toxicities. Of patients receiving TAC 96.4% had G-CSF support compared to 71.5% receiving FEC-D ($p < 0.001$). Overall, the incidence of febrile neutropenia (FN) was 12.0% for TAC and 16.0% for FEC-D ($p = 0.29$). G-CSF-supported vs. G-CSF-unsupported FN occurred in 11.1% vs. 33.3% of patients receiving TAC, 2.9% vs. 8.1% of patients receiving the FEC portion of FEC-D and 4.1% vs. 17.6% of patients receiving the D portion of FEC-D. There was one treatment-related death in each cohort. During the follow-up period, there was one case of acute leukemia in the FEC-D cohort and no documented cardiac events.

Conclusion: We could not detect any differences between the TAC and FEC-D cohorts in terms of DFS, OS, or adverse events. This study supports the use of prophylactic G-CSF for the prevention of FN in patients receiving TAC chemotherapy. With respect to FEC-D chemotherapy, primary G-CSF support could be limited to the docetaxel portion of chemotherapy, leading to potential cost savings.

Disclosure of Interest: No significant relationships.

P097

Does the mode of presentation impact on distress levels in early stage breast cancer?

L.J. McSweeney[1], J. Battley[1], L. Sheehan[1], E. Lee[2], D. O'Mahony[1], S. O'Reilly[3] *. *[1]cork University Hospital, Cork, Ireland, [2]South Infirmary Victoria Hospital, Cork, Ireland, [3]Department of Medical Oncology, Cork University Hospital, Cork, Ireland*

Goals: To investigate whether or not a statistically significant difference exists between levels of psychological distress in women diagnosed with breast cancer through routine screening in a national screening program (Breastcheck) versus those with a symptomatic presentation. The goals of the study included 1. To examine the impact of mode of presentation on distress levels 2. To determine whether levels of distress in the study subjects were in line with with internationally reported statistics 3. To facilitate discussion of the need for routine distress screening in this population.

Methods: We assessed levels of distress in 93 female patients with either screen detected or symptomatic breast cancer being treated with curative intent. The Hospital Anxiety and Distress Scale (HADS) scores were used as a marker of distress. HADS-A and HADS-D measure anxiety and depression respectively. Demographic and clinical data were compiled from patient files and an additional 12 item questionaire. Data were analysed using SPSS software. Ethical approval was received from the regional ethics committee.

Results: After adjusting for confounding factors no statistically significant difference was observed between HADS score between the 2 cohorts. 47% of screen detected patients were HADS-A positive compared with 43% of the symptomatic cohort. HADS-D positive scores were observed in 19% of screened and 15% of symptomatic patients. 50.5% of patients scored above the threshold for HADS-A, HADS-D or both. Age over 60 years was associated with concomittant positive HADS-A and HADS-D screening results. Financial stress was associated with positive HADS-D scores.

Conclusion: The majority of patients in the study experienced distress. Mode of presentation did not impact on this incidence. Consideration should be made for routine screening in newly diagnosed patients with early stage breast cancer particularly those over 60 years or who are in financial distress.

Disclosure of Interest: No significant relationships.

P098

Scalp cooling system to prevent hair loss in breast cancer patients receiving chemotherapy

T. Kinoshita[1] *, K. Tamura[2], A. Hashimoto[3], T. Ogura[1], A. Hironaka[4], S. Arai[3], M. Asanabe[3]. *[1]Division of Breast Surgery, National Cancer Center Hospital, Tokyo, Japan, [2]National Cancer Center Hospital, Japan, Tokyo, Japan, [3]National Cancer Center Hospital, Tokyo, Japan, [4]Pathology, National Cancer Center Hospital, Japan, Tokyo, Japan*

Goals: Most common chemotherapeutic agents are often used to treat breast cancer patients with severe hair-loss, but since there are no preventive measures for hair loss, only symptomatic therapies such as the use of wigs or hats, hair loss significantly reduces patients' quality of life (QOL). We have to confirm the efficacy of hair loss prevention and the safety of scalp cooling equipment, and thus enhance patient recovery and QOL.
Methods: This study used scalp-cooling equipment (Paxman Cooler, U.K.), and targeted female breast cancer patients scheduled to receive 4 cycles of postoperative adjuvant chemotherapy using either AC (60/600 mg/m^2) or TC (75/600 mg/m^2). The primary outcome was the proportion of patients able to complete 4 cycles of postoperative adjuvant AC or TC therapy. Secondary outcomes were the degrees of comfort, satisfaction, and hair loss prevention, as well as the rates of adverse events and metastases to the scalp in patients who used the scalp cooling equipment.
Results: We had evaluated 21 cases: 11 who received AC therapy and 10 who received TC therapy. Protocol completion rates were 81.8% (9 cases) for AC therapy and 100% (10 cases) for TC therapy. Hair loss was graded using the WHO classification scheme; the numbers of cases for each Grade from 0–4, respectively, were 0, 3, 2, 5, and 1 during AC therapy, and 0, 3, 3, 4, and 0 for TC therapy. A wig is not considered necessary for hair loss up to Grade 2. The proportion of patients with Grade 1–2 hair loss was 5/11 cases (45.5%) in the AC group, and 6/10 cases (60%) in the TC group, or 11/21 cases (52.4%) overall. Furthermore, scalp cooling resulted in greater hair loss prevention during TC therapy than during AC therapy.
Conclusion: We will continue studying the effects of scalp cooling in breast cancer patients undergoing chemotherapy, and work to improve on the design of the original scalp cooling equipment.
Disclosure of Interest: No significant relationships.

P099

Breast cancer treatment and assisted reproductive intervention

H. Takuwa *, Y. Yoshimoto, R. Hagiwara, S. Takahara, A. Yamauchi. *Breast Surgery, the Tazuke Kofukai Medical Research Institute Kitano Hospital, Osaka, Japan*

Background: We report that the average age of Japanese women at first child birth is constantly increasing. According to the Japanese Ministry of Health, Labour and Welfare, it is over 30 years of age since 2011. Generally, the onset of breast cancer is young compared to other carcinomas. Younger patients often wish to maintain their fertility when they start their breast cancer therapy. In patients who wish to become pregnant after completion of their therapy, assisted reproductive technologies (ART), such as embryo freezing or ovarian freezing are performed. However the success rate is not so high.
Purpose: We investigated the success rate of pregnancy and childbirth after their completion of breast cancer treatment, and the relationship between the delay of breast cancer treatment and breast cancer recurrence.
Methods: We enrolled 24 young patients (≤35 years of age) of early breast cancer treated in our hospital in 2006–2012, who have a chance to be pregnant after their completion of their therapy. 8 of them (33.3%) had deliveries already. We compared 8 cases who received ART intervention before breast cancer treatment and 16 cases who did not.
Results: Five cases (2 TNBCs, 2 luminal types, 1 DCIS) could deliver without any complications during pregnancy after breast cancer treatment. All cases were not in ART intervention group, and they did not experience breast cancer recurrence so far. Mammary gland development and feeding of treated breast is not sufficient for any patient, and childcare was performed using the artificial feeding. On the other hand, patients with ART started breast cancer treatment with mean of 2 months delay (1–7 months) because of their intervention. Because the patient began to choose ART intervention since 2008, we need to observe their prognosis longer.
Conclusion: We report that there is a possibility of natural pregnancy if young breast cancer patients (younger than 35 years old) wish deliveries after completion of breast cancer therapy. These might be an advantage to ART intervention.
Disclosure of Interest: No significant relationships.

P100

The role of microRNAs in resistance to breast cancer hormone therapy

F. Homaeishandiz[1] *, M. Mojarad[2], A. Aldawood[1], M.M. Kianisharif[1], A. Babaei[1]. *[1]Radiation Oncology, Mashhad University of Medical Sciences, Mashhad, Iran, [2]Genetic, Mashhad University of Medical Sciences, Mashhad, Iran*

Goals: Tumor resistance to the selective estrogen receptor modulator tamoxifen remains a serious clinical problem. Multiple mechanisms responsible for endocrine resistance have been proposed, including deregulation of various components of the estrogen receptor (ER) pathway, alterations in cell cycle and cell survival signaling molecules, and the activation of escape pathways. Dysregulation of miRNA expression has been associated with experimental and clinical endocrine therapy resistance. The purpose of this study was to evaluate the relation of three mi-RNAs with resistant to tamoxifen in breast cancer patients.
Methods: miRNA analysis was performed on 60 ER+ primary tumors from breast cancer patients (30 resistant and 30 sensitive to tamoxifen). miRNA-342, miRNA30c and miRNA200a were measured by means of quantitative Real Time PCR. All patients had received adjuvant tamoxifen as mono-therapy.
Results: There was no significant difference between two groups according to demographic and clinical information. Analysis showed lower expression levels of miR-342, miR-200a in tamoxifen resistant group, but there was no significant different in levels of miRNA-30c between two groups. miRNA-200a showed a significant relation with recurrence. There was no significant relation between mi-RNAs and estrogen, progestron and HER2 receptors, there was only a significant relation between mi-RNA-200a and HER2.
Conclusion: Our findings suggest that miR-342 and miR-200a regulates tamoxifen response in breast tumor cells and our clinical data indicates a trend towards reduced miR-342 and miR-200a suppression and tamoxifen resistance. Considering these two biomarkers may represent a novel therapeutic approach to sensitizing and suppressing the growth of tamoxifen refractory breast tumors.
Disclosure of Interest: No significant relationships.

P101

Effect of statins on recurrence of breast cancer: a meta-analysis of cohort studies

S. Jung[1]*, E.S. Lee[1], J.I. Kim[2], S. Myung[3]. [1]*Center for Breast Cancer, National Cancer Center, Goyang, Korea,* [2]*Ilsan Paik Hospital, Inje University College of Medicine, Goyang, Korea,* [3]*Molecular Epidemiology Branch, Research Institute, National Cancer Center, Goyang, Korea*

Goals: Several cohort studies have reported inconsistent findings for the association between statin use and breast cancer recurrence. We investigated the effect of statin use on breast cancer recurrence using a meta-analysis of cohort studies.
Methods: We searched MEDLINE (PubMed) and EMBASE in October 2014. Two evaluators independently reviewed and selected articles, based on pre-determined selection criteria. The primary endpoint was breast cancer recurrence, and the second endpoints were overall mortality and disease related mortality.
Results: Out of 593 articles meeting our initial criteria, seven cohort studies (five for breast cancer recurrence and three for mortality) involving 77, 660 participants (13, 730 cases and 63, 930 controls) were included in the final analyses. In a fixed-effects meta-analysis of all the studies, breast cancer patients with statin use showed a decreased recurrence [hazard ratio (HR) 0.79, 95% confidence interval (CI) 0.70–0.90, $I^2 = 0\%$], compared with those without statin use. In the subgroup meta-analysis, lipophilic statins reduced the recurrence of breast cancer (HR 0.75, 95% CI 0.64–0.87, $I^2 = 0\%$), whereas hydrophilic statins did not (HR 1.12, 95% CI 0.79–1.59, $I^2 = 0\%$). Also, the longer use of statins reduced breast cancer recurrence (HR 0.81, 95% CI 0.69–0.95, $I^2 = 0\%$ for more than 2 years of medication). However, statins did not reduce mortality (HR 0.81, 95% CI 0.54–1.19, $I^2 = 87.5\%$ in overall mortality; HR 0.73, 95% CI 0.46–1.14, $I^2 = 82.8\%$ in disease related mortality).
Conclusion: The current meta-analysis showed that statin use reduced the recurrence of breast cancer. More prospective cohort studies and randomized controlled trials providing a higher level of evidence are needed.
Disclosure of Interest: This work was supported by the National Cancer Center, Republic of Korea [National Cancer Center Grant NCC-1210102].

P102

Outcomes in postmenopausal women with T2N0 breast cancer without adjuvant chemotherapy

J.W. Kim[1]*, Y.S. Kim[1], B.S. Ko[2], K.C. Kim[1]. [1]*Surgery, Chosun University Hospital, Gwangju, Korea,* [2]*Asan Medical Center, Seoul, Korea*

Goals: Cytotoxic chemotherapy for breast cancer after surgery is one of the most important systemic therapy to reduce the recurrence rates and mortality rates. However, chemotherapy in elderly women with low risk, hormone receptor positive breast cancer is still inspires controversy. We report the outcomes in postmenopausal women with hormone receptor positive, HER-2 negative T2N0 breast cancer without adjuvant chemotherapy.
Methods: We analyzed retrospectively 207 postmenopausal women with hormone receptor positive, HER-2 negative T2N0 invasive breast cancer who underwent surgery at our center from January 2000 to December 2008. The patients were devided two groups: endocrine therapy only (ET, n = 71) and adjuvant chemotherapy followed by endocrine therapy (CET, n = 136).
Results: ET group was older (p = 0.000) and less received adjuvant radiotherapy (p = 0.003) than CET group. There was more lymphovascular invasion in CET group than ET group (p = 0.001). ET group showed a higher degree of progesterone receptor expression (p = 0.048). In multivariate analysis, lymphovascular invasion was the only factor affecting risk of death and recurrence. There was no statistical significance in disease free survival rate, overall survival rate and disease-specific survival rate between two groups.
Conclusion: Some postmenopausal women with hormone receptor positive, HER-2 negative T2N0 breast cancer may avoid chemotherapy on the basis of biologic characteristics, comorbidity, social support, functional status, and patient's preferences. Tailored adjuvant therapy for early-stage breast cancer patients is an important goal.
Disclosure of Interest: No significant relationships.

P103

Subcutaneous trastuzumab plus chemotherapy for early breast cancer: interim safety from SafeHer

J. Gligorov[1]*, M. De Laurentiis[2], M. Verrill[3], K.H. Jung[4], H.A. Azim[5], B. Ataseven[6], N. Al-Sakaff[7], D. Heinzmann[8], M. Shing[9], X. Pivot[10]. [1]*Institut Universitaire De Cancérologie, Sorbonne Université, APHP Hôpital Tenon and UPMC, Paris, France,* [2]*Breast Oncology Department, National Cancer Institute "Fondazione Pascale", Naples, Italy,* [3]*Medical Oncology Department, Northern Centre for Cancer Care, Newcastle, United Kingdom,* [4]*Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea,* [5]*Clinical Oncology Department, Cairo University, Cairo, Egypt,* [6]*Department of Obstetrics and Gynaecology, Kliniken Essen-Mitte, Essen, Germany,* [7]*Global Pharma Development, F. Hoffmann-La Roche Ltd, Basel, Switzerland,* [8]*Biostatistics, F. Hoffmann-La Roche Ltd, Basel, Switzerland,* [9]*Global Pharma Development, Genentech, Inc., South San Francisco, United States of America,* [10]*Chemotherapy–Oncology, CHU Jean Minjoz, Besançon, France*

Goals: To evaluate safety and tolerability of subcutaneous (SC) trastuzumab (Herceptin® SC [H SC], F. Hoffmann-La Roche Ltd) plus chemotherapy in patients with HER2-positive early breast cancer (EBC) using a handheld syringe in Cohort A of the Phase III, non-randomised, multinational, open-label SafeHer study (NCT01566721); one of the largest studies to investigate H SC for HER2-positive EBC.
Methods: Patients received 600 mg fixed-dose H SC every 3 weeks (q3w) for 18 cycles, with a chemotherapy partner at the investigators' discretion (~10% could receive H SC only). Results from first dose until 4 weeks after the last H SC dose are presented. Follow-up will continue for 5 years. Adverse events (AEs) and serious AEs (SAEs) were recorded/graded according to National Cancer Institute Common Terminology Criteria for AEs (NCI-CTCAE) 4.0, congestive heart failure (CHF) according to NCI-CTCAE 4.0/New York Heart Association functional classification. Laboratory parameters, vital signs and electrocardiogram data were also collected. A second cohort is ongoing, where H SC is administered using a single-use injection device.

	Patients receiving H SC + chemotherapy, n (%)	
	Concurrent (n = 1074)	Sequential (n = 604)
Any grade AE	1000 (93)	465 (77)
SAE	170 (16)	42 (7)
NCI-CTCAE ≥ grade 3	332 (31)	66 (11)
NCI-CTCAE ≥ grade 3 of interest		
Blood/lymphatic	139 (13)	8 (1)
Gastrointestinal	46 (4)	5 (1)
Infections	44 (4)	7 (1)
General/administration site	28 (3)	3 (1)
Vascular	28 (3)	8 (1)
Respiratory	12 (1)	3 (1)
Cardiac	11 (1)	10 (2)
CHF	1 (<1)	1 (<1)

Results: N = 2578 patients were enrolled across both cohorts. The Cohort A safety population consists of 1864 patients with 1554 (83%)

receiving 18 H SC cycles; 193 patients (10%) withdrew and 121 (7%) were still on treatment (4 did not receive treatment). Concurrent chemotherapy was received by 1074 patients (58%) and sequential chemotherapy by 604 (32%). One hundred and eighty-six patients (10%) did not receive any chemotherapy and these data will be reported later. Main safety results during the treatment period are shown in the table.

Conclusion: SafeHer Cohort A interim results confirm the safety and tolerability of H SC 600 mg q3w with concurrent and sequential chemotherapy for HER2-positive EBC. No new safety signals were identified and H SC results are consistent with the known safety profile of adjuvant H.

Disclosure of Interest: Consultant/advisor: Roche/GNE (JG, MDL, MV, HAA, BA, XP); Novartis/Celgene/Amgen (MDL). Stock/royalties/equity: Roche/GNE (NAS, DH). Research/travel: Roche/GNE (JG, MDL, MV, HAA, BA); Novartis/Celgene/Amgen (MDL); Eisai KR (KHJ). Employment: Roche/GNE (NAS, DH, MS).

P104

Patterns of recurrence and survival in HER2+ patients relapsing after receiving adjuvant trastuzumab

M. Hattori*, T. Fujita, M. Sawaki, N. Kondou, A. Yoshimura, M. Ichikawa, J. Ishiguro, H. Iwata. *Department of Breast Oncology, Aichi Cancer Center, Nagoya, Japan*

Goals: Although 1 year of adjuvant trastuzumab improves survival in patients with HER2+ breast cancer, some patients will develop recurrent disease. The objective of this study was to examine the association between the patterns of recurrence and survival after relapse in HER2+ breast cancer patients who have relapsed after receiving adjuvant trastuzumab.

Methods: We utilized data from 321 HER2+ breast cancer patients identified as having received adjuvant trastuzumab at our institution between 2003 and 2012. Patients with ipsilateral breast tumor recurrence were excluded from analysis. The impact of patterns of recurrence and clinicopathologic factors on overall survival (OS) after relapse were analyzed with Cox regression model, and OS after relapse was estimated by Kaplan–Meier method.

Results: At a median follow-up of 45.5 months, 29 patients had developed recurrent disease and 17 patients had died. The median treatment free interval from the end of adjuvant trastuzumab in patients with recurrent disease was 10.3 months, response rate to first anti-HER2 therapy for metastatic disease was 53.8%, and the median OS after relapse was 25.4 months. In univariate analysis, hormone receptor status, clinical stage at first diagnosis, treatment-free interval (≤6 months) and visceral metastases as first site of relapse had no significant influence on OS after relapse. Multivariate analysis revealed that response to first anti-HER2 therapy for metastatic disease (41.6 vs. 22.6 months, HR 2.8; p = 0.059) and brain metastasis as first site of relapse (22.5 vs. 32.9 months, HR 4.3; p = 0.086) were associated with OS after relapse but low in statistical significance.

Conclusion: Our findings indicate response to initial anti-HER2 therapy after relapse and brain metastasis as first site of relapse were prognostic factors for survival after relapse in HER2+ breast cancer patients who have relapsed after receiving adjuvant trastuzumab. On the other hand, treatment-free interval (≤6 months) did not impact on survival after relapse.

Disclosure of Interest: No significant relationships.

P105

The MAGIC survey in HR+, HER2− breast cancer (BC): when might multigene assays be of value?

M. Aapro[1]*, M. De Laurentiis[2], B. Linderholm[3], E. Mamounas[4], C. Markopoulos[5], M. Martin[6], P. Neven[7], D. Rea[8], R. Rouzier[9], C. Thomssen[10]. *[1]Medical Oncology, Institut Multidisciplinaire d'Oncologie, Clinique de Genolier, Genolier, Switzerland, [2]Department of Senology, National Cancer Institute G. Pascale Foundation, Naples, Italy, [3]Department of Oncology, Sahlgrenska Academy and University Hospital, Gothenburg, Sweden, [4]University of Florida Health Cancer Center at Orlando Health, Orlando, United States of America, [5]Department of Surgery, Athens University Medical School, Athens, Greece, [6]Medical Oncology Service, Hospital General Universitario Gregorio Marañón, Madrid, Spain, [7]Multidisciplinary Breast Centre and Gynaecological Oncology, UZ Leuven, Leuven, Belgium, [8]School of Cancer Sciences, University of Birmingham, Birmingham, United Kingdom, [9]Department of Surgery, Institut Curie-Université Versailles-Saint-Quentin, Paris-Saint-Cloud, France, [10]Department of Gynecology, Martin-Luther-University Halle-Wittenberg, Halle (Saale), Germany*

Goals: The MAGIC survey evaluated which criteria clinicians use regarding the need for adjuvant chemotherapy (AdjCT) and showed that there was substantial heterogeneity across clinicians and countries in treatment decisions (Aapro et al, EBCC 2014, abstract 24). Multigene assays (MGA) can help to make more-informed decisions by providing prognostic and predictive information beyond traditional parameters. We here present data on BC patient profiles with a high heterogeneity in treatment recommendations based on traditional parameters.

Methods: From August 2013 until January 2014, physicians with ≥5 years' experience in BC treatment and participating in multidisciplinary teams were invited for the MAGIC survey capturing treatment recommendations for randomly generated early BC patient profiles (n = 672). A conjoint analysis was used to assess which patient attributes were considered for treatment decisions.

Results: The survey was completed by 911 physicians from 52 countries, of whom 72% had >10 years' experience. Their treatment recommendations showed that for BC patient profiles with only high-risk or only low-risk characteristics, there was a high consensus to recommend AdjCT or no AdjCT (endocrine treatment alone); 42% of the profiles had >75% probability of being recommended AdjCT and 6% had >75% chance of being recommended no AdjCT. There was substantial uncertainty for 52% of patient profiles with at least every fourth patient likely to receive a different treatment recommendation if visiting a different physician. 15% of patient profiles had a very high uncertainty with <50% probability to be recommended either chemotherapy and endocrine treatment or the latter alone. These patient profiles tended to have the following characteristics: >50 years old, tumor size <3 cm, Grade 1 or 2 tumor, high ER expression, and Ki67 expression <20%.

Conclusion: There was substantial heterogeneity in treatment recommendations and an overall tendency to give chemo-endocrine rather than endocrine treatment alone. The highest uncertainty in treatment decisions was seen in patients with intermediate risk by clinical and pathological parameters. MGAs may facilitate decision-making in these situations.

Disclosure of Interest: MA: consultant for Amgen, Astellas, BMS, Celgene, GSK, Helsinn, Hospira, Novartis, Merck, Merck Serono, Pfizer, Pharmacosmos, Pierre Fabre, Roche, Sandoz, Teva, Vifor; honoraria for lectures at symposia received from Amgen, Bayer Schering, Cephalon, GSK.

P106

Time to adjuvant chemotherapy in high-risk breast cancer: local outcomes and influences

A. Hamid*, S. White. *Medical Oncology, Northern Health, Epping, Australia*

Goals: A key component of therapy for women with "high-risk" breast cancer is the administration of adjuvant chemotherapy after breast surgery. There is increasing evidence that time to chemotherapy (TTC) among women with high-risk breast cancer can influence survival outcomes, with worse outcomes observed when chemotherapy is significantly delayed (Gagliato et al, JCO 2014). Furthermore it remains unclear if other specific factors including age, stage, surgery type, nodal status and receptor status influence TTC in this patient population. We aim to assess the TTC in a local population of women with high-risk non-metastatic breast cancer and to assess factors (age, stage, surgery type, nodal status, receptor status, date of oncology review) that may influence TTC within this population.
Methods: All patients receiving adjuvant, curative-intent chemotherapy associated with high-risk disease (AC (doxorubicin, cyclophosphamide); TCarboH; TCycloH; FEC-D; FEC-DH, other trastuzumab regimen) between 2009–2014 at an academic centre were identified and these cases were reviewed for demographic data, stage, pathological findings, date(s) and type(s) of surgery, date of oncology review and date of chemotherapy initiation.
Results: 164 patients were identified of which 52 received AC-containing regimen, 19 TCarboH, 19 TCycloH, 43 FEC-D, 18 FEC-DH and 13 other trastuzumab-containing regimen. Overall, 77 of 165 patients (46.7%) analysed had Her2-positive breast cancer. Of the 52 patients who received AC chemotherapy, 11 (21.2%) had "triple-negative" receptor status, 8 (15.4%) were Her2-positive and most (94.2%) had node-positive disease. During initial analysis, the median time from breast surgery to chemotherapy initiation in patients receiving AC chemotherapy was 44 days. The median time from specialist oncology consultation to chemotherapy in these patients was 19.5 days. Further analyses of TTC in other regimens and the relationship to patient, pathological and treatment factors will be presented at the meeting.
Conclusion: TTC appears to have an important influence on outcomes in patients with high-risk breast cancer. We postulate that clinical and pathological factors influence TTC in this patient population.
Disclosure of Interest: No significant relationships.

P107

Predicting factor for HER-2 gene status in immunohistochemistry-equivocal (2+) breast cancer

S.K. Kim*, S.Y. Kang, H.J. Youn, S.H. Jung. *Surgery, Jeonbuk National University Hospital, Jeonju City, Korea*

Goals: Human epidermal growth factor receptor 2 (HER2) is a member of the epidermal growth factor receptor family having tyrosine kinase activity. Amplification or overexpression of HER2 occurs in approximately 15–30% of patients with breast cancers and serves as a prognostic and predictive biomarker. HER-2 2+ score is regarded as an equivocal status and requires further examination by fluorescent in situ hybridization (FISH). We aimed to establish clinocopathologic factors for prediction of the presence of HER-2 expression.
Methods: Between January 2011 and June 2014, 93 patients with HER-2 2+ by immunohistochemistry (IHC) invasive breast cancer were enrolled in this study. A retrospective chart review was conducted and comparison between the clinicopathologic factors and whether the presence of the HER-2 amplification was performed.
Results: Mean age of patients was 49.2 years (range, 29–78 years). Estrogen receptor (ER) was positive in 64 (68.8%) patients. 66.7% of patients were progesterone receptor (PR) positive. The mean Ki67 value was 17.5% (range, 3–90%). 15 of all patients were HER-2 FISH amplified (positive). Tumors with HER-2 amplified were less likely to harbor ER positive (46.7% vs. 73.1%, $P = 0.015$) or PR positive (40.0% vs. 71.8%, $P < 0.001$). A significant high level of Ki67 was detected in HER-2 amplified groups ($P = 0.005$).
Conclusion: Hormonal receptor status and Ki-67 level of breast cancer tissue may be used as predictive factors of HER-2 expression. Further larger studies must confirm the significance of our results.
Disclosure of Interest: No significant relationships.

P108

Subjective health complaints in women on adjuvant breast cancer therapy compared to healthy controls

K.B. Hagen[1]*, T. Aas[1], J. Gjerde[2], J.T. Kvaløy[3], H. Søiland[4], R.A. Lind[5]. *[1]Breast and Endocrine Surgery, Haukeland University Hospital, Bergen, Norway, [2]Hormone Laboratory, Haukeland University Hospital, Bergen, Norway, [3]Mathematics and Natural Science, University of Stavanger, Stavanger, Norway, [4]Surgery, Stavanger University Hospital, Stavanger, Norway, [5]Medicine, Haukeland University Hospital, Bergen, Norway*

Goals: Subjective health complaints (SHC), or self-reported complaints without objective pathological findings, are very common [1]. Studies show that adherence to endocrine therapy in breast cancer women declines significantly during the first 18 months of treatment [2], and that information about side effects of therapy, and normal symptoms in menopausal women, may increase adherence to treatment [3]. The aim of the study was to examine 29 SHC, during the last month, in breast cancer patients compared to healthy controls.
Methods: One hundred and ninety-six breast cancer patients, 1–2 years after surgery, and a control group formed by 101 self-reported postmenopausal blood donors filled in four questionnaires; Subjective Health Complaints (SHC), Functional Assessment of Cancer Therapy-Endocrine Subscale (ES), Fatigue – Functional Assessment of Cancer Therapy-Fatigue subscale (FACIT-F), and the Fatigue Visual Analog Scale (Fatigue VAS).
Results: The breast cancer women scored significantly higher than controls on sum scores of SHC, $P < 0.001$, menopausal symptoms (ES), $P < 0.001$, and fatigue (FACIT-F and Fatigue VAS), $P < 0.001$. The sum scores of SHC correlated significantly with the sum scores of ES, FACIT-F and Fatigue VAS. Leg pain during activity, tiredness, sleep problems, heat flushes, dizziness and diarrhea were the significant reported complaints. The other 23 complaints recorded, did not differ significantly.
Conclusion: The patients reported more frequent and severe SHC compared to controls. The recognition of common SHC may be of importance in order to identify these patients' specific needs, which may prevent non-adherence to breast cancer therapy.

Reference(s)

[1] Ihlebaek C, Eriksen HR, Ursin H. Prevalence of subjective health complaints (SHC) in Norway. Scand J Public Health 2002; 30: 20–9.
[2] Bender C., et al. Influence of Patient and Treatment Factors on Adherence to Adjuvant Endocrine Therapy in Breast Cancer. Oncology Nursing Forum 2014; 4: 274–285.
[3] Wouters H, van Geffen EC, Baas-Thijssen MC, Krol-Warmerdam EM, Stiggelbout AM, Belitser S, et al. Disentangling breast cancer patients' perceptions and experiences with regard to endocrine therapy: nature and relevance for non-adherence. Breast 2013; 22: 661–6.

Disclosure of Interest: The authors declare no commercial or financial conflict of interest.

P109

Adjuvant chemotherapy for elderly HER2/neu positive breast cancer patients

G. Miryusupova[1]*, N. Shayusupov[2]. [1]*Breast Cancer Surgery, Tashkent City Oncology Center, Tashkent, Uzbekistan,* [2]*Oncology, Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan*

Goals: The purpose of our study is to investigate side effects in adjuvant chemotherapy (CT) for elderly breast cancer (BC) patients.
Methods: In 21 operable BC patients 63–75 years old, included in trials of adjuvant therapy in our center, 9 women were treated with BC conserving therapy and 12 women received mastectomy. Tumor tissue was defined by negative estrogen receptor and progesterone receptor and positive Her2/neu. All of them were having adjuvant CT with paclitaxel (P) 175 mg/m^2 and trastuzumab (T) (8 mg/kg–6 mg/kg) both every 3 weeks (4 cycles P+T – 6 month T).
Results: After 1st cycle of this CT 2 patients had grade 3–4 hematological toxicity (anemia, neutropenia, thrombocytopenia and febrile neutropenia) and 3–4 non-hematological toxicity (abdominal pain, mucositis, neuropathy). We had to reduce P dose by 20% for these patients after 1st cycle of CT. After 2nd cycle of this CT 3 patients had side effects. We had to reduce P dose by 20% too.
In this analysis of patients receiving adjuvant CT (P+T) – 5 patients (23.8%) had grade 3–4 hematological and non-hematological side effects. They finished adjuvant CT after reduction of the P dose.
Conclusion: Elderly Her2/neu positive BC patients will have need to correct P dose before to starting the adjuvant CT.
Disclosure of Interest: No significant relationships.

P110

9-week versus 52-week trastuzumab treatment for HER2-positive breast cancer

J. Kim*, J. Lee, H. Jeong, W. Byeon. *General Surgery, Chungnam National University Hospital, Daejeon, Korea*

Goals: Trastuzumab has established efficacy against breast cancer with overexpression or amplification of the HER2 oncogene. The current recommendation is 1 year of adjuvant trastuzumab. We compared 9 weeks of treatment with trastuzumab with 52 weeks of treatment in terms of efficacy and toxicity.
Methods: This study is a retrospective study comparing treatment with trastuzumab for 9 weeks (every week) and 52 weeks (every 3 weeks) after standard neoadjuvant chemotherapy or adjuvant chemotherapy in 220 patients with HER2-positive breast cancer. Patients who received trastuzumab in the adjuvant treatment were evaluated for disease-free survival (DFS), overall survival (OS), efficacy, and toxicity.
Results: There were 90 (40.9%) and 130 (59.1%) patients in the 9- and 52-week trastuzumab groups, respectively. Median follow-up was 73.8 months (14–100) in the 9-week trastuzumab group and 44.5 months (32–61) in the 52-week trastuzumab group. 5-year DFS was 90 and 85% (P = 0.226) in the 9- and 52-week trastuzumab treatment groups, respectively, and 5-year OS was 97.8 and 99.2% in the 9- and 52-week trastuzumab groups, respectively (P = 0.361). There were 9 (10.0%) recurrences and 4 (4.4%) deaths in the 9-week trastuzumab treatment group, and 19 (14.6%) recurrences and 4 (3.1%) deaths in the 52-week trastuzumab treatment group. Toxicity was not observed in the 9-week trastuzumab group and symptomatic cardiotoxicity was observed in 5 (3.8%) patients in the 52-week trastuzumab group.
Conclusion: In this study, similar outcomes were found in 9-week group when compared with 52-week trastuzumab treatment group.
Disclosure of Interest: No significant relationships.

P111

The effectiveness of low-dose olanzapine against CINV caused by anthracycline-containing regimen

M. Kashiwaba[1]*, H. Komatsu[1], K. Ishida[1], R. Kawagishi[1], Y. Matsui[1], H. Otsuki[1], T. Kawasaki[2], N. Uesugi[2], T. Sugai[2], G. Wakabayashi[1]. [1]*Surgery, Iwate Medical University, Morioka, Japan,* [2]*Molecular Diagnostic Pathology, Iwate Medical University, Morioka, Japan*

Goals: Anthracyciline-based regimen (A-regimen) is still important for breast cancer regarding the high risk of CINV. We utilize A-regimen with anti-emesis triplet consisted with aprepitant, dexamethasone and palonosetron, but we observe at least 10% Pts with resistant CINV.
Methods: Therefore, we planed to examine the effectiveness of low-dose Olanzapine 2.5 mg/day for four days as a phase II study with resistant CINV after A-regimen treated with anti-emesis triplet in Japanese Pts.
Results: Forty patients were entered and it showed significant improvement to resistant CINV (29/40: 72.5%) and no Pts discontinued by adverse events (AE). However, NCCN guideline recommended Olanzapine 10 mg/day for four days, it often shows AE i.e. weight gain, sleepiness and abnormal glucose tolerance.
Conclusion: Present study may suggest that even low-dose Olanzapine is an important option for treatment of resistant CINV. Final detailed results will be presented at meeting.
Disclosure of Interest: No significant relationships.

P112

The effectiveness of tamoxifen based on the experience of male breast cancer in our institution

Y. Yoshimura*, M. Fujihara, Y. Kajiwara, M. Kochi, M. Ito, S. Ohtani, K. Higaki. *Breast Surgery, Hiroshima City Hiroshima Citizens Hospital, Hiroshima, Japan*

Goals: For male breast cancer, tamoxifen treatment is suggested to improve disease free survival and overall survival when uesd as adjuvant therapy for 5–10 years. We examined about it in our institution.
Methods: 15 male breast cancer patients were operated at our hospital between 1973 and 2014. The median age of them was 69 years (range: 52–79) when they were operated. 2 patients had breast cancer family history. 13 patients had invasive ductal carcinoma, 1 patient had non invasive ductal carcinoma, and 1 patient had mucinous carcinoma. Hormone receptor was determined in 10 patients, all of them were estrogen reseptor positive, 9 of them were progesterone receptor positive, and all of them were human epidermal growth factor receptor negative. All patients had Luminal A like.
Total mastectomy performed in 13 patients, partial mastectomy performed in 2 patients. Since 2003, as adjuvant therapy, 8 patients were treated from only tamoxifen (4 of them were treated for over 5 years), 1 patient was treated from FEC (5-FU + epirubicin + cyclophosphamide) and tamoxifen (for over 5 years), and another patient was treated with abraxane, FEC and tamoxifen (for over 5 years). There was no patient treated from aromatase inhibitor.
Results: Disease free survival was median 58 months (range: 5–120 months): median 58 months (range: 29–58 months) in not tamoxifen treatment group (5 patients), median 117 months (range: 5–120 months) in tamoxifen treatment group (10 patients) (p = 0.210). Overall survival was median 120 months (range: 5–134 months): median was not reached (range: 29–75 months) in not tamoxifen treatment group, median was not reached (range: 5–134 months) in tamoxifen treatment group. 10 patients are alive, 1 patient died from another disease, and 4 patients are unknown. 4 patients had recurrence or metastasis after median 48 months (range: 31–117 months) from operation. All of them had Luminal A like, 3 of them

had adjuvant therapy including tamoxifen. 3 of 13 patients (23%) who performed from total mastectomy, and 1 of 2 patient (50%) who performed from partial mastectomy had recurrence or metastasis (p = 0.229). After recurrence, they were treated from EC (epirubicin + cyclophosphamide), TC (docetaxel + cyclophosphamide), letrozole, or abraxane, and 3 of them are alive, 1 of them is unknown.
Conclusion: It is suggested that tamoxifen treatment as adjuvant therapy may improve disease free survival. Almost all patients are estrogen receptor positive at male breast cancer, therefore tamoxifen can be effective at male breast cancer therapy.
Disclosure of Interest: No significant relationships.

Epidemiology/Prevention/Diagnosis

P115
Does trastuzumab increase ONJ development due to zoledronic acid treatment in breast cancer?

K.N. Pilanci[1] *, G. Alco[2], C. Ordu[1], F. Celebi[3], D. Sarsenov[4], Z. Erdogan Iyigun[5], F. Agacayak[6], S. Ilgun[4], V. Ozmen[7]. *[1]Medical Oncology, Bilim University, Istanbul, Turkey, [2]Radiation Oncology, Gayrettepe Florence Nightingale Hospital, Istanbul, Turkey, [3]Radiology, Gayrettepe Florence Nightingale Hospital, Istanbul, Turkey, [4]Surgery, Istanbul Florence Nightingale Hospital, Istanbul, Turkey, [5]Physical Therapy and Rehabilitation, Bilim University, Istanbul, Turkey, [6]Radiology, Istanbul Florence Nightingale Hospital, Istanbul, Turkey, [7]Surgery, Istanbul Medical Faculty, Istanbul, Turkey*

Goals: One of the most important adverse effects of Zoledronic acid (ZA) is osteonecrosis of the jaw (ONJ). In the present study, our aim was to evaluate the frequency of this adverse effect, the risk factors influencing its development, and the characteristic features.
Patients and Method: Our study included 97 patients with breast cancer recorded in the archives of the Istanbul Florence Nightingale Breast Study Group, who received ZA therapy between March 2006, and December 2013, due to bone metastases. We also recorded the patients' age, weight, duration of treatment with ZA, number of ZA infusions, dental procedures, concurrent chemotherapy, aromatase inhibitor and/or trastuzumab use, diabetes mellitus, renal dysfunction and smoking habits.
Results: The mean age of the patients was 54±10 years and the mean time of exposure to the ZA therapy was 37±18 months. Thirteen patients (13.4%) had developed ONJ. Among the patients with ONJ, the mean time of exposure to ZA was 41 months (range: 13–82 months) and the mean number of ZA infusions was 38 (range: 15–56). The duration of treatment with ZA and the use of trastuzumab were observed to be two factors that influenced the development of ONJ (p = 0.049, p = 0.028, respectively).

Table: Multivariate logistic regression analysis (ForwardStepwise)

Influential factors in the development of ONJ	OR (95% CI)	p
Trastuzumab use	4.08 (1.159–14.069)	0.028
Zoledronic acid use (months)	1.032 (1.00–1.065)	0.049

Conclusion: The development of ONJ may solely be associated with the duration of treatment with ZA but with anti-angiogenic agents received by the patients. We are of the opinion that patients receiving ZA should be followed up with regular dental examinations every 6 to 12 months in order to detect any possible development of ONJ.
Disclosure of Interest: No significant relationships.

P116
Alkaline water is ineffective in preventing breast cancer

T. Kiskova[1] *, V. Demeckova[1], J. Topitzerova[1], S. Gancarcikova[2], D. Mudronova[2], Z. Jendzelovska[1], B. Velika[3], V. Tomeckova[3], M. Backor[1]. *[1]Faculty of Science, Pavol Jozef Safarik University in Kosice, Kosice, Slovak Republic, [2]University of Veterinary Medicine and Pharmacy, Kosice, Slovak Republic, [3]Faculty of Medicine, Pavol Jozef Safarik University in Kosice, Kosice, Slovak Republic*

Goals: The information explosion about the impact of an alkaline diet on cancer increased in a few years; up to 4 million web sites are found via the Internet. One of the most popular ways to get more alkaline is to drink alkaline water (pH 8–10). However, there is no credible evidence in scientific literature to support claims that alkaline water (AW) has any greater health effects than drinking regular water. The aim of the study was to evaluate whether daily intake of alkaline water could prevent breast cancer in experimental rats.
Methods: Female Sprague-Dawley rats (n = 22) were used in the experiment. Breast cancer was induced with 2 doses of N-methyl-N-nitrosourea (NMU, 50 mg/kg body weight) on the 43rd and the 50th postnatal day. The prevention with AW began 2 weeks before the 1st NMU dose and its administration ran until the end of the experiment (16 weeks). Rats with NMU-induced mammary tumours were divided into 2 groups: Group 1 (AW, n = 8) was treated with AW (Alkaline Water Pitcher, Yalong Trade, China) ad libitum on a daily basis. Group 2 (NMU, n = 8) was the control untreated group. The intact group (INT, n = 6) consisted of healthy control animals. Basic parameters of carcinogenesis, blood analysis, reactive oxygen species (ROS) in circulating phagocytes, as well as serum biochemistry analyses were determined.
Results: The tumour incidence in the AW group reached the incidence of the untreated NMU group (100%) already in the 10th experimental week. The tumour frequency increased significantly ($P < 0.05$) without influencing the tumour volume. Neither blood nor serum analyses confirmed the protective effect of alkaline water. On the contrary, our data showed a negative effect of AW on selected blood/serum parameters compared to untreated animals. Serum LDL-cholesterol and alkaline phosphatase (ALP) levels were significantly higher ($P < 0.05$) in the AW group than in the untreated NMU group. The number of blood erythrocytes was significantly lower ($P < 0.05$) in the AW group compared to the INT group. ROS formation by blood phagocytes in both AW and NMU groups was significantly decreased ($P < 0.01$) compared to the INT group. Both treated and untreated animals suffered from hypoproteinemia, hypercreatinemia, and hypercalcemia.
Conclusion: Our results did not confirm the preventive potential of AW on breast cancer in rats. In contrast, drinking AW alone for an extended period could actually make more damage than help and should therefore be used with caution in patients with breast cancer. An elevated alkaline phosphatase is indicative of bone and liver abnormalities. Recently, it has been shown that high LDL-cholesterol levels promote breast cancer progression. It is therefore not surprising that the only group, where we observed death during the experimental period, was the AW group. Our work is the first scientific evidence that alkaline water is not only ineffective primary prevention of breast cancer but can promote the process of carcinogenesis.
Disclosure of Interest: No significant relationships.

P117

The evaluation of the breast cancer screening programme in Western Siberia

N. Zakharova[1], J. Belaya[2]*, S.W. Duffy[3], S. Pyankin[4], A. Pestryakova[4]. *[1]Khanty-Mansiysk State Medical Academy, Khanty-Mansiysk, Russian Federation, [2]Breast Cancer and Oncogynecology Surgery, Khanty-Mansiysk State Clinical Hospital, Khanty-Mansiysk, Russian Federation, [3]Wolfson Institute of Preventive Medicine, Queen Mary University of London, London, United Kingdom, [4]State Cancer Registry, Khanty-Mansiysk, Russian Federation*

Goals: Breast cancer is the most common cancer in the female population, and one of the leading causes of cancer deaths in women. Almost 12 million new cancer cases were diagnosed in 2008 across the world and of these, 1.38 million women were diagnosed with breast cancer. In many areas, breast cancer mortality has decreased in recent decades due to improving treatment and implementation of mammography screening. The main aim of this study is to evaluate the results of the Breast Cancer Screening Program implemented in the Khanty-Mansiysky Autonomous Okrug – Ugra in 2007.
Methods: Mammography screening covers women over 40 years old, the screening interval is 2 years, and two-view mammography and single reading. Data number of screened are obtained annually from the reports for the State Healthcare Department. The information on the female population, all screen-detected and symptomatic detected breast cancer cases, deaths cases due to breast cancer has been obtained from the State Cancer Registry for years 2002–2013. The target population of women aged 40+ has increased from 273,100 in 2002 to 336,189 in 2013. We studied incidence of node positive breast cancer over the years 2002 to 2013, comparing observed incidence in 2007 to 2013 with that expected from the observed trend in 2002 to 2006. We also estimated the effect of screen detection on node positivity in the 4,229 cancers diagnosed in the target age group in 2002–2013, using logistic regression and taking account of confounding factors.
Results: During 2007–2013 within the Program, 284,854 women were screened in the region. The screening coverage rate (ever-screened) is approximately 67.5%. 9.7% of screened women were referred for further assessment. The prevalence at first screen was 2.7 per 1000 screened women. The test sensitivity for the first round was estimated as 80%. The number of node positive breast cancers in 2007 to 2013 was 1,171, 13% lower than the 1,345 expected from the 2002–2006 trend. Screen detected cancers were significantly less likely to be node positive after adjusting for district and year of diagnosis, and for tumour size (OR = 0.69, 95% CI 0.54–0.87). In women over age 50 there was a significant decreasing trend of node positivity over 2002–2013, which was no longer observed after adjusting for detection mode, suggesting that the reduction in node positive disease over time is due to the screening.
Conclusion: The quality evaluation of the Screening Program shows that the main criteria are within the international standards. Mammographic screening has contributed to a major reduction in node positive breast cancer and is likely to produce a corresponding breast cancer mortality reduction in the future.
Disclosure of Interest: No significant relationships.

P118

The beliefs, knowledge, understanding and treatment access to breast cancer amongst women in Nigeria

M.O. Tagbarha*. *Public Health, University of Abuja, Abuja, Nigeria*

Goals: The goal of this study is to ascertain the beliefs, knowledge, understanding, attitudes and treatment access to breast cancer among rural women in Nigeria.
Methods: An interview guide was designed specifically for this study in which 200 rural women in Northern Nigeria, age 45 and over took part in. It contained questions about beliefs, knowledge, understanding and attitudes about Breast Self-Examination (BSE), Clinical Breast Examination (CBE) and mammogram. In addition, questions assessing the variables of the Health Belief Model and health motivations also were included. The data were obtained during face-to-face interviews in the primary language of the participating woman. The interviews were transcribed and translated into English.
Results: Out of the 200 women who participated, only 1% two (2) of the participants practiced BSE monthly, 8% had undergone at least one CBE during their lives, and 91% had never had a mammogram. There were little or no access to treatment even at early detection in these rural areas causing thereby vulnerability to loss of life. Majority of these rural women (95%) said they knew little or nothing about breast cancer. While 15% of the women said detecting cancer early was important, only 3% reported that cancer could be cured. Age, education, or mother tongue showed no statistically significant relationship with the breast health practice scores. However, proficiency with the English language ($p = 0.009$) and number of years exposed to awareness and education ($p = 0.009$) had a significant relationship with the breast health practice scores. The significant explanatory factor for the variable breast health practices was a cue to action ($p = 0.009$).
Conclusion: The level of awareness and treatment access to breast cancer amongst Northern Nigeria's rural women is extremely low thereby making them not to engage in screening and/or detection practices. This alarming situation calls for urgent intervention of medical/health organizations to provide immediate breast cancer awareness, screening and care so as to reduce incidences or threat at early detection.
Disclosure of Interest: No significant relationships.

P119

Molecular essence and treatment strategy of ER-negative/PgR-positive/HER2erhyphen;negative breast cancer

K. Yu*, Z. Shao. *Department of Breast Surgery, Cancer Center and Cancer Institute, Shanghai Medical College, Fudan University, Shanghai, China*

Goals: The clinical significance of progesterone receptor (PgR) expression in estrogen receptor (ER)-negative breast cancer is controversial, and the clinical practice guidelines such as 2013 St. Gallen consensus of early-stage breast cancerr fail to categorize the ER−/PgR+/HER2− phenotype into four known intrinsic subtypes. Here, we systemically investigated the clinicopathologic features, molecular essence, and endocrine responsiveness of this phenotype.
Methods: This study included four cohorts. The first and second cohorts were from the Surveillance, Epidemiology, and End Results database (n = 67,932) and Fudan University Shanghai Cancer Center (n = 2,338), respectively, and were used for clinicopathologic and survival analysis. The third and fourth cohorts were from two independent publicly available microarray datasets including 837 operable cases and 483 cases undergoing neoadjuvant chemotherapy, respectively, for clinicopathologic and survival analysis and gene-expression analysis. Characterized genes defining subgroups within the ER−/PgR+/HER2− phenotype were determined and further validated.
Results: Clinicopathologic features and survival outcomes of the ER−/PgR+ phenotype fell in between the ER+/PgR+ and ER−/PgR− phenotypes but were more similar to ER−/PgR−. Among the ER−/PgR+ phenotype, 23–33% were luminal-like and 56–65% were basal-like. We further refined the characterized genes for subtypes within the ER−/PgR+ phenotype and developed a feasible immunohistochemistry-based method that could determine the molecular essence of ER−/PgR+ using three markers, TFF1, KRT5,

and EGFR. After adjustment for other prognostic factors, the three-marker defined subgroup was an independent prognostic factor for relapse (HR 2.4, 95% CI 1.17–5.03, P = 0.017). Moreover, patients with a luminal-like ER−/PgR+ subtype probably benefited more from sufficient endocrine therapy (log-rank P = 0.06). In contrast, the basal-like subgroup did not benefit from endocrine therapy (log-rank P = 0.61).

Conclusion: The majority of the ER−/PgR+/HER2− phenotype are basal-like and a minority is luminal-like. Detecting immunohistochemical TFF1, CK5, and EGFR helps to identify the intrinsic subgroups within this phenotype. Basal-like ER−/PgR+ tumors obtain limited benefit from endocrine therapy, thus these patients may avoid this treatment. Further large-scale studies will be necessary to validate our findings.

Disclosure of Interest: No significant relationships.

P120

Efficacy of group logo therapy on decreasing hopelessness of women with breast cancer

S. Mohabbat-Bahar[1], M. Golzari[1], M.E. Akbari[2], M. Moradi-Joo[2]*. [1]*Faculty of Psychology and Educational Sciences, Allame Tabatabai University, Tehran, Iran,* [2]*Cancer Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

Goals: Breast cancer is the most incident cancer and the fifth cause of death due to malignancies among Iranian women. A strong sense of meaning and purpose in life of breast cancer patients appears to decrease hopelessness in their life. The present study has investigated effectiveness of group logo therapy on decreasing hopelessness in women with breast cancer who were covered by the Cancer Research Center (CRC), Shahid Beheshti University of Medical Sciences.

Methods: The research was quasi-experimental with pre-test, post-test and control group. For this purpose, 30 patients with breast cancer were selected by convenience sampling and divided into two experimental and control groups. Then, all 30 patients completed Beck Hopelessness Scale (BHS). The experimental group participated in 8 sessions of counseling through group logo therapy; however, the control group did not receive any type of psychological training. In the end, both groups were tested again. After collecting questionnaires, data was analyzed using analysis of covariance and by eighteenth edition of statistical software (SPSS).

Results: The research result has shown that group logo therapy was significantly effective in reducing hopelessness in women with breast cancer ($p < 0.0005$). In other words, this intervention could reduce hopelessness in experimental group.

Conclusion: According to the result obtained, it can be concluded that Psychological interventions such as group logo therapy could reduce the amount of hopelessness in patients with breast cancer. Hence, this intervention can be used to reduce hopelessness in breast cancer patients, in line with current medical treatments.

Disclosure of Interest: No significant relationships.

P121

Cost effectiveness study on pre-operative sentinel lymph node biopsy in patients with early breast cancers

M. Co[1]*, A. Kwong[2], V. Ma[3], K.K. Ma[1]. [1]*Department of Surgery, Queen Mary Hospital, Hong Kong, Hong Kong,* [2]*Surgery, The University of Hong Kong, Hong Kong, Hong Kong,* [3]*Department of Radiology, Queen Mary Hospital, Hong Kong, Hong Kong*

Goals: Sentinel lymph node biopsy is currently the gold standard of diagnostic workup in early breast cancers. Identification of sentinel lymph nodes by pre-operative scintigraphy has been carried out to improve the detection of sentinel lymph nodes intraoperatively. Here we analyze the cost-effectiveness of the use of scintigraphy in detection of sentinel lymph nodes in two university hospitals in Hong Kong.

Methods: Clinical and operative details were retrieved from a prospectively maintained database. The resources and cost data from all patients, who had undergone sentinel lymph node biopsy, were retrieved and analyzed.

Results: From January 2008 to December 2012, a total of 400 patients have undergone sentinel lymph node biopsy for breast cancer in two university-affiliated hospitals. 329 had pre-operative sentinel lymph node mapping with scintigraphy, while 71 patients did not receive pre-operative sentinel lymph node mapping due to logistic reasons. Baseline patient demographic data (primary tumor size and type of breast surgery received) were comparable on both arms (P = 0.15 and P = 0.22). The relapse and recurrence rate were not statistically different on both arms (Axilla relapse P = 0.64, metastasis P = 0.89, chest wall relapse P = 0.7). Detection rate of sentinel lymph nodes were the same (100%), However there was an additional cost to each patient who had undergone sentinel lymph node mapping (US$ 345.8).

Conclusion: In conclusion, pre-operative sentinel lymph node mapping does not further improve the sentinel lymph node detection rate. In addition, it does not affect the surgical outcomes in terms of local relapse and recurrence. The use of pre-operative sentinel lymph node mapping is therefore no longer cost-effective.

Disclosure of Interest: No significant relationships.

P122

Reliability of ER, PR, and HER2 status in core needle biopsy

H.C. Shin*, H. Sohn, S.J. Park. *Department of Surgery, Chung-Ang University Hospital, Seoul, Korea*

Goals: It has become increasingly important in the preoperative work up of breast cancer patients to analyze estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), and Ki67 in core needle biopsy (CNB). These factors reflect response or resistance to endocrine therapy, chemotherapy and target therapy. Furthermore, factors help to select adjuvant or neoadjuvant treatment. For accuracy of ER, PR, HER2, and Ki67 in CNB, we compared the results of CNB and those of surgical specimen.

Methods: We retrospectively reviewed data from 161 breast cancer patients whose ER, PR, HER2, and Ki67 were analyzed in both CNB and surgical specimen between 2013 and 2014. Patients who received neoadjuvant chemotherapy were exclued in this study. ER, PR, and Ki67 were determined by immunohistochemistry (IHC) and reported as percentage. The cut-off point for ER and PR was 1%, and for Ki67 was 14%. HER2 was determined by IHC and/or fluorescence in situ hybridization (FISH). HER2 positive was defined as IHC 3+ or FISH (+).

Results: The mean value in CNB and surgical specimen were 59.4% and 58.9% for ER, 46.1% and 44.6% for PR, and 24.0% and 26.8% for Ki67. The expression difference between CNB and surgical specimen for ER and PR were not statistically significant (P = 0.681 and P = 0.455, respectively). However, Ki67 level in surgical specimen was higher than that in CNB with statisticall significant (P = 0.038). According to criteria for ER, PR, HER2, and Ki67, the sensitivity of ER, PR, HER2 and Ki67 in CNB were 92.4%, 96.3%, 100%, and 81.7%, respectively. The specificity of ER, PR, HER2 and Ki67 in CNB were 85.7%, 81.7%, 97.9%, and 91.2%, respectively.

Conclusion: The ER, PR, HER2, and Ki67 in CNB were generally well correlated with surgical specimen. Among them, HER2 status of CNB was the most accurate factor compared with surgical specimen. However, Ki67 level in CNB was lower than that in surgical specimen.

Disclosure of Interest: No significant relationships.

P123

FDG-PET, MRI and USG in the assessment of axillary lymph node metastases in breast cancer

W. Byon[1]*, E. Kim[1], J. Kwon[1], B.J. Song[2], C. Park[1]. [1]*Breast & Thyroid Cancer Center, Department of Surgery, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea,* [2]*Department of Surgery, Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, Korea*

Goals: ^{18}F fluorodeoxyglucose positron emission tomography (FDG-PET) is a noninvasive imaging modality that can identify nodal metastases in women with primary breast cancer. The aim of this study was to compare the accuracy of FDG-PET with MRI and sonography scanning to determine axillary lymph node status in patients with breast cancer undergoing sentinel lymph node biopsy or axillary lymph node dissection.
Methods: Between January and December 2012, ninety-nine patients with breast cancer and clinically negative axillary nodes were evaluated. All patients underwent FDG-PET, MRI, ultrasound followed by sentinel lymph node biopsy (SLNB) or axillary lymph node dissection (ALND).
Results: Using axillary lymph node assessment as the gold standard, the sensitivity and specificity of FDG-PET were 51.4% (95% CI, 41.3% to 65.6%) and 92.2% (95% CI, 82.7% to 97.4%) respectively. The sensitivity and specificity of MRI and ultrasound were 57.1% (95% CI, 39.4% to 73.7%), 67.2% (95% CI, 54.3% to 78.4%) and 42.86% (95% CI, 26.3% to 60.7%), 92.2% (95% CI, 82.7% to 97.4%). Stratification according to hormone receptor status showed an increase in specificity when negative (FDG-PET: 42.3% to 77.8%, MRI 50% to 77.8%, ultrasound 34.6% to 66.7%). Also, positive HER2 status was associated with an increase in specificity (FDG-PET: 42.9% to 85.7%, MRI 50% to 85.7%, ultrasound 35.7% to 71.4%).
Conclusion: The sensitivity and specificity of FDG-PET compared with MRI and ultrasound was high. However, FDG-PET is not sufficiently accurate to appropriately identify lymph node metastases. This study suggests that FDG-PET scanning cannot replace histologic staging in early stage breast cancer, but might have a role in evaluating axillary lymph node status in hormone receptor negative or HER-2 overexpressing subtypes.
Disclosure of Interest: No significant relationships.

P124

Pro-neurotensin and pro-enkephalin predict breast cancer risk under hormone replacement therapy

O. Melander[1], M. Orho-Melander[1], J. Manjer[1], B. Hedblad[1], G. Engström[1], O. Hartmann[2], J. Struck[2]*, P. Nilsson[1], A. Bergmann[2], M. Belting[3]. [1]*Dept. of Clinical Sciences, Lund University, Malmö, Sweden,* [2]*Research & Development, Sphingotec GmbH, Hennigsdorf, Germany,* [3]*Dept. of Oncology, Lund University, Malmö, Sweden*

Goals: Improved risk stratification for guiding hormone replacement therapy (HRT) is an unmet need. Plasma pro-Neurotensin (pro-NT) and pro-Enkephalin (pro-ENK) have emerged as suitable markers to predict the risk of development of incident breast cancer in the general population. In a subgroup analysis of two large population based studies we assessed how pro-NT and pro-ENK in women receiving HRT are associated with the development of incident breast cancer.
Methods: We measured pro-ENK and pro-NT in fasting plasma from 1929 women (mean age 58±5.9 years) of the population based Malmö Diet and Cancer Study (MDC) free from breast cancer. We used Cox proportional hazards models to relate pro-ENK and pro-NT to first breast cancer events (n = 123) within 15 years of follow-up. In a case cohort design we measured pro-ENK and pro-NT in fasting plasma samples from 1569 women (mean age 70±4.4 years) of the population based Malmo Preventive Project (MPP), who were free from breast cancer. Multivariate adjusted logistic regression models were used to relate pro-ENK and pro-NT to first breast cancer events (n = 130) during the observation period (inclusion: 2002–2006, till end of 2010). Performance of both markers was assessed in subgroup analyses for women having received HRT at inclusion (20.3% in MDC and 11.9% in MPP).
Results: Both pro-NT and pro-ENK provide new and independent information on top of breast cancer risk factors (all $p < 0.001$): In MDC, the c index of the risk factors alone was 0.565. Adding pro-NT, pro-ENK, or both, increased the c index to 0.608, 0.594 and 0.632, respectively (all $p < 0.001$ for added value). In MPP, the c index of the risk factors alone was 0.591. Adding pro-NT, pro-ENK, or both, increased the c index to 0.730, 0.649 and 0.761, respectively (all $p < 0.001$). Within the multivariable models, pro-NT and pro-ENK are the strongest contributors, followed by HRT in both studies. In multivariable models including either pro-NT or pro-ENK, HRT, as well as their interaction term, the interaction term remained non-significant ($p > 0.287$ in all models). Kaplan–Meier plots of pro-NT >180 pmol/L and pro-ENK <44 pmol/L illustrate that the observed breast cancer risks for HRT and the biomarkers are almost 100% multiplicative.
Conclusion: Measurement of plasma pro-NT and pro-ENK can aid in the risk assessment for incident breast cancer and can contribute in the decision making on the use of HRT.
Disclosure of Interest: Dr Bergmann is CEO and holds shares in Sphingotec GmbH, which holds the patent rights for use of pro-Neurotensin and pro-Enkephalin in risk prediction of breast cancer. Dr Melander is co-inventor on the same patent applications.

P125

Breast carcinoma in situ in women with BRCA1 and BRCA2 mutations: a single institution review

C.C. Cardoso*, A. Luís, P. Machado, A. Clara, A. Opinião, S. Bento, J.L. Faria, J.C. Marques, S. Santos, F. Vaz. *Medical Oncology, Instituto Português de Oncologia Lisboa – Francisco Gentil, Lisboa, Portugal*

Goals: Germline mutations in BRCA1 and BRCA2 genes are known to cause an increase of invasive breast cancer and more recently, these mutations were found to increase the risk of breast carcinoma in situ (BCIS). Many studies in BRCA carriers showed that the preinvasive phase may be shortened or even absent in hereditary breast cancers, particularly those associated with BRCA1 mutations.
Methods: Clinical and genetic files of all BRCA 1/2 carriers registered in our Clinic were reviewed. Carriers were identified between January 2000 and December 2013 and all BCIS cases, either in breast cancer (BC) survivors or in healthy carriers, were registered. We described the pathological characteristics of BCIS, diagnosis methodology and treatment plan.
Results: Four hundred and forty-eight BRCA1/2 mutation carriers (115 BRCA1 and 333 BRCA2) were identified and reviewed (195 healthy carriers and 253 with previous cancer diagnosis). BCIS was observed in 20 patients (pts), all females and median age of 41.7 yrs. Five BCIS pts were BRCA 1 positive (4.3%), 15 BRCA2 positive (4.5%) and 7/15 BRCA2 pts were diagnosed with the Portuguese founder mutation: c.156–157insAlu. Median menarche age was 12 yrs. Five pts are childless and 15 pts had her first child at a median age of 27 yrs. For BRCA1 carriers, histological grade was high in 3 cases and intermediate in 2; estrogen receptors (ER) were positive in 2 pts, negative in 2 and not done in 1 patient (pt). For BRCA 2 carriers (1 pt with bilateral BCIS), histological grade was either high (3), intermediate (8) or low-grade (5); ER were positive in 11 cases tested and negative in 1 (4 were not done). From the 20 BCIS pts, 6 were previously non-cancer pts having their diagnosis while on surveillance. These 6 pts were diagnosed with 7 BCIS cases: 3 cases detected by MRI or mammography and 4 cases detected in prophylactic surgery specimens (one pt with bilateral

BCIS). Treatment: all 6 pts underwent bilateral mastectomy and 5 pts prophylactic adnexectomy (1 pt with 35 yrs plans for future pelvic preventive surgery). All patients are alive without disease. From the 20 BCIS pts, 14 were BC survivors and the diagnosis of BCIS was done by clinical observation (2 cases), MRI or mammography (10 cases) and by prophylactic contralateral breast surgery (2 cases). Only 6 of these 14 pts have done bilateral mastectomy. Eight had either previous conservative surgery or opted for that treatment for their BCIS and keep MRI and mammography surveillance. Seven of 14 (50%) had prophylactic adnexectomy. All pts are alive but 2 have metastatic disease under chemotherapy treatment.

Conclusion: In our BRCA1/2 carrier population, breast carcinoma in situ was detected in similar proportions in BRCA 1 or 2 mutation carriers (4.3% vs 4.5%) The frequency of BCIS in BRCA carriers is reduced 20/448 pts (4.4%). Our data confirms the relevance of radiological surveillance for detection of BCIS, although some cases were only detected after prophylactic surgeries.

Disclosure of Interest: No significant relationships.

P126

Incidence of vitamin D deficiency during breast cancer treatment

J. Lee[1]*, M.H. Lee[1], S.Y. Kim[2]. *[1]Surgery, Soonchunhyang University Hospital, Seoul, Korea, [2]Surgery, Soonchunhyang University Hospital, Chunnan, Korea*

Goals: Vitamin D levels has been considered to be inversely related to breast cancer development, recurrence risk, and mortality. Mean vitamin D levels in Korean population is lower than western countries due to higher incidence of lactose intolerance and lower exposure to sunlight. The purpose of this study was to assess incidence of vitamin D deficiency during breast cancer treatment with comparison of general population.

Methods: Breast cancer patients seen at a single tertiary cancer center were enrolled (n = 280). Serum 25-hydroxyvitamin D [25(OH)D] was measured at the time of surgery and after completion of adjuvant chemotherapy. Non-cancer controls were selected from Korean National Health and Nutrition Examination Surveys 2011 (n = 3316). Statistical analyses used chi-square test, Fisher's exact test, t-test, and ANOVA.

Results: The 25(OH)D levels were deficient (<20 ng/ml) in 190 patients (67.9%), insufficient (20–29 ng/ml) in 51 patients (18.2%), and sufficient (30–150 ng/ml) in 39 patients (13.9%). There was no difference ($p = 0.022$) of serum 25(OH)D level between breast cancer patients (mean 18.5 ng/ml) and non-cancer controls (17.4 ng/ml). A notable decrease in 25(OH)D concentration was observed (17.4 ng/ml vs 13.1 ng/ml, $p < 0.001$) after chemotherapy but was not related to chemotherapy regimens. It was found significant lower 25(OH)D levels at winter season (from October to March, $p = 0.030$). Subjects with invasive carcinoma had significantly lower circulating levels of 25(OH)D than those with ductal carcinoma in situ (DCIS) ($p = 0.010$).

Conclusion: A decrease of serum vitamin D level was observed after chemotherapy in breast cancer patients. Most of the breast cancer patients showed deficient or insufficient serum vitamin D concentration. Consideration should be given to the supplement of vitamin D to those patients.

Disclosure of Interest: No significant relationships.

P127

Metabolic syndrome and breast cancer risk by molecular subtype

E. Esposito[1]*, M. De Laurentiis[1], M. Montella[2], N. Maurea[3], M. D'Aiuto[1], E. Cavalcanti[4], M. Grimaldi[2], G. D'Aiuto[1], G. Ciliberto[1], I. Capasso[1]. *[1]Department of Breast Surgery and Cancer Prevention, Istituto Nazionale per lo Studio e la Cura dei Tumori "Fondazione Giovanni Pascale", IRCCS, Naples, Italy, [2]Department of Epidemiology, Istituto Nazionale per lo Studio e la Cura dei Tumori "Fondazione Giovanni Pascale", IRCCS, Naples, Italy, [3]Department of Cardiology, Istituto Nazionale per lo Studio e la Cura dei Tumori "Fondazione Giovanni Pascale", IRCCS, Naples, Italy, [4]Department of Med Lab and Clinical Pathology, Istituto Nazionale per lo Studio e la Cura dei Tumori "Fondazione Giovanni Pascale", IRCCS, Naples, Italy*

Goals: Metabolic syndrome (MS) has been shown to increase the risk of breast cancer. Existing data suggest that the strength of metabolic syndrome-breast cancer link varies by intrinsic molecular subtype, but results from worldwide literature are controversial. Primary endpoint of the study was to assess whether MS is a predictor of specific breast cancer subtype. Secondary endpoint was to determine whether components of MS can individually increase the risk of specific breast cancer subtype.

Methods: Anthropometric and metabolic variables were correlated to breast cancer specific subgroups, retrospectively. Statistical significance was considered when $p \leq 0.05$ and 95% CI.

Results: Data analysis suggests MS per se prevalence is higher among Luminal breast cancers in postmenopausal [OR 1.37 (95% CI 1.07–2.80), $p = 0.03$]. Body Mass Index alone is associated to Luminal A subtype breast cancer risk [OR 1.12 (95% CI 0.96–2.19), $p = 0.2$]. Waist Circumference >88 cm has been shown to be specifically and statistically significant associated to HER-2+ breast cancer subtypes in postmenopausal [OR 2.72 (95% CI 1.69–10.72), $p = 0.01$], whilst in Luminal B it was only marginally statistically associated [OR 2.21 (95% CI 0.77–2.60), $p = 0.1$]. Insulin resistance showed statistical significant linkage to HER-2+ and Luminal B tumours [OR 2.11 (95% CI 1.66–6.69), $p = 0.05$, and OR 2.33 (95% CI 1.2–4.2), $p = 0.006$, respectively]. Hence, it has emerged that BMI is weakly associated to Luminal A breast cancers in this case series, whereas visceral obesity and insulin resistance are likely to be linked to more aggressive breast cancer subtypes.

Conclusion: The newest concept of breast cancer as a metabolic disease will impact approaches to cancer management and prevention. Personalised risk assessment and tailored therapies should be now considered in the light of the patient's metabolic profile in both chemopreventive and adjuvant settings. Further studies on larger samples are needed in order to increase the pre-clinical and clinical research.

Disclosure of Interest: No significant relationships.

P128

Nipple aspirate fluid (NAF) cytology in the IBIS-model prediction of breast cancer (BCA) risk

J.W. Kylstra[1]*, M. Kalnoski[2], S. Quay[3], S. Chen[3], T. Vo[2], J. Cuzick[4]. *[1]Clinical Research, Atossa Genetics, Seattle, United States of America, [2]Natl. Reference Lab for Breast Health, Seattle, United States of America, [3]Atossa Genetics, Seattle, United States of America, [4]Centre for Cancer Prevention, Queen Mary University of London, London, United Kingdom*

Goals: Ductal Hyperplasia, along with familial factors and reproductive history, is part of most BCa predictive algorithms including the Gail and IBIS (Tyrer-Cuzick) models, conferring a 1.9–4.2 fold risk increase for benign- and atypical hyperplasia, respectively [Hartmann et al., NEJM 2005; 353: 229–37). However, absent of prior biopsy, information on ductal pathology is usually

absent, leading to underestimation of BCa risk with consequent failure to identify many who could benefit from preventive strategies. We explored the contribution made by ductal pathology information to IBIS' ability to classify women to low-, intermediate-, and high 10-year risk groups. Per current UK-guidelines (e.g. NICE, 2013), women classified in the upper 2 risk strata are eligible for counseling or preventive strategies, incl. chemoprevention.
Methods: IBIS risk factors were recorded from asymptomatic women without prior history of BCa during routine periodic wellness exams. To assess ductal hyperplasia, bilateral NAF-specimens were collected with the ForeCYTE Breast Aspirator. Alcohol spray-fixed and stained per Papanicolaou, paper filters containing NAF-specimens were placed directly under the microscope. Cytology was graded per King Classification (Class II = hyperplasia w/o atypia; Class III = atypical hyperplasia). IBIS risk was calculated with and without hyperplasia information in the model, and each woman classified to one of 3 groups: high (≥8%), intermediate (>5≤8%), and low (≤5%) 10-year risk. Analysis was stratified by age (<45 vs ≥45).
Results: Complete information on IBIS parameters incl. hyperplasia was available for 832 women age ≥45 and 509 age <45. Absent hyperplasia information in the model, IBIS classified 3.7% (19/509) of women age <45 and 20.6% (171/832) age ≥45 as having >5≤8% 10-year risk; 1.4% (7/509) women age <45 and 4.2% (35/832) women age ≥45 were classified to ≥8% 10-year risk. Low risk were 483 women age <45 and 626 women age ≥45. With hyperplasia information for all women added to IBIS, the number classified to ≥8% 10-year risk increased to 13.9% (71/509) for women age <45 and 11.2% (93/832) for age ≥45. 11 women age <45 (2.3%) and 15 women age ≥45 (2.4%) moved from low (≤5%) to intermediate (>5≤8%) 10-year risk with addition of ductal pathology information. No NAF-collection was interrupted or aborted because of discomfort.
Conclusion: In an asymptomatic population, availability of ductal pathology information aids the IBIS model in identifying substantially more women at increased risk for BCa. Screening programs identifying women for preventive strategies or trials can greatly improve their efficiency or "catchment ratio" by having ductal pathology status available for all women evaluated, with NAF a convenient method to obtain such information. Among various risk factors in BCa predictive algorithms, hyperplasia is the most actionable, as it presents a potential target for therapeutic intervention.
Disclosure of Interest: Atossa Genetics employee.

P129
Breast cancer screening by evaluating amino acid levels in the blood

M. Suzuki*. *Breast Center, Kitamurayama Hospital, Higashine Yamagata, Japan*

Goals: In healthy people, the concentrations of amino acids in blood plasma are maintained at stable levels while they are metabolized among various organs. We know that cancers disturb the balance of amino acids in the blood. AICS (AminoIndex® Cancer Screening) is a test that measures the concentration of amino acids in the blood and statistically analyzes the differences in the balance of amino acid concentration between healthy people and those with cancer. The alteration in amino acid balance is unique for each type of cancer, so AICS can evaluate multiple types of cancer simultaneously from a single blood test. The test is easy to perform because only 5 ml of blood are needed. Currently, AICS is able to aid in the detection of gastric cancer, lung cancer, colorectal cancer, prostate cancer, breast cancer and uterine/ovarian cancer. The aim of this study is to assess the usefulness of AICS for breast cancer screening.
Methods: AICS counts the balance of amino acids as an AICS value, using numerical figures between 0.0 and 10.0, which represents the probability that a person may have cancer. The larger the value, the higher the probability. Patient results are assigned to three rank categories: An AICS value between 0.0 and 4.9 is Rank A, a value between 5.0 and 7.9 is Rank B, and a value between 8.0 and 10.0 is Rank C. In our hospital, 115 healthy women were tested both with AICS and also by mammography to detect breast cancer.
Results: Out of 115 women, 82 were in Rank A, 24 were in Rank B and 9 were in Rank C. The mammography screening showed that two women had malignant shadows – one in Rank B and one in Rank C. Both were diagnosed with breast cancer (invasive ductal carcinoma) by pathological examination. No breast cancer was found in Rank A. So, in this study at our hospital, the rate of occurrence was 0.00% in Rank A, 4.17% in Rank B, and 11.1% in Rank C. From these results, in the case of Rank B or Rank C in AICS, we have to push forward inspection such as mammography.
Conclusion: AICS can aid to detect breast cancer and it may be useful for breast cancer screening.
Disclosure of Interest: No significant relationships.

P130
Investigation by questionnaire of the employment of Japanese breast cancer patients

H. Kotani*, N. Kondou, J. Ishiguro, T. Hisada, Y. Adachi, M. Ichikawa, A. Yoshimura, M. Hattori, M. Sawaki, H. Iwata. *Department of Breast Oncology, Aichi Cancer Center Hospital, Nagoya, Japan*

Goals: Breast cancer (BC) is the most common cancer among women and its survival rate has been improved. As the number of cancer survivors increases, it is important to support their social comeback during and after their treatment. The purpose of this study is to reveal the changes in the working style through-out the treatment of Japanese BC patients with work.
Methods: The questionnaires were distributed to the BC patients treated or followed-up in Aichi Cancer Center Hospital between June and November 2014. Eligibility criteria were age 20–65 years, having operation for BC at least 1 year earlier and under employment at the time of diagnosis. Patients were divided into 3 groups according to the adjuvant therapy (Group A: none, B: endocrine therapy, C: chemotherapy). Three hundred patients in total and 100 patients in each group were scheduled to enroll. The questionnaire includes patient's background, treatment given, kind of occupation, changes in working situation (i.e. quit, duration of absence, shortened work time) and any anxiety about working.
Results: The study included 233 patients who returned the questionnaire until this analysis (Groups A, B, C: 62, 79, 92 respectively). Of these patients, 29 (12.4%) did not tell their employer about their cancer and 43 (18.5%) quit their job during or after the treatment. As to the time of quitting, most patients had quit their jobs at the time of diagnosis (7.3%) followed by those undergoing chemotherapy (5.4%) and at the time of operation (4.7%). In each group, the quit rate was the highest in group C (28%) followed by group B (20%) and lastly group A (8%). At the time of operation, 127 patients (55%) were absent from work, the duration of absence varied according to the method of operation. [Median absence duration (weeks): Bp+SLNB 3, Bp+ALND 4, Bt+SLNB 6, Bt+ALND 7]. The rates of patients currently working who have anxiety are 34%, 26% and 9.7% in groups C, B and A, respectively.
Conclusion: As the quit rate was highest at the time of diagnosis, consultation about working is necessary immediately after diagnosis. The patients treated heavily have higher quit rates and more anxiety about working, therefore, more careful consultation is needed for these patients. The study results provide the useful information about their working style for Japanese BC patients with work.
Disclosure of Interest: No significant relationships.

P131

Targeted ultrasonography for MRI-detected lesions of preoperative breast cancer patients

S. Hayama[1]*, M. Sakakibara[1], H. Takishima[2], T. Nagashima[1], T. Sangai[1], K. Fujimoto[1], M. Miyazaki[1]. [1]*General Surgery, Chiba University Graduate School of Medicime, Chiba shi Chuuou ku, Japan,* [2]*Radiology, Chiba University Graduate School of Medicime, Chiba shi Chuuou ku, Japan*

Goals: Magnetic resonance imaging (MRI) is commonly performed to preoperatively evaluate the extent of breast cancer. However, proper management of secondary lesions detected by using MRI is sometimes challenging. Although MRI-guided biopsy is recommended to examine such lesions, the procedure is rarely performed. Therefore, these lesions are often investigated by using ultrasonography (US). Furthermore, the treating physicians might not always be familiar with the MRI lexicon by the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) for the management of MRI-detected lesions, possibly because MRI and US findings do not always correspond. The aim of this study was to examine the identification and malignancy rates of MRI-detected lesions by using US in preoperative breast cancer patients based on the BI-RADS lexicon.
Methods: Of the 725 primary breast cancer patients who underwent preoperative breast MRI at Chiba University Hospital between November 2011 and June 2014, 102 were detected with secondary lesions and included in this study. We retrospectively analysed the identification rate of these lesions by using US and their malignancy frequency based on the BI-RADS classification.
Results: MRI detected a total of 111 lesions, including 24 belonging to category 2, 40 of category 3, 45 of category 4, and 2 of category 5. The identification rates on US for each category were 50%, 60%, 89%, and 100%, respectively. Biopsy was performed to examine all lesions detected on US, and the malignancy rates for each category were 0%, 29%, 55%, and 100%, respectively. One patient who was diagnosed with category 4 lesions on MRI but undetectable on US eventually showed a relapse.
Conclusion: The application of US for MRI-detected lesions is useful and convenient. However, approximately 10% of the cases with an MRI category of ≥4 were undetectable on US, especially non-mass enhancement lesions. Therefore, it is critical to improve detection capability, for example, by using real-time virtual sonography or repeating MRI within a short time period.
Disclosure of Interest: No significant relationships.

P132

Medical conditions of long term breast cancer survivors

J. Lee[1], J.E. Lee[2]*, S.Y. Kim[2], M.H. Lee[1], H.K. Jung[1]. [1]*Surgery, Soonchunhyang University Hospital, Seoul, Korea,* [2]*Surgery, Soonchunhyang University Hospital, Chunnan, Korea*

Goals: Breast cancer survival has been increased due to awareness of screening and development of treatment. Survivors experiences persistent or late effects of cancer treatment such as lymphedema, osteoporosis, and cardiovascular diseases. Those complications affect their quality of life. In this study, we assessed medical conditions of long term breast cancer survivors to evaluate prevalence of persistent and late effects of breast cancer treatment.
Methods: Selected data from The Korea National Health and Nutrition Examination Survey (2009–2012) was used for evaluation. We identified long term breast cancer survivors (diagnosed more than 5 years ago) in the survey population. Non-cancer control group were selected with 1:4 matching of age, sex and the survey year. Medical examination and questionnaire were evaluated.
Results: Long term breast cancer survivors (n = 90) and non-cancer controls (n = 360) were included in this study. Except breast feeding history (81.8% in survivors and 92.6% in controls, p = 0.015), both groups were balanced in menopausal status, history of pregnancy, area of residence, and educational status. Self-estimated health status was better in breast cancer survivors (67.91±17.20) than in non-cancer controls (44.84±21.47) but it was not statistically significant (p = 0.143) No difference was found in incidence of cardiovascular diseases (myocardial infarction, hypertension, and angina diagnosed by doctor). Smoking, alcohol intake, and intensity of physical activity did not show differences. Incidence of osteopenia and osteoporosis measured by bone marrow density examination was not significantly different between survivors and controls (33.3% vs 40.6%, and 59.0% vs 40.6%, p = 0.121). Mean vitamin D levels were deficient (18.35±7.37 vs 17.53±6.71) in both groups, and there were no difference in hemoglobin level, fasting glucose, and lipid profiles.
Conclusion: No significant difference was found in health status between long term breast cancer survivors and non-cancer population based on health survey and examination. Specified questionnaire and medical record review is required for evaluation of late effects in breast cancer survivors.
Disclosure of Interest: No significant relationships.

P133

Evocative epidemiology of female breast cancer in Delhi, India

P.K. Julka[1]*, N. Manoharan[2], O. Nair[1], G.K. Rath[1]. [1]*Department of Radiation & Oncology, All India Institute of Medical Sciences, New Delhi, India,* [2]*Department of Cancer Registry, All India Institute of Medical Sciences, New Delhi, India*

Goals: To describe the epidemiology and trends in breast cancer incidence in Delhi using population based cancer registry data.
Methods: A total of 15244 cancer cases were registered during the period 1st January 2009 to 31st December 2009. This recently completed cancer data of the year 2009 was collected by Delhi Population Based Cancer Registry (PBCR) from more than 162 government hospitals/centers and 250 private hospitals and nursing homes situated in Delhi and has been utilized to discuss descriptive epidemiology of breast cancer. Crude rate, Age-standardized incidence rates (ASR) and age-specific incidence rates has been calculated. Time trends have been studied using twenty-two years of data collected by Delhi PBCR from the year 1988 to 2009. Breast cancer trend was analysed using Joinpoint regression.
Results: Among 15244 cancer registered cases 8122 were males and 7122 females in 2009. Breast cancer was the leading site of cancer among females and it constituted about 1927 (27.1%) cases with a median age of 51 years. The crude and age standardized incidence rates for breast cancer were 23.4 and 32.9 per 100,000 females respectively. The age specific incidence rates increased with age and attained a peak at 60–64 years age group. Invasive ductal carcinomas are the most frequently reported histology. A statistically significant increase in ASR with an annual percentage change (APC) of 1.1% was observed. From the age group 45–54 years onwards a significant increase was noted.
Conclusion: Breast was the second most common site of cancer in Delhi (576 cases) with ASR of 24.8 per 100,000 preceded by carcinoma of cervix (ASR 25.9 per 100,000) in 1988. In two decade the median age which was 46 years in 1988 has become 51 years in 2009. Over the years the incidence of breast cancer increased gradually and surpassed cancer of cervix. The same trend was also noted in other metropolitan cities viz. Bangalore, Bhopal and Chennai except Mumbai where breast cancer remains the leading site of cancer since inception of the registry in 1982. Though the age standardized incidence rate of breast cancer in Delhi is comparable with other metropolitan cities of India, it is low compared to Western countries. Changing life styles in metropolitan cities like delayed marriage, late age at first child birth, lower parity and higher socio

economic status, may be some of the probable primary cause for higher incidence of breast cancer in urban areas.
Disclosure of Interest: No significant relationships.

P134
The IEO breast cancer data base: two decades of breast cancer treatment

B. Santillo*, N. Rotmensz. *Data Quality Control Unit Division of Epidemiology and Biostatistics, European Institute og Oncology, Milan, Italy*

Goals: After its first 20 years of activity, the 'young' European Institute of Oncology (IEO), has become a pole of attraction for oncological cure in general and breast cancer in particular. Over 33% of the patients in our Institute are treated for breast cancer. This anniversary is the occasion to take stock of the situation.
Methods: Since all data of patients operated are prospectively recorded in an institutional data base, and used for weekly multidisciplinary discussions, we decided to photograph the change of patient status at presentation, change in type of surgery performed and adjuvant treatment proposals. It has been chosen to present the results freezed at 1st year (mid 1994–1995), after 10 years (2004) and at the 20th year since beginning (2014). For homogeneity of analysis, only invasive disease has been considered.
Results: If during the first years only a few hundreds of patients were operated yearly, in 2004, the peak of 2000 new cases was reached and remained relatively stable up to 2014. Geographic origin (increase number of far away living and foreign patients), age (elder), type of surgery (more mastectomy), histological type and subtypes, stage and obviously treatment proposal have changed over the years and will be discussed.
Conclusion: Our long lasting data collection has offered the possibility of retrospectively analyse our population, detect change in characteristics, stage of disease and clinical practice, orient new strategy and last but not least has resulted in more than 150 articles published in peer reviewed journals.
Disclosure of Interest: No significant relationships.

P135
Regular image follow up of contralateral breast in metachronous bilateral breast cancer

S.H. Kang*, H. Kim. *General Surgery, Breast Division, Keimyung University School of Medicine, Daegu, Korea*

Goals: Regular mammographic follow up is recommended to patients with previous history of breast malignancy in many clinics to detect contralateral breast cancer development. We aimed to evaluate the effect of regular radiologic follow up on early detection of contralateral breast cancer and prognosis in patients with metachronous bilateral breast cancer.
Methods: We reviewed medical record of all breast malignant patients in our institute from 1983 to June 2014 and we found 49 (1.7%) patients of metachronous bilateral breast cancer. Patients with bilateral breast cancer within 6-month interval, bilateral cancer through direct spread, non-compliance who had delayed surgery were excluded, so that 44 patients were included. We divided these 44 patients into two groups whether or not regular radiologic follow up and compared clinicopathologic factors including age, stage, time interval of 1st and 2nd cancer, operation method and breast cancer specific survival. We used SPSS for statistical analysis. The significance for difference between two groups was performed with chi-square test. The significance for survival was performed with Kaplan–Meier method, log rank test and Breslow test.
Results: Mean age of 1st and 2nd breast cancer diagnosis in total patients was 43.8 years and 49.2 years. Mean time interval between 1st and 2nd cancer was 68.9 months. In situ carcinoma was found in 5 (11.4%) patients, stage 1 in 11 (25%), stage 2 in 21 (47.7%), stage 3 in 6 (13.6%) as stage at diagnosis of 1st breast malignancy. Median follow up period was 150 months. Recurrences in total cohort were found in 13 patients (29.5%), seven patients' deaths were breast cancer specific. Regular radiologic follow up with annual mammography with or without ultrasonography was performed in 28 patients (63.6%, group 1), however, 12 patients (27.3%, group 2) did not have regular follow up. Another four patients (9.1%) had no medical information about follow up.
With regard to second breast cancer, stage 0 and 1 malignancies were more in group 1 than in group 2 (82.1% vs 25.0%, $p = 0.006$) and patients with same or decreased stage were more in group 1 than group 2 (71.4% vs 33.3%, $p = 0.042$). However, time interval between 1st and 2nd cancer did not show statistical difference (68.7 and 74.1 months, $p = 0.801$) and breast cancer specific survival between two groups showed minimal superior to group 1 with borderline significance ($p = 0.043$).
Conclusion: Regular radiologic follow up for contralateral breast of known breast cancer patients can absolutely lead to early detection for second cancer. However, time interval between 1st and 2nd cancer is no difference and the benefit of breast cancer specific survival is slightly better with borderline significance.
Disclosure of Interest: No significant relationships.

P136
Diagnostic impact of magnetic resonance imaging in ultrasound occult breast calcification

W. Wang*. *Comprehensive Breast Health Center, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China*

Goals: X-ray mammography (XRM) is important for breast calcification detection, especially for some ultrasound occult calcification. However, false-positive findings occur and lead to unnecessary biopsy. The purpose of this investigation was to identify the values of magnetic resonance imaging (MRI) in this part of patients.
Methods: The study involved 226 calcified lesions in 207 asymptomatic patients admitted between January 2011 and March 2014. Eligible for investigation were ultrasound occult breast calcification classified as BI-RADS 4–5 in the initial mammography that all had MRI test and histopathologic verification. Accordingly, 207 patients with 42 malignant and 184 benign lesions were enrolled. Two blinded observers reviewed the MRI images of the calcification and categorized lesions into mass or nonmass and used BI-RADS to classify the lesions.
Results: In the diagnosis of breast cancer in ultrasound occult calcification, sensitivity for mammography and MRI were 69% vs. 85.7% ($p = 0.068$), and specificity were 64.7% vs. 88% ($p < 0.001$). The diagnostic sensitivity was significantly higher for combined MRI+XRM (100%, $\chi^2 = 11.08$, $P < 0.005$) than for XRM alone, and the negative predictive value was increased from 90.2% to 100%. In the malignant calcification, 11.9% (5/42) had no abnormality in MRI and 78.6% (33/42) were nonmass-like enhancement, while 78.3% benign calcification had no abnormality in MRI ($p < 0.001$). 78.5% malignant calcifications were carcinoma in situ (CIS) or had CIS part, and 81% were hormone-receptor positive.
Conclusion: Additional breast MRI can improve the diagnostic sensitivity of mammography in ultrasound occult calcification. According to the high negative predictive value, some patients may avoid biopsy or operation. Nonmass-like enhancement in MRI is more common in malignant calcification. Most of ultrasound occult malignant calcification had carcinoma in situ and were hormone-receptor positive.
Disclosure of Interest: No significant relationships.

P137

Sexuality, childbearing, parenting concerns – needs in young breast cancer patients

M. Burgmann[1], R. Wuerstlein[1]*, K. Hermelink[1], F. Van Meegen[1], J. Engel[2], N. Harbeck[1]. [1]*Breast Center, University Hospital Munich – Grosshadern, Munich, Germany,* [2]*Medical Informatics, Biometry and Epidemiology, Munich Cancer Registry of the Munich Cancer Center, Munich, Germany*

Goals: By definition, young breast cancer (BC) patients are <40 years old at diagnosis. These patients, who are affected by cancer in a particularly active period of life, have special concerns regarding sexuality and partnership, fertility and childbearing, cancer-related distress of minor children, and professional career. This study aimed to evaluate special needs and psychosocial problems of young women with BC to improve support strategies for this group of patients.

Methods: Patients <40 years old at diagnosis who had been treated at LMU Breast Center between 2006 and 2013 were eligible for participation. Standardized questionnaires assessing life satisfaction (Life Satisfaction Questionnaire, Fahrenberg et al., 2000) and cancer-specific distress (Questionnaire on Stress in Cancer Patients, Herschbach et al., 2003), as well as a self-developed questionnaire on partnership, desire for children, parenting concerns, employment situation, and demographic and medical data were sent by mail in January 2014.

Results: 88 patients (mean age 34.5) were enrolled (55% response rate). Compared with population data stratified for age and sex, patients showed significantly less satisfaction in the domains of health ($p < 0.001$) and sexuality ($p = 0.002$) but not in any other domains or overall life satisfaction. The most pronounced cancer-specific problems were cancer-related fears, psychosomatic problems like fatigue or nervousness, and reduced sexual activity. Current desire to have children was reported by 45.8% of patients and another 15.6% were uncertain, but only 21.7% actually planned to have children. The most frequently reported reasons to refrain from childbearing were shortened life expectancy, negative impact of pregnancy on prognosis, and treatment-related infertility. Of 55 patients who retrospectively evaluated their decision for or against fertility preservation, 76.4% were satisfied with their choice while 5.5% expressed regret and 18.2% were not sure. Of mothers of minor children, 41.7% indicated that they had had counselling needs regarding parenting concerns that had not been met.

Conclusion: Young BC patients have unmet counselling needs regarding childbearing after BC treatment and minor children's cancer-related distress while fertility issues seem to be well established and sufficiently implemented in medical consultations. Cancer-related fears, psychosomatic problems, and sexual problems considerably stress young patients and need to be implemented in supportive care programs for these patients.

Disclosure of Interest: No significant relationships.

P138

Comparison of breast cancer disease characteristics between female and male elderly patients

V. Posarac[1]*, M. Jevric[1], S. Susnjar[2], O. Djokic[3], S. Pupovac[2], D. Gavrilovic[4]. [1]*Surgical Oncology, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia,* [2]*Medical Oncology, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia,* [3]*Medical Center Sabac, Sabac, Serbia,* [4]*Data Center, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia*

Goals: To compare the disease characteristics between female and male elderly breast cancer (BC) patients (pts).

Methods: We identified 98 elderly (≥65 years) BC female pts diagnosed and treated for stage 1–3 BC during 2001/2002 and 61 elderly male BC pts diagnosed with stage 1–3 BC from 1994 to 2010. All of them were treated with curative intent by surgery +/− pre- or postoperative radiotherapy (RT) +/− (neo)adjuvant chemotherapy (CHT). Hormone receptor (HR) status was determined either by classical biochemical DCC method (ER-pos if ≥10 fmol/mg protein and PR-pos if ≥20 fmol/mg protein) or by immunohistochemistry (IHC) and HER2 status by IHC method. Statistics included: Pearson χ^2 test and Fisher exact test.

Results: BC characteristics in elderly female and male pts are presented in Table 1.

Table 1.

Disease characteristic	Female pts	Male pts
Age (median, range) years	70 (65–79)	72 (65–84)
BC Stage		
stage 1	19%	12%
stage 2	52%	48%
stage 3	27%	40%
BC Histology		
Ductal invasive	50%	79%
Lobular invasive	39%	7%
Tumor size		
≤20 mm	43%	31%
>20 mm	45%	38%
Tumor grade		
Grade 1	4%	8%
Grade 2	90%	74%
Grade 3	4%	5%
Nodal status		
Node negative	42%	34%
Node positive	42%	39%
HR status		
HR negative	16%	5%
HR positive	62%	54%
HER2 status		
HER2 negative	–	16%
HER2 positive	–	–
HER2 unknown	100%	84%
Follow up (median, range) mos	109 (7–148)	46 (5–199)
Disease relapse	32%	59%
Death	52%	48%
Death w/o disease relapse	28%	0

All female and almost all male BC pts who were treated with adjuvant systemic therapt received CMF and endocrine therapy with tamoxifen.

Conclusion: Generally, our results showed that there are no substantial differencicies of BC disease characteristics between elderly male and female pts. However, male BC pts are presented more frequently in stage 3 disease compared to female pts and all male pts who died experienced disease relapse compared to female population where 28% died w/o BC progression.

Disclosure of Interest: No significant relationships.

P139

Prognostic value of troponin I for chemotherapy-induced cardiac dysfunction in breast cancer patients

Y. Adachi*, A. Yoshimura, M. Ichikawa, J. Ishiguro, H. Kotani, T. Hisada, M. Hattori, N. Kondou, M. Sawaki, H. Iwata. *Breast Oncology, Aichi Cancer Center Hospital, Nagoya, Japan*

Goals: Although anthracycline (ADR) and trastuzumab (T) are effective drugs for breast cancer patients, the use of these drugs sometimes cause severe left ventricular dysfunction. Monitoring by using echocardiography is usually recommended to follow the patients treated by ADR and/or T. However, a routine echocardiography may be an inconvenience for the patients, therefore the use of biochemical marker methods has been

suggested. Some paper reported that elevation of troponin I was associated with cardiac dysfunction in patients with malignancies who are undergoing chemotherapy. However, its impacts on the clinical outcome of troponin I in Japanese breast cancer patients who are administered ADR and/or T have never been investigated. The aim of this study was to assess the usefulness of high sensitivity cardiac troponin I [hs-cTnI] in the identification of ADR and/or T induced cardiotoxicity in Japanese breast cancer patients.

Methods: This retrospective study involved primary (78%) or metastatic breast cancer patients (22%) who were administered ADR and/or T from February 2013 to December 2013 at Aichi Cancer Center Hospital (ADR: 20%, ADR+T: 50%, T: 30%, median age: 58 years). Two patients had cardiac arrhythmia and 2 patients had carcinomatous pericarditis. We evaluated serum hs-cTnI by using preserved blood samples in 198 patients for whom echocardiography was performed within seven days from sampling blood. Pearson's correlation between log hs-cTnI and left ventricular ejection fraction (LVEF) and sensitivity and specificity of hs-cTnI in diagnosis of cardiac dysfunction were evaluated. Cardiac dysfunction was defined as LVEF ≤45.

Results: Cardiac dysfunction was diagnosed in 3 patients (1.5%). Two of these patients had asymptomatic cardiac dysfunction. Although a modest correlation was identified between log hs-cTnI and LVEF ($r = -0.24$, 95% confidence interval [CI]: −0.37 to −0.11), hs-cTnI had a good diagnostic performance in identifying patients with cardiac dysfunction (AUC: 0.91, 95% CI: 0.85 to 0.97). When the cut off level of hs-cTnI was defined as 7.5 pg/ml, it provided the highest sensitivity and clinical benefit for identifying all of the patients with cardiac dysfunction, including asymptomatic cardiac dysfunction (sensitivity: 100%, specificity: 86%).

Conclusion: hs-cTnTI might be used for identification of cardiotoxicity induced by ADR and/or T in Japanese breast cancer patients.

Disclosure of Interest: No significant relationships.

P140
Identification of BRCA1/2 germline mutations by integrated approach

A. Kwong[1] *, J. Chen[1], V. Shin[1], F. Law[2], T. Chan[2], J. Ford[3]. [1]*Surgery, The University of Hong Kong, Hong Kong, Hong Kong,* [2]*Pathology, The Hong Kong Sanatorium and Hospital, Happy Valley, Hong Kong,* [3]*Oncology, Stanford University School, California, United States of America*

Goals: Germline BRCA gene mutations have been demonstrated to be associated with hereditary breast cancer and ovarian cancer. Identification of BRCA mutations would greatly improve the preventive strategies and management of breast cancer. Sanger sequencing has been the gold standard in identifying these mutations. However, 4–28% of inherited BRCA mutation may due to large genomic rearrangements (LGRs) of these genes which could be missed by using Sanger Sequencing alone. This study aims to evaluate the pick-up rate of LGRs in our cohort. Germline BRCA gene mutations have been demonstrated to be associated with hereditary breast cancer and ovarian cancer. Identification of BRCA mutations would greatly improve the preventive strategies and management of breast cancer. Sanger sequencing has been the gold standard in identifying these mutations. However, 4–28% of inherited BRCA mutation may due to large genomic rearrangements (LGRs) of these genes which could be missed by using Sanger Sequencing alone. This study aims to evaluate the pick-up rate of LGRs in our cohort.

Methods: A total of 1,463 clinically high-risk patients with breast cancer and/or ovarian cancer based on age of onset, family history of breast and ovarian cancer, tumor biological subtype including triple negative breast cancer (TNBC) were recruited through The Hong Kong Hereditary Breast Cancer Family Registry from 2007 to 2014. Full gene sequencing (either Sanger sequencing or Next-generation sequencing) and multiplex ligation-dependent probe amplification (MLPA) were performed.

Results: From 2007 to 2014, we identified 126 deleterious BRCA mutations in the recruited high-risk probands. A total of 56 (3.83%) gene mutations were in BRCA1 and 70 (4.78%) in BRCA2. BRCA1-positive probands had a significantly younger age of diagnosis when compared with BRCA2-positive probands ($p = 0.03$). The frequency of TNBC is significantly higher in BRCA-positive than in BRCA-negative probands ($p = 0.0001$) and TNBC are more likely to be associated with BRCA1-positive than BRCA2-positive probands ($p = 0.01$). Overall these LGRs accounted for 6.35% (8/126) of all BRCA mutations in our cohort, in which 8.93% (5/56) of BRCA1 mutations and 4.29% (3/70) of BRCA2 mutations. One of the mutations was de novo and only identified in proband but not in any of the family members.

Conclusion: Through this integrated approach, both small nucleotide variations and LGR could be detected. We suggest MLPA should incorporate in the standard practice for genetic testing to avoid false negative results which would greatly affect the management of these high-risk families.

Disclosure of Interest: No significant relationships.

P141
3-D temporal resolution characteristics of breast lesions from breast MRI

R. Lin[1] *, J. Ouyang[1], P. Huang[2], H. Lee[3]. [1]*Institute of Medical Sciences, Tzu Chi University, Hualien, Taiwan,* [2]*Taitung Women's Breast Health Center, St. Mary's Hospital, Taitung, Taiwan,* [3]*Department of Medical Informatics, Tzu Chi University, Hualien, Taiwan*

Goals: Breast Magnetic Resonance Imaging (breast MRI) better predicts breast malignancy by using the dynamic contrast enhanced kinetic patterns of the Breast MRI. Traditionally, radiologists write MRI reports by reading a series slice by slice using two-dimensional (2D) information, which cannot judge the whole mass morphology robustly. The purpose of this research is to provide 3-D temporal resolution characteristics of breast lesions from breast MRI to specialists for diagnosis.

Methods: From an IRB approved project, this study collected MR images and clinical records of 93 patients with an unclear mass, including a total of 129 breast lesions. The numbers of benig and malignant lesions were 44 and 85 respectively. All MR studies were conducted at Aurora 1.5T breast-dedicated MRI contains three sets of volumetric data in a specific order of time before and after contrast agent was injected into the patient. The various kind of enhancements might show three types of the kinetic curve resulting from 3-D temporal resolution (3D-TR), that is, persistent pattern (type I), plateau pattern (type II) and washout pattern (type III). Types II and III have higher percentage of malignant breast cancer lesions in recent study. The kinetic cancer volume (KCV) for each type of kinetic curves is define as their ratio between the pixels of each type and the pixels of total mass, which was used after the lesion ROIs were drawn. ANOVA was used to find the correlation among the three KCVs.

Results: In the groups of benign mass and malignant lesions, the KCV ratio of type II was higher than those of types I and III (p-value <0.05). In the benign group, the Post Hoc test showed a significant difference between the KCV ratios of types II and III (p-value <0.05), but not between those of type II and type I (p-value >0.05). In the malignant group, the KCV ratio of type II was much higher than those of types I and III (p-value <0.05). After pixels of types II and III (II–III) were classified into the same group, their KCV ratio was compared to that of type I. The difference of the KCV ratio between the type II–III and type I in the malignant group is higher than that in the benign group.

Conclusion: 3D Temporal Resolution characteristics can provide radiologists another factor to analyze the breast MRI objectively. Many previous studies showed that tumors with washout pattern strongly suggested malignancy. In this study, it was discovered that the KCV ratios from the plateau pattern was higher than those from the washout pattern. After the washout pattern and plateau pattern were classified in the same group, their KCV ratio is larger than that of persistent pattern. The larger the difference, the higher the chance of malignancy. The 3D temporal resolution characteristics can thus be used as a reference to determine whether the tumor is benign or malignant.
Disclosure of Interest: No significant relationships.

P142
Clinicopathological assessment of metachronous bilateral breast cancer

D. Takabatake[1]*, K. Ohisi[1], S. Kiyoto[2], M. Takahashi[2], Seiki Takashima[2], K. Aogi[2], S. Ohsumi[2], N. Taira[3], Shigemitsu Takashima[2]. *[1]Breast Oncology, Kochi Health Science Center, Kochi, Japan, [2]Breast Surgery, Shikoku Cancer Center, Matsuyama, Japan, [3]Breast Surgery, Okayama University Graduate School of Medicine, Okayama, Japan*

Goals: Primary breast cancer (BC) patients often develop metachronous bilateral BC where cancer develops in the contralateral breast postoperatively. The goals of this study is to review and analyse the incidences and clinicopathological features of metachronous bilateral BC.
Methods: We reviewed and analysed in 3,336 cases of stages 0–III primary BC treated surgically at our facilities between 1994 and 2008.
Results: Among surgically treated patients, the mean cumulative incidences of BC on the contralateral side were 1.6%, 3.4%, and 5.2% within 5, 10 years, and 15 years, respectively. The postoperative incidence of contralateral BC was 1.6% within the first 5 years, 1.7% between 6–10 years, and 1.6% between 11–15 years. Detailed data, including pathological findings, were available for 98 patients who developed contralateral BC (CBC) postoperatively in or after 2000; these cases were analysed clinicopathologically. The median DFI was 63 months. Of all the cases, 26.3% had a family history of BC. Systemic therapy was administered postoperatively to 54.5% of cases. The subtype of the contralateral tumour was identical to that of the initial tumour in 70.9% of all cases and differed in the remaining 29.1%. Within the latter group, luminal-type cancer in one breast was followed by non-luminal-type development in the other breast in 21.7% of cases, while non-luminal-type cancer in one breast was followed by luminal-type development in the other breast in 55.6% of cases. Among patients treated with hormone therapy for the initial BC, the CBC was often the non-luminal type. The incidence of early onset CBC within 5 years postoperatively was low among patients who received systemic therapy for the initial BC, while systemic therapy did not suppress late onset CBC (developing ≥6 years after surgery). Family and breastfeeding histories were significant factors predicting CBC onset ($p < 0.0001$ and $p = 0.0003$, respectively), but there was no significant difference in the timing of CBC onset according to these factors.
Conclusion: Family and breastfeeding histories were identified as significant factors associated with metachronous CBC onset. Postoperative systemic therapy contributed to suppression of early onset CBC. The incidence of CBC showed no tendency to decrease over time, signifying the necessity of long-term monitoring for possible onset of cancer in the contralateral breast post-treatment of the initial BC, especially for patients who have BC family histories.
Disclosure of Interest: No significant relationships.

P143
Can differences in tumor biology explain better prognosis of screen-detected breast cancers?

S.M. Ess[1]*, C. Herrmann[1], M. Rössle[2], F. Otto[3], H. Frick[1]. *[1]Krebsregister, Krebsliga Ostschweiz, St. Gallen, Switzerland, [2]Institut für Pathology, Kantonsspital Graubünden, Chur, Switzerland, [3]ZeTuP, St. Gallen, Switzerland*

Goals: Screen-detected (sd) breast cancers (BC) show better prognosis than non-screen detected (nsd) cancers. We analyzed to which extent differences can be explained by tumor biology rather than by shifts in size and stage only.
Methods: We analyzed data from two population-based cancer registries in Eastern Switzerland. We included all stage I–II carcinomas diagnosed between 2010 and 2013. Tumors were classified as luminal-A-like (LumA), luminal-B-like (LumB), HER2-enriched (H-en) and triple negative (TN) using the surrogate definitions of intrinsic subtypes adopted by the 13th St. Gallen Breast Cancer Conference (Goldhirsch, 2013).
Results: In 2010–2013 1603 women were diagnosed with stage I–II BC in the catchment area. 410 (26%) were sd of which 58% (n = 237) were detected within the newly introduced organized mammography screening program (MSP). sd BC showed seldom TN phenotype [3% (n = 12) vs. 8% (n = 100) among nsd, $p < 0.001$), HER2 overexpression (6%, n = 22 vs. 10%, n = 116 among nsd, $p = 0.008$) or histological high grade (17%, n = 69 vs 35% n = 420 among nsd, $p < 0.001$). The choice of the cut point for "low" vs. "high" for the Ki-67-proliferation index influenced the proportion of LumA/LumB cancers in both groups sd and nsd. Using a cut point of 14%, 158 (39%) sd BC and 249 (21%) nsd BC were LumA ($p < 0.001$). With a cut point of 20%, 185 (45%) sdBC and 331 nsd BC (28%) were classified LumA ($p < 0.001$). The differences persisted when restricting the analysis to stage I BC or to BC with size <15 mm. Sd BC showed the same characteristics independent of whether detected within MSP or by opportunistic screening.
Conclusion: Better survival of sd BC can only partially be attributed to shifts in tumor size and stage. A high proportion of sdBC show biological characteristics associated with low-progression risk which could explain the better prognosis associated with sdBC in observational studies.

Reference(s)

[1] Goldhirsch et al. 2013. Personalizing the treatment of women with early breast cancer. AnnOncol 24(9): 2206.

Disclosure of Interest: No significant relationships.

P144
Venous thromboembolic events in early breast cancer patients receiving chemotherapy in India

V.S. Chauhan*, B.D. Pathak. *Surgical Disciplines, Metro Hospital, Faridabad, India*

Goals: Chemotherapeutic agents and cancer are related to venous thromboembolic events. They occur commonly in patients receiving standard chemotherapy of 5 Fu, cyclophosphamide and epirubicin (FEC) or FEC followed by taxanes (FEC-T). These are a source of significant morbidity particularly in the upper limbs. There is a dearth of data on the rates of venous thromboembolic events (VTEs) in the Indian settings with standard chemotherapy regimens and there are no standard practices of management or prophylaxis of these morbid events. This study aims at identifying the risk factors and develop management guidelines for such events.
Methods: All patients who received FEC and FEC-T at Metro Hospital, Surgical and Medical Oncology Unit from January 2009 till January 2014 were retrospectively analysed to identify patients who had a possible VTE. Analysis and possible correlation of age,

symptoms, tumor stage, grade, BMI, menopausal status was done. Identification of the treatment which was done was also reviewed.
Results: Seventy-two patients were identified of whom 45 had received FEC-T. Out of these, 20 patients had developed symptoms suggestive of VTEs. A venous Doppler USG had diagnosed a thrombus in the upper limb on the side of chemotherapy administration. Two patients (10%) had deep venous thrombosis (DVT), the others had superficial thrombus (90%). Out of the 27 patients who received FEC, 10 patients developed VTEs with 2 patients having DVT and the other 8 patients having superficial thrombus. The median time to symptoms was 2 cycles in FEC-T and 3 cycles in FEC. Age, menopausal status, tumor grade were not found to be correlated as there was no statistically significant association.
Conclusion: A significant proportion of patients receiving chemotherapy develop upper limb VTEs, particularly due to phlebitis caused by these agents, particularly epirubicin. In India, access to rapid scanning is limited and one needs to have a high index of clinical suspicion. Also, there is a need to develop prophylaxis and treatment protocols for VTEs which are lacking in India.
Disclosure of Interest: No significant relationships.

P145
Breast cancer awareness and early detection practices among Omani women: a pilot study

E.M. Al Khasawaneh[1], S.T. Siddiqui[1]*, V. Seshan[1], A. Al Ajmi[2], Y. Al Farsi[1]. *[1]College of Nursing, Sultan Qaboos University, Muscat, Oman, [2]Oncology, Sultan Qaboos University Hospital, Muscat, Oman*

Goals: This study was conducted to assess Omani women's general awareness of breast cancer and early detection behavior to develop a national breast cancer awareness intervention which would empower women with better early detection practices and improve survival.
Methods: We conducted a cross-sectional survey of 1372 Omani women of at least 20 years of age from five governorates of Oman. Women were recruited using stratified random sampling. The survey collected demographic information and scored variables of early detection behavior and general awareness of breast cancer. The scores were compiled into overall early detection and general awareness scores as proportions of 1. The mean scores for general awareness and early detection were calculated for each age group, level of education and income level. The correlations between each demographic variable and scores of awareness and early detection were estimated. The extent of belief in "evil eye" or envy as a risk factor for breast cancer was also estimated for each demographic variable.
Results: The overall mean score for early detection scores was 0.59 with a standard deviation of $\pm$0.26. The overall mean score for general awareness was 0.47, with a standard deviation of $\pm$0.21. The mean general awareness score was found to increase with increasing levels of education and income; in terms of age, the mean peaked at the 40–49 years age group (0.52$\pm$0.21) and then tapered. The early detection mean did not show any such trends, and was the highest for the 40–49 years age group, secondary education level and the OMR500–999 income level. The correlations between general awareness and income level ($r = 0.147$), education level ($r = 0.090$) and age group ($r = 0.067$) – albeit quite low – were found to be significant ($p < 0.05$). Early detection had no correlation with these demographic variables. Overall, an overwhelming majority of women 59.5% agreed or strongly agreed with the belief in "evil eye" or envy as a risk factor for breast cancer. This belief held true across all demographics.
Conclusion: The significant positive correlations between awareness and socioeconomic factors such income and education demonstrate that there is an awareness gap between the different demographics of Omani society. The overall dismal awareness and early detection results, and the survey of local beliefs highlight a severe necessity for a contextually-tailored breast cancer awareness intervention program in Oman.
Disclosure of Interest: No significant relationships.

P146
Long term follow up of elderly women diagnosed with breast cancer

S. Susnjar[1]*, O. Djokic[2], S. Pupovac[1], J. Mladenovic[3], D. Gavrilovic[4]. *[1]Medical Oncology, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia, [2]Medical Center Sabac, Sabac, Serbia, [3]Radiotherapy Oncology, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia, [4]Data Center, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia*

Goals: To evaluate long-term survival of elderly patients (pts) diagnosed with breast cancer (BC) at the Institute for Oncology and Radiology of Serbia.
Methods: This analysis includes a group of elderly (≥65 years old) women diagnosed with stage 1–3 BCs during 2001/2002. They were treated with surgery +/− radiotherapy and adjuvant (adj) endocrine (tamoxifen, TAM) and CMF chemotherapy (CHT). Hormone receptor (HR) status was determined by classical biochemical DCC method (ER-pos if ≥10 fmol/mg protein and PR-pos if ≥20 fmol/mg protein). The main end points were disease-free survival (DFS) and overall survival (OS). Statistics included: Pearson Hi^2 test, Fisher exact test, Kaplan–Meier product-limit method and Log-rank test.
Results: We identified 98 pts of median age 70 years (range 65–79) diagnosed with stage 1–3 BC during 2001/2002. Nineteen percent of pts were diagnosed in stage 1, 52% in stage 2 and 27% in stage 3 BC. The most frequent histology was ductal invasive BC (50%), followed by lobular invasive BC (39%). Majority of pts had T2 (45%) grade 2 (90%) HR-pos (84%) BCs equally divided between node (N)-neg and N-pos subgroups (42% each). Significantly higher number of pts with more than 4 lymph nodes (N≥4) involved received adj CMF CHT (9/15 pts) compared to N-neg pts (6/41 pts), $p = 0.002$. Similarly, significantly more pts with HR-pos BCs did not receive adj CMF (51/61 pts) compared to pts with HR-neg BCs (7/16 pts), $p = 0.001$. The use of adj TAM was influenced only by HR status, not by tumor size or N status. After median follow up period of 109 mos (range 7–148) 31/98 (32%) pts relapsed and 51/98 (52%) died, among which 28/98 (28.5%) died w/o disease progression. Median DFS and OS were 95 mos (95% CI 74–121), and 118 mos (95% CI ≥95), respectively. Pts outcome was influenced by following factors: tumor size [patients with T1 BCs had significantly longer OS compared to pts with T2 BCs ($p < 0.05$)]; N status (N≥4 pts had significantly shorter DFS and OS compared to N1–3 ($p = 0$) and N-neg ($p = 0$) pts]; HR status [HR-neg BC pts had significantly shorter DFS compared to HR-pos BC pts ($p < 0.05$)].
Conclusion: Our results confirmed that a substantial portion of elderly BC pts diagnosed with stage 1–3 BC died w/o disease relapse. Survival analysis showed that disease extent (larger tumor size and N≥4 status) and HR-neg status significantly influenced pts outcome despite received adj CMF/TAM.
Disclosure of Interest: No significant relationships.

P147
Quality of life (QOL) and symptom burden (SB) in breast cancer patients across the continuum

S. Verma[1]*, J. Hamer[2], C. Ecclestone[2], A. Leahey[2], L. Zhang[2], C. Deangelis[2], E. Rakovitch[2], E. Chow[2]. *[1]Medical Oncology, Sunnybrook Odette Cancer Centre, Toronto, Canada, [2]Sunnybrook Odette Cancer Centre, Toronto, Canada*

Goals: To determine the Quality of Life (QOL) and Symptom burden (SB) among breast cancer patients related to disease stage, type of treatment, and disease free interval.

Methods: Patients completed the Edmonton Symptom Assessment System (ESAS) and the Functional Assessment of Cancer Therapy for Breast Cancer (FACT-B). Patients were categorized into 4 groups based on their stage of cancer: DCIS, early stage, locally advanced or metastatic. Patients within these groups were divided into subsequent cohorts based on their last day of treatment: <2 years, 2–<5 years, 5–<10, ≥10 years, age at time of enrollment: ≤50, 51–60, 61–70, and ≥70 years, surgery type: lumpectomy or mastectomy, radiation type: 5000 cGy/25, 4256 cGy/16 or 4250 cGy/16 and 9000 cGy/1, chemotherapy and hormone therapy. Patients were also stratified by recurrence status and time since diagnosis of primary cancer.
Results: From January to August 2014, a total of 1,513 patients were enrolled. Metastatic patients (n = 178) had highest ESAS scores compared to all other patient groups and higher scores of depression and anxiety compared to DCIS (n = 141) and early stage patients (n = 769). Patients in the 2–5 years (n = 255) or 5–10 years post treatment cohort (n = 214) have lower QOL score compared to those in the ≥10 years cohort (n = 101). Young patients ≤50 with early stage cancer (n = 171) or locally advanced cancer (n = 145) have higher ESAS scores for tiredness, depression, and anxiety compared to all other age cohorts and overall lower QOL. Patients treated with a lumpectomy (n = 790) have significant higher QOL scores, except for Social/Functional well-being, comparing to those treated with mastectomy (n = 611). Early stage patients who received chemotherapy (n = 373) reported more ESAS symptoms and an overall lower QOL compared to those with no chemotherapy (n = 389). Patients taking SERM treatments (n = 438) have higher depression and lower QOL compared to those not on SERM (n = 528).
Conclusion: This is one of the largest QoL analysis conducted in the current framework of breast cancer treatment. Patients, who were <50 years old, 2–10 years post-treatment, treated with mastectomy, chemotherapy or SERM hormone therapy had increased SB and decreased QOL. Individualized interventions and programs can be developed to tailor to physical, educational, and psychosocial needs identified across the breast cancer continuum.
Disclosure of Interest: No significant relationships.

P148
Feasibility of ultrasound-guided vacuum-assisted breast biopsy system for intraductal papilloma

J.W. Kim*, Y.S. Kim, K.C. Kim. *Surgery, Chosun University Hospital, Gwangju, Korea*

Goals: Intraductal papillomas (IDPs) of the breast can be commonly presented with a variety of clinical symptoms and radiologic findings. Surgical excision is commonly recommended because of the possibility of an associated high grade lesion such as adjacent carcinoma. We performed this study to validate the feasibility and safety of ultrasound-guided vacuum-assisted breast biopsy system (Mammotome) for diagnosis and minimally invasive excision of IDPs instead of surgical excision.
Methods: We retrospectively reviewed the clinical information of twenty-six patients who underwent excision of solitary intraductal papilloma using the 8-gauge probe with the ultrasound-guided Mammotome system between January 2007 and December 2012 at Chosun University Hospital.
Results: Mean age of the patients were 44.6±9.2 years old (age range 23–70 years). Mean follow-up duration were 56.2±19.8 months (range 29–92 months). Mean size evaluated by ultrasonogram preoperatively were 1.0±0.5 cm (range 0.5–2.0 cm). Preoperative diagnosis using ultrasonogram were intraductal papilloma (7 patients, 26.9%), fibroadenoma (3 patients, 11.5%), fibrocystic change (15 patients, 57.7%) and malignancy (1 patient, 3.8%). There was local recurrence in only one patient. We performed Mammotome excision additionally, and pathologic diagnosis was intraductal papilloma.
Conclusion: Our study suggests that ultrasound-guided Mammotome excision for diagnosis and treatment of solitary IDPs was feasible and safe. This technique appears to be an alternative to surgical excision for IDPs. Further prospective studies to better estimate the feasibility of Mammotome excision for IDPs may be helpful.
Disclosure of Interest: No significant relationships.

P149
BRCA mutations and haplotypes in high risk Lebanese Arab breast cancer patients

N.S. El Saghir[1]*, N.K. Zgheib[2], H. Assi[1], K. Khoury[1], Y. Bidet[3], R.N. Charara[1], R.A. Farhat[1], A. Shamseddine[1], F.Y. Kreidieh[1], N. Uhrhammer[4]. *[1]Internal Medicine, American University of Beirut Medical Center, Beirut, Lebanon, [2]American University of Beirut, Beirut, Lebanon, [3]Centre Jean Perrin, University of Auvergne, Clermont-Ferrand, France, [4]Laboratoire Diagnostique Génétique Et Moléculaire, Centre Jean Perrin, Clermont-Ferrand, France*

Goals: Study aims to determine the incidence of BRCA1 and BRCA2 mutations in breast cancer Lebanese and Arab patients (pts) at high risk for hereditary disease.
Methods: 250 Lebanese women with breast cancer, of young age with or without family history (FH), were recruited between 2009 and 2012 at the American University of Beirut Medical Center (AUBMC). BRCA gene sequencing of all coding exons and intron-exon boundaries was performed at the Centre Jean Perrin, France. Study was approved by IRB and funded by an Ethnic Research Initiative (ERI) grant awarded by GSK.
Results: 14 of 250 patients (5.6%) had deleterious BRCA mutations and 31 (12.4%) had variants of uncertain significance (VUS). 8 out of 74 (10.8%) patients ≤40 with FH+ had deleterious mutations (6 BRCA1 and 2 BRCA2). Only 1 out of 74 (1.4%) pts ≤40 with FH− had a mutation (BRCA1), 4 of 75 (5.3%) pts 41–50 with FH+ had a mutation (1 BRCA1, 3 BRCA2), and only 1 of 27 (3.7%) pts >50 with FH+ had a mutation (BRCA2).
All 7 BRCA1 mutation carriers had a positive FH, were between 32 and 48 years, and had Grade 3 IDC with negative ER, PR, and HER2 receptors (TNBC). 6 BRCA2 mutation carriers had IDC with positive hormone receptors (HR), and 2 were HER2-positive. Eight BRCA1 haplotypes had frequency of >1%; this is including H1, the most frequent haplotype (50% of alleles) that presented the default nucleotide at all positions. We observed 17 BRCA2 haplotypes with a frequency of >1%, with the most common at 27.5%. 14 major types accounted for 99% of these haplotypes; the remaining 1% consisted of six rare allele combinations.
Conclusion: This first large study of ethnic Lebanese Arab women with breast cancer shows a lower than expected rate of mutations when compared to similar patient populations. Age ≤40 combined with positive FH gave the highest BRCA mutation prevalence rate of 10.8%. High rates of VUS are noted and need to be clarified by additional studies. The need to evaluate additional genes such as PALB2, CHEK2, and TP53 is emphasized. Haplotype analysis shows significant diversity.
Disclosure of Interest: No significant relationships.

P150
Clinical outcome of pregnancy associated breast cancer: Hacettepe University experience

D. Basaran[1], M. Turgal[1], K. Beksac[2]*, O. Ozyuncu[1], O. Aran[2], M.S. Beksac[1]. *[1]Obstetrics and Gynecology, Hacettepe University, Ankara, Turkey, [2]General Surgery, Hacettepe University, Ankara, Turkey*

Goals: The primary goal of this study was to evaluate the clinicopathological characteristics of patients with pregnancy-

associated breast cancer (PABC) and outcome following surgical intervention plus chemotherapy. In addition maternofetal health and the survival rates were also analyzed.
Methods: Clinical and pathological data of patients diagnosed with breast cancer manifesting during pregnancy or postpartum first year or any time during lactation in the period of 2003–2014 at Hacettepe University Hospital were reviewed retrospectively.
Results: Twenty patients diagnosed with PABC were analyzed. Diagnosis were made during 8–38 weeks of pregnancy or untill month 24. All patients were biopsied or operated for the investigation of a palpable mass in the breast. Tumor size ranged 1.5–8.3 cm. The pathological examination revealed invasive ductal carcinoma (80%) and advanced-stage disease (75%) as dominant features. Diagnostic delay was a frequent observation. Diagnosis was delayed due to symptoms of pregnancy and lactation or due to negligence. All patients diagnosed during pregnancy received chemotherapy. Half of these diagnosed during pregnancy are alive with no evidence of disease with a median follow-up of 11 months. 75% of patients diagnosed during the post-partum period are alive with no evidence of disease with a median follow-up of 4 years. Chemotherapy associated fetal loss was not observed. No significant adverse side effects were observed in the pregnant women and their fetuses during and after treatment with chemotherapy.
Conclusion: PABC often presents with advanced-stage disease and there can be a significant delay before these patients receive treatment. Survival of the patients diagnosed postpartum are better than those diagnosed during pregnancy. Successful surgery and adjuvant or neoadjuvant chemotherapy can be curative without harming fetal outcome.
Disclosure of Interest: No significant relationships.

P151
The role of radiologic evaluation for detection of axillary lymph node metastasis

J.I. Kim[1]*, B.S. Kwak[2]. [1]*Surgery, Inje University Ilsan Paik Hospital, Goyang, Korea,* [2]*Surgery, Dongguk University Ilsan Hospital, Goyang, Korea*

Goals: Axillary lymph node metastasis (ALNM) is a key prognostic factor of breast cancer, thus, diagnostically accurate methods for determining ALNM are very important. The purpose of this study was to evaluate the availability of preoperative breast ultrasonography (US), contrast-enhanced magnetic resonance imaging (MRI), and ^{18}F-fluorodeoxyglucose positron emission tomography-computed tomography (PET-CT) for detection of ALNM in early breast cancer (tumor size ≤5 cm).
Methods: The medical records of patients with breast cancer who underwent sentinel lymph node biopsy or axillary lymph node dissection after preoperative breast US, MRI and PET-CT between January 1, 2012 and October 31, 2014, were retrospectively reviewed. We analyzed positive predictive value (PPV), negative predictive value (NPV), sensitivity and specificity of each radiologic modality.
Results: Of 105 patients with early breast cancer underwent axillary surgery, 71 patients evaluated all radiologic modalities preoperatively. The mean age of patients was 50.7±11.0 years (range 30–80 years). 55 patients underwent planned sentinel lymph node biopsy (SLNB), and 16 patients underwent planned axillary lymph node dissection (ALND). 8 patients underwent SLNB needed additional ALND after frozen biopsy. In total, 28.2% (20/71) of patients exhibited ALNM on pathologic report. The PPV was 52.2%, 61.9%, and 92.3%, and the NPV was 83.3%, 86.0%, and 86.2%, respectively. The sensitivity was 60.0%, 65.0%, and 60.0%, and specificity was 78.4%, 84.3%, and 98.0%, respectively.
Conclusion: There are no definitive modalities for detecting ALNM in early breast cancers to replace SLNB. However, PET-CT seems to be a predictive radiologic modality for detection of axillary LN metastasis considering higher PPV and specificity. If ALNM is suspected based on PET-CT, ALND without SLNB might be a better option.
Disclosure of Interest: No significant relationships.

P152
Diagnostic accuracy of axillary lymph node metastasis using FDG PET/CT in stage I/II breast cancer

Masahiro Ito[1]*, Masatoshi Ito[2], X. Duan[2], H. Hirakawa[1], M. Amari[1], K. Fukamachi[1], T. Ishida[3], N. Ohuchi[3]. [1]*Breast Surgery, Tohoku Kosai Hospital, Sendai, Japan,* [2]*Sendai Medical Imaging Center, Sendai, Japan,* [3]*Surgical Oncology, Tohoku University School of Medicine, Sendai, Japan*

Goals: The aim of this study is to assess axillary lymph node status of stage I/II primary breast cancer using 2-[^{18}F]Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (PET/CT).
Methods: In this retrospective single institute study, 249 women newly diagnosed with operable breast cancer underwent PET/CT before surgery, followed by counting standard uptake value (SUV) of primary tumor and axillary lymph node and assessing pathologically lymph node metastasis. All women underwent axillary lymph node dissection.
Results: Primary tumor (range:0.1–4.7 cm) was identified by PET/CT in 225 patients. Using logistic regression, SUV of primary tumor was significantly associated with histological grade, ki-67 Labeling index ($p = 0.006558, 0.000406$) Axillary lymph node metastasis were found in 64 (28.4%) of 225 patients. (macrometastases 53, micrometastases 11) The sensitivity was 43.8 (95% CI, 31.4% to 56.7%), specificity was 90.1% (95% CI, 84.4% to 94.2%), positive predictive value was 63.6% (95% CI, 47.8% to 77.6%), negative predictive value was 80.1% (95% CI, 73.5% to 85.7%), and prevalence was 28.4% (95% CI, 22.6% to 34.8%). The sensitivity for micrometastases was 0%, and for macrometastases was 45.2%.
Conclusion: SUV reflect the tumor activity such as histological grade and ki-67 Labeling index. PET/CT doesn't have enough sensitivity and specificity so as to be alternative to sentinel lymph node biopsy.
Disclosure of Interest: No significant relationships.

P153
Understanding barriers to Serbian women with breast cancer seeking medical advice

S. Vasović[1]*, S. Mamula Mašić[2], I. Ujfeljan Ristić[3], M. Bodlović Kladar[4], N. Andrašić[5], L. Milovanović[6], N. Milić[7]. [1]*Medical Oncology, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia,* [2]*Roche d.o.o., Belgrade, Serbia,* [3]*General Hospital Zrenjanin, Zrenjanin, Serbia,* [4]*Institute for Oncology of Vojvodina, Sremska Kamenica, Serbia,* [5]*General Hospital Subotica, Subotica, Serbia,* [6]*General Hospital Kruševac, Kruševac, Serbia,* [7]*Institute for Statistics, Medical University of Belgrade, Belgrade, Serbia*

Goals: Delay in potentially preventable help-seeking behavior has a major effect on the prognosis and survival of patients with breast cancer. The aim of this study was to determine the causes of delay longer than 3 months in seeking help among patients with breast cancer from Serbia.
Methods: In this cross-sectional study 800 breast cancer patients were interviewed about potential risk factors and markers of delayed seeking for medical advice by uniform questionnaire. Patient delay was defined as time from onset of symptoms to first consultation with a health care provider. Logistic regression analysis was used for the constructing of the delaying profile patient model.
Results: Among the 800 patients, 21% delayed seeking consultation for longer than 3 months. In multivariate logistic regression model, a significant increase in patient delay was associated with older age, lack of trust in the health care system and the success of

the treatment, lack of time for seeking medical advice, as well as poor knowledge or awareness of the severity of the breast cancer disease ($p < 0.05$). Regarding stage of breast cancer, there were significant associations of breast cancer advanced stage and delayed first consultation with a health care provider ($p < 0.05$).
Conclusions: A set of variables, mainly related to psychological and behavioral patient attributes, are impacting delay time for seeking medical advice. Defining the personal profile of women with breast cancer symptoms to whom psychological counselling are recommended, would be helpful for both clinicians, by improving their understanding when managing patients, and for policy makers that can formulate strategies and implement targeted activities to prevent delaying in the diagnosis and treatment of breast cancer.
Disclosure of Interest: One of the authors (Sarina Mamula Mašić) is fully employed by Roche d.o.o. Roche d.o.o. is sponsor of the project BreastCare from which data are generated.

P154
Use of complementary medicine, CAM compliance and lifestyle interventions

D. Paepke[1]*, E. Klein[1], K. Kramer[2], M. Kiechle[1]. *[1]Frauenklinik rechts der Isar, TU München, München, Germany, [2]Chirurgie, Universitätsklinik Ulm, Ulm, Germany*

Introduction: 50–70% of breast cancer patients use methods of complementary medicine. These are mainly young women, highly educated and in a curative situation. The data regarding CAM compliance, benefit of CAM-therapies and lifestyle interventions is limited.
Methods: Survey with primary breast cancer patients (n = 286) operated in the breast cancer center at the University Hospital TU-München, Klinikum rechts der Isar in the year 2012. Two questionnaires – one for CAM users with 72 questions and one for NON-CAM users with 52 questions – were conducted via telephone interview with 192 patients. The questionnaire contains questions about the disease situation, the use and effect of CAM including compliace and questions about lifestyle interventions.
Results: 192 patients are interviewed. 56% (n = 107) of the patients used CAM methodes. 79% reported an improvement of quality of life. In 96% (n = 103) CAM is applied consistently and as often as recommended. 78% of CAM users is their complementary medical treatment as important – or more important than the conventional medical therapy. 44% (n = 85) did not apply CAM but 54% of them would have been liked to be informed about CAM facility. This means 80% of all breast cancer patients are interested in CAM and wish to have CAM advice from their physicians. 58% (n = 112) of all the patients have changed their lifestyle after the diagnosis and live more healthier. 67% of the CAM users and 33% of the NON-CAM users. 72% (n = 138) of all the patients feel less stressed of wich 80% through a conscious stress reduction. Looking back 70% of the patients answered that their disease made a sense or brought something positive in their lives. Those were mostly the younger patients (average 59 years) and CAM users.
Conclusion: Breast cancer patients are highly interessed in CAM. Useful CAM methodes should be integrated in the therapy of breast cancer patients.
Disclosure of Interest: No significant relationships.

P155
Small solid non palpable breast carcinomas: can they be excised in total by BLES?

I.K. Papapanagiotou[1]*, V. Kalles[1], P. Liakou[1], A. Nonni[2], D. Koulocheri[1], A. Pazaiti[1], K. Migkli[3], G. Theodoropoulos[1], E. Menenakos[1], G.C. Zografos[1]. *[1]1st Propaedeutic Surgery Department, Hippokrateion Hospital, University of Athens, Athens, Greece, [2]Pathology Department, University of Athens, Athens, Greece, [3]3rd Gynecology Department, Attikon Hospital, University of Athens, Athens, Greece*

Goals: Breast Lesion Excision System (BLES) is an automated vacuum-assisted breast biopsy device, used for the removal in an intact specimen of suspicious, non palpable mammographic lesions utilizing radiofrequency technology. The current study was performed to evaluate the effectiveness of this device in retrieving completely and with clear margins small solid breast carcinomas.
Methods: This study includes 23 consecutive patients with suspicious non palpable solid mammographic lesions that underwent a breast biopsy with the use of BLES. All procedures were performed between 2008–2010 at the Breast Unit of the 1st Department of Propaedeutic Surgery, University of Athens, at Hippokrateion Hospital, using the Fischer stereotactic table and the Intact 8G biopsy needle with 15 mm and 20 mm diameter of the basket. Histological evaluation of the BLES specimens indicated 2 DCIS and 21 Invasive Carcinomas. According to each patient's histological result, appropriate surgical procedure was performed. Furthermore, Pathologists examined the surgical specimen in order to evaluate the possible existence of residual disease in the cavity formatted by the basket of BLES.
Results: As mentioned before, all patients underwent appropriate surgical procedure. Lesions excised from 13 patients (57%) had clear margins (≤1 mm) at their histological evaluation, and no residual disease was found in the cavity formatted by the basket. In 7 cases (30%) the lesion exceeded the size (>2 cm) of the retrieving basket and residual disease existed in the surgical specimen. In 3 patients (13%), targeting of the lesion was incorrect, the majority of the lesion was excised but on the other hand residual disease was found in the surgical specimen. These occurred in the first months of application of the BLES system, due to our initial small experience.
Conclusion: According to our initial experience and findings, if a small carcinoma lesion of the breast (<2 cm) is targeted correctly, it can be safely and effectively removed in total, leaving no residual disease in the formatted cavity of the breast. We must emphasize however, that our sample is very small and further research is ongoing to obtain safer conclusions.
Disclosure of Interest: No significant relationships.

P156
Variations in breast screening in BRCA/high risk mutation carriers in a dedicated breast centre

L.M. Houlihan*, N.M. Foley, M. Jinih, Z. Khan, A. Khan, N. Relihan, H.P. Redmond. *Breast Research Centre, Cork University Hospital, Cork, Ireland*

Goals: The recommended screening of BRCA and other genetic carriers at high risk of breast cancer has been subject to debate and change recently. A UK guideline has set out recommendations for both the intensity and type of imaging recommended in different risk categories. Our aim was to characterise the screening of a high risk population in a dedicated breast centre and to compare the interval and type of screening with international guidelines.
Methods: A database has been prospectively maintained since 2003 and includes confirmed mutation carriers (BRCA1, BRCA2, p53, CDH1) and untested patients with a greater than 30% carrier probability. This database was consolidated with additional

information including patient demographics, frequency and type of surveillance imaging, whether patients availed of risk reduction surgery and breast cancer status.
Results: Women who underwent risk reduction surgery or those who had a diagnosis of breast cancer were excluded from further analysis. 26 women were included for analysis. The average age was 44 years (range 21–63). The intention for patients between the ages of 30 and 50 is annual mammography and MRI, while in those over 50 years it is annual mammography. In our cohort, 12/19 patients under 50 years of age have had at least one MRI, with 14/19 having annual mammography. All patients in the over 50 group have had annual mammography.
Conclusion: Identification of BRCA/genetic mutation carriers at higher risk of breast cancer is increasing. Factors such as, the limited availablity of public MRI, coupled with competition for slots with women embarking on neoadjuvant treatment, pregnancies, symptomatic episodes and appointment defaulters are hindering our ability to adhere strictly to screening intervals.
Disclosure of Interest: No significant relationships.

P157
Life satisfaction and biographic changes in young breast cancer survivors

R. Wuerstlein[1], K. Hermelink[1], A. Heiduschka[1], J. Engel[2], N. Harbeck[1] *, M. Burgmann[1]. *[1]Breast Center, University Hospital Munich – Grosshadern, Munich, Germany, [2]Medical Informatics, Biometry and Epidemiology, Munich Cancer Registry of the Munich Cancer Center, Munich, Germany*

Goals: Breast cancer impacts on many aspects of life that are of particular importance for young patients, like sexuality and childbearing, partnership/marriage, and professional career, and may hence negatively affect these patients' life satisfaction. Treatment of young breast cancer patients therefore requires special support that takes these issues into account. The intention of this cross-sectional study was to analyze life satisfaction and the effect of breast cancer (BC) diagnosis on the private and professional situation of young breast cancer patients.
Methods: We initiated a cross-sectional study using the standardized Life Satisfaction Questionnaire (Fahrenberg et al, 2000), the Questionnaire on Stress in Cancer Patients (Herschbach et al, 2003) and a self-developed questionnaire on partnership, employment situation, family planning, demographic and medical data. Patients who had been <40 years old at diagnosis of breast cancer and had been treated at LMU Breast Center between 2006 and 2013 were eligible for participation.
Results: Of 160 contacted patients, 88 returned the questionnaires. Compared to population data, no differences of general life satisfaction were found; however, the BC patients showed significantly lower satisfaction in the subdomains health status ($p < 0.001$) and sexuality ($p = 0.002$). The patients' most pronounced cancer-specific problems were fear of cancer recurrence or further hospital stays, psychosomatic problems like nervousness or fatigue, and reduced sexual activity. Most patients (71.6%) did not report any changes in partnership status. A similar percentage of patients (10.2%) had divorced/separated from or married the person they had been in a relationship with at diagnosis, and 7.9% had entered into a new relationship or marriage. Time to return to work was 9.98 (SD 5.72) months after diagnosis, depending on receipt of chemotherapy (no chemotherapy: 3.6 months, chemotherapy: 11.4 months). If patients with metastatic disease were excluded, the proportion of patients who were employed at diagnosis and at assessment was similar.
Conclusion: The general life satisfaction of young breast cancer survivors shows no difference from women without cancer. Yet, these patients were not satisfied with their general health status and with their sexuality. As both topics are closely associated with psychological and physical well-being, further interdisciplinary support and specific counseling are needed in that context.
Disclosure of Interest: No significant relationships.

P158
Low awareness of breast cancer, common subtypes and treatment options among Hong Kong women

J. Tsang[1] *, S.T. Yung[1], K. Ng[2], R.K.C. Ngan[3], C.W. Leung[3], C.C. Kwok[3], J.J. Suen[3], T.Y. Ng[3], I.S. Soong[3], W. Yeo[3]. *[1]Department of Clinical Oncology, Queen Mary Hospital, The University of Hong Kong and Hong Kong Breast Oncology Group, Hong Kong, Hong Kong, [2]Social Sciences Research Centre, The University of Hong Kong, Hong Kong, Hong Kong, [3]Hong Kong Breast Oncology Group, Hong Kong, Hong Kong*

Goals: We aimed to better understand the breast cancer awareness and attitudes towards preventive measures among Hong Kong well women and to enhance the general awareness of breast cancer prevention and treatment among Hong Kong women in the community.
Methods: We conducted a cross-sectional survey on "Breast Cancer Awareness among Hong Kong Well Women" through telephone interview with Hong Kong female residents aged 20–65 using the CATI system with trained research assistants at the Social Sciences Research Centre during the 3-week period of 28/2/2014–18/3/2014.
Results: Altogether, a sample of 12,316 telephone numbers was drawn to contact our respondents and only 764 were valid numbers, among which 503 were successfully completed subjects with 65.8% response rate. About 40% of all respondents perceived breast cancer as the most important health threats for their age but the perceived life-time risk of having any breast cancer was relatively low, with nearly half 49.2% of the respondents perceived herself as having no or low risk of breast cancer. Education level ($p = 0.0008$), occupation ($p = 0.0068$) and monthly household income ($p = 0.0361$) were found to have correlation with the perceived breast cancer life-time risk: subjects with primary education level had lowest mean score 3.115, while the mean of secondary and tertiary levels were 4.155 and 4.176 that were quite similar. Working people, professionals, generally have a higher mean assessment score (ranging from 4.25 to 4.90) while those were not at work had much lower assessment score (students: 3.687, housewives: 3.431, retired: 3.90). People with lower monthly household income had lower mean assessment score (3.67, 3.14), while others had generally higher assessment scores (ranging from 3.8 to 4.45). Family history of breast cancer, of course, was expected to have impact with subjects having known family history of breast cancer also had higher perceived life-time risk ($p \leq 0.0001$, mean 5.31 vs 3.79). In the era of established "personalized medicine" for breast cancer with easy access to media information, it was a bit surprising that majority of the respondents have low awareness of common breast cancer subtypes: 92.8% have never heard of the most aggressive type of HER-2 positive breast cancer, and over half 56.8% either did not know or did not understand hormone therapy is a valid option for hormone positive breast cancer which accounts for 60–70% of all breast cancer patients.
Conclusion: Hong Kong women have still relatively low awareness for breast cancer common subtypes and treatment options with low perceived life-time risk despite the relatively high incidence in Hong Kong. Further intervention and public health education is warranted to bridge the knowledge gap and enhance breast health awareness.
Disclosure of Interest: No significant relationships.

Locally advanced and metastatic disease

P160
Adenoid cystic carcinomas of the breast

M.S. Mahendra*. *William Harvey Hospital, South Thames Foundation School, TN LZ, United Kingdom*

Goals: Adenoid cystic carcinoma (ACC) of the breast is rare. The aim of this study is to review cases of ACC treated in a DGH.
Methods: This database was searched for all cases of ACC of the breast from January 2002 to December 2013. Their demographics, tumour characteristics, treatment and survival were reviewed.
Results: There were 9 patients giving an incidence of 0.1%. The mean age at diagnosis was 65 years (53–82). The mean tumour size was 2.48 cm (1.5–5 cm). The tumour grading: GI 6, GII 2, GIII 1. 7 patients were oestrogen receptor (ER) negative and two ER positive. All were progesterone receptor (PR) negative (1 unrecorded). 6 of the patients were HER2 receptor negative (3 unrecorded). 7 were node negative (2 unrecorded). Of 7 patients who had surgery, two had mastectomies and five wide local excisions. 4 patients received radiotherapy and none chemotherapy. Mean follow up was 36 months (3–69). There was 1 breast cancer death in a patient with advanced disease.
Conclusion: Adenoid cystic carcinomas of the breast are rare, tend to be triple negative and node negative and have a favourable prognosis. They may represent a subset of patients who can be treated with less axillary surgery and less chemotherapy.
Disclosure of Interest: No significant relationships.

P161
Prognostic value of pretreatment neutrophil–lymphocyte ratio in metastatic breast cancer

A. Mazouz[1]*, N. Adil[2], N. Chakib[2], A. Samia[1], M. Nawfel[1]. [1]*Hassan II University Hospital, Department of Medical Oncology, Fez, Morocco,* [2]*Faculty of Medicine and Pharmacy, Laboratory of Epidemiology, Fez, Morocco*

Goals: The neutrophil–lymphocyte ratio (NLR) has been reported to reflect systemic inflammation and to have independent prognostic value for patients with various cancers. In this study, we analyzed the prognostic significance of the preatment NLR in a retrospective cohort of patients with metastatic breast cancer (MBC).
Methods: Data from 200 MBC patients diagnosed between January 2009 and December 2013 in our department were evaluated retrospectively. The pretreatment NLR was defined as the neutrophil count divided by lymphocyte count and NLR cut-off values of ≥2.5 and <2.5 were used according to previous studies. Kaplan Meier method was used to analyze survival according to NLR level. Others covariate (performance status, recurrent disease, metastasis to viscera,…) were also studied using this method. Cox hazard model was performed for adjusting in confounding factors. Significance level was $p \leq 0.05$.
Results: The average age of these patients was 48 years-old [23–84]. The tumor was classified T3-T4 in 64% of cases with lymph node involvement in 49% of cases. The breast cancer was ductal histologic and undifferentiated type in 94% and 40% of cases respectively. The expression of hormonal receptor (HR) was noted in 71% of cases. The human epidermal growth factor-2 (HER2) was over expressed in 20% of cases. The disease was metastatic at diagnosis in 70% of cases. Overall, the most common sites of metastasis were the bone (54%), lung (52%), liver (36%), pleura (12%) and brain (7%). The average of NLR was 2.3 and 40% of patients had a higher NLR. The chemotherapy was given as a first line in 84% of cases. Trastuzumab was given in 17% of cases. Endocrine therapy was given especially on consolidation after response to chemotherapy in 25% of cases. Grade 3/4 toxicity was observed in 10% of patients (mainly hematological). Control of metastatic disease was noted in 67% of cases. After a median follow up of 19 months, the median of progression free survival (PFS) and overall survival (OS) were 10 months and 20 months respectively. In the univariate analysis, an increased pretreatment NLR was associated with shorter overall survival with $p = 0.06$ such as, recurrent disease, multi-organ involvement and metastasis to viscera with respectively $p = 0.04$, $p = 0.02$ and $p < 0.01$. In the multivariate analysis, we identified an increased pretreatment NLR as in independent predictor for overall survival with HR = 1.7, 95% CI = [1.02–2.83] and $p = 0.04$ such as metastasis to viscera with HR = 3, 95% CI = [1.36–6.69] and $p = 0.07$.
Conclusion: This is a first Moroccan report that had demonstrated the pronostic value of pretreatment NLR in patients with MBC to the best of our knowledge. Pretreatment NLR may be an independent prognostic factor with less overall survival. This combined index should be considered as a potential prognostic biomarker in future.
Disclosure of Interest: The authors declare that they have no competing interests.

P162
Tumor resection using near-infrared indocyanine green fluorescence in nonpalpable breast mass

H.J. Choi[1]*, H.J. Shin[1], S.K. Kim[2], E.Y. Ahn[1]. [1]*General Surgery, Breast & Thyroid Care Center, Myongji Hospital, Goyang, Korea,* [2]*National Cancer Center, Ilsan, Korea*

Goals: As a new technology that can be used for sentinel lymph node biopsy for breast cancer, near-infrared fluorescence imaging and lymph node mapping using indocyanine green (ICG) has been reported to provide feasible and safe real-time observation of lymph node signaling. One-third of breast cancer cases present as non-palpable lesions. The current gold standard treatment for these cancers is wide excision using wire-guided localization. In addition to breast surgery, this imaging technique can provide resection margins in non-palpable breast masses. We report that near-infrared ICG-fluorescence can be successfully applied for imaging of the resection margins by direct injection into non-palpable breast tumors, making it possible to accurately identify resection lines.
Methods: Between March and November 2014, 20 patients diagnosed with early breast cancer or non-palpable benign breast tumors were enrolled in the study. Prior to the operation, we injected ICG intratumorally 1 cm from the tumor margin under the guidance of ultrasonography. Resection was monitored using a specially designed near-infrared ICG camera. We reviewed specimens for tumor size, resection margin (positive or negative), and operation time.
Results: Among the 20 patients, 6 patients were diagnosed with early breast cancer and 14 patients with benign tumors. In early breast cancer, all cases had negative resection margins. The median operation time was 98 min. The medians of resection specimen size and tumor size were 8.1*6.6*2.2 cm and 2.0*1.7*5.9 cm, respectively. The median of specimen to tumor size (resection margin size) was 2.2/2.4/2.0/0.5 (superior/inferior/medial/lateral) cm. For the benign cases, the median operation time was 37 min. The medians of resection specimen size, tumor size, and specimen to tumor size was 4.0*3.1*1.6 cm, 1.2*1.0*1.0 cm, 2.7*1.9*0.5 cm, respectively.
Conclusion: Near-infrared ICG-fluorescence detection of breast tumor margins was successful in both non-palpable masses and early breast cancer. It was shown to be an efficient method of obtaining a high proportion of negative margins and optimum resection volumes in patients undergoing breast conserving surgery.
Disclosure of Interest: No significant relationships.

P163

Denosumab-induced hypocalcaemia in metastatic breast cancer

J. Fenech*, I. Macpherson, M. Rizwanullah, G. Lumsden, M. Alfayez. *Oncology, Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom*

Goals: Denosumab is a monoclonal antibody used in the prevention of skeletal-related events (SREs) in patients with bone metastases from breast cancer. Hypocalcaemia is a rare and dangerous side effect of the drug denosumab. A few cases of severe hypocalcaemia have been reported in the literature. Some reports have suggested that denosumab-induced hypocalcaemia is associated with renal impairment. Here, we report episodes of hypocalcaemia and its management in patients receiving denosumab for metastatic breast cancer in our institution.
Methods: We retrospectively collected the data of one hundred and sixty-five breast cancer patients with bony metastasis who are receiving 120 mg of denosumab subcutaneously every 4 weeks to prevent SREs. Each patient will be prescribed 1 Adacl-D3 tablet (calcium carbonate), 1.5 g (calcium 600 mg), and colecalciferol (10 mcg) daily. The patients will have their kidney function tests and adjusted calcium level checked before each dose of the denosumab injection is given. The data were collected from the chemotherapy electronic prescribing system (chemocare) and the patients' electronic records.
Results: Eighty-seven out of one hundred and sixty-five patients (53%) found to have hypocalcaemia while on denosumab. Thirty-six patients (41%) recorded the first episodes of hypocalcaemia after the first dose of denosumab. Thirteen patients (15%) developed hypocalcaemia after the second dose of denosumab. All of the patients were asymptomatic with the first episodes of hypocalcaemia. No changes in the estimated glomerular filtration rate (EGFR) associated with the episodes of hypocalcaemia have been recorded. After the first dose of denosumab, only eight patients had serum calcium less than 2.00 mmol/l (8 mg/dl). All patients were asymptomatic and were treated with a doubling of the dose of Adcal-D3. The lowest calcium level recorded after the first dose of denosumab was 1.79 mmol/l (7.17 mg/dl). Further episodes of hypocalcaemia were recorded in subsequent treatments with denosumab. Only one patient recorded a calcium level less than 2.00 mmol/l (8 mg/dl) in a subsequent treatment of denosumab. The calcium level was 1.68 mmol/l (6.73 mg/dl). The patient experienced symptoms of hypocalcaemia. He was treated with an IV calcium replacement therapy.
Conclusion: This case series demonstrated that denosumab could be administered safely in breast cancer patients with bony metastasis. All the patients reported in this series who received denosumab have normal kidney function tests as a baseline. Interestingly, half of the patients have hypocalcaemia, which is more likely to be recorded after the first dose of denosumab. These episodes of hypocalcaemia are not associated with a change in the kidney function test. Only one patient required IV calcium replacement. Hypocalcaemia can be managed safely by doubling the dose of Adcal-D3 tablets in this population.
Disclosure of Interest: No significant relationships.

P164

Physician's considerations for re-biopsy in patients with recurrent metastatic breast cancer

S. Strulov Shachar*, G. Fried, K. Drumea, N. Shafran, G. Bar-Sela. *Oncology, Rambam Health Care Campus, Haifa, Israel*

Goals: Several retrospective studies have shown that biopsies taken in recurrent metastatic breast cancer (RMBC) could differ from those at initial diagnosis. While re-biopsy in RMBC is often recommended, the impact of this procedure is questionable. *Purpose:* Evaluation of factors affecting physicians' decision to re-biopsy RMBC patients and the impact of this procedure on survival.
Methods: Retrospective data of 262 RMBC patients in 2000–2014 were analyzed by univariate and multivariate regression tests. Data included patient demographics, pathological reports and physicians' notes regarding the decision.
Results: Re-biopsy was performed in 182/262 patients (69%). The decision-making process was documented in 76 patients in whom re-biosy was performed (42%), but in none of the 80 patients without re-biopsy. A positive decision to re-biopsy was associated with early initial stage (84% in DCIS, I, IIA vs. 64.5% in IIB, III, $p = 0.003$); negative HER2 status (76% vs. 42% in HER2 positive, $p < 0.001$); fewer involved sites at recurrence (82% if single vs. 61%, $p = 0.003$); and the time period when diagnosed (p-trend = 0.004 for recent years). In multivariate analysis, only a more recent year of diagnosis (OR = 4.2, p-trend = 0.028, 95% CI 1.4–12.5) and initial HER2 negative status (OR = 4.5, $p < 0.001$, 95% CI 2.1–9.9) were found to be significant. Pathological reports for both initial disease and recurrence were available for ER in 55%, PR in 53%, and HER2 in 46% of patients. ER status changed from positive to negative in 11 patients and from negative to positive in 16 patients. The corresponding changes were 34 and 13 for PR, and 1 and 5 for HER2. Overall survival was not related to performance of re-biopsy ($p = 0.8$). Risk factors for mortality included older age (>70 years, OR = 1.90), advanced stage at diagnosis (OR = 1.6), number of disease sites at recurrence (OR = 1.6), brain metastasis (OR = 5.1), and shorter interval from initial diagnosis (OR = 2.2).
Conclusion: The decision-making process regarding the performance of re-biopsy in RMBC was documented in less than half the files. Factors positively affecting the re-bipopsy decision were early stage at diagnosis, negative HER2 status at diagnosis, and lower tumor burden at recurrence. There was a higher tendency to re-biopsy in the more recent years of the study period.
Disclosure of Interest: No significant relationships.

P165

cStage IIIc BC patients diagnosed by PET/CT can get good prognosis with intensive treatment

A. Watanabe*, T. Shien, Y. Abe, T. Nogami, T. Iwamoto, T. Motoki, N. Taira, H. Doihara. *Breast and Endocrine Surgery Department, Okayama University Hospital, Okayama, Japan*

Goals: Pretreatment clinical staging of breast cancer became easy and correct by PET/CT. Especially, regional lymph node metastases which could not be detected by conventional examination diagnosed exactly by using pretreatment PET/CT for locally advanced breast cancer, and treatment strategy and prognosis of these cStage IIIC patients is under debate.
Methods: We started to perform pretreatment PET/CT for locally advanced breast cancer patients from April 2009. There were 50 patients who underwent neoadjuvant chemotherapy (NAC) after pretreatment PET/CT and 8 patients were diagnosed cStage IIIC because of detection of parasternal and/or supraclavicular lymph node metastases. We analyzed clinicopathological features, response of NAC and radiotherapy and prognosis of these patients and discuss about treatment strategy of cStage IIIC patients diagnosed PET/CT.
Results: Median age was 41 (range 31–58). Clinical T stage was cT1, 2 (25%); cT2, 3 (37.5%); cT3, 2 (25%); and cT4b, 1 (12.5%); all patients had axillary lymph node metastases. The immunopathological diagnoses by core needle biopsy from primary tumor were ER positive, 6 (75%); HER2 positive, 3 (37.5%); and Ki67 > 15%, 5 (62.5%). All patients underwent NAC using anthracycline and taxane. After NAC, all regional lymph nodes uptake of FDG in PET/CT examination disappeared. Surgery (mastectomy 6, partial mastectomy 2, immediately breast reconstruction 5). All

patients underwent axillary lymph node dissection, but surgery of parasternal and/or supraclavicular lymph node metastases were not performed. Pathological responses of NAC were G3, 2 (25%); G2, 4 (50%); and G1, 2 (25%). Postoperative radiotherapy to supraclavicular and chest wall were performed to 7 patients and 6 patients underwent additional radiation therapy to parasternal lymph node area. There was no important adverse events of radiotherapy. There was no local and distant metastases followed by PET/CT. Median follow up period was 12 months (range 8–60).
Conclusion: Regional lymph node metastases which diagnosed by preoperative PET/CT can be controllable by intensive therapy including NAC, surgery and additional radiation therapy.
Disclosure of Interest: No significant relationships.

P166
Thymidylate synthase is a significant predictive factor of S-1 in metastatic breast cancer patients

H. Seki[1]*, H. Jinno[2], T. Hayashida[2], M. Takahashi[2], F. Asanuma[1], M. Osaku[1], Y. Kitagawa[2]. *[1]Breast Center, Kitasato University Kitasato Institute Hospital, Tokyo, Japan, [2]Department of Surgery, Keio University School of Medicine, Tokyo, Japan*

Goals: S-1, an oral fluoropyrimidine formulation that combines tegafur, 5-chloro-2,4-dihydroxypryidine, and potassium oxonate in a molar ratio of 1:0.4:1, has been widely used against solid cancers including gastric, colorectal, pancreatic, lung and breast cancer in Japan. In a phase II study, the response rate (RR) was 41.7% and the median survival was 872 days among taxane-pretreated patients with metastatic breast cancer (MBC). However, the predictive factor of S-1 in patients with MBC has not been determined yet. The purpose of this study is to investigate the correlation between 5-FU-related enzyme and clinical efficacy of S-1 in patients with MBC.
Methods: Forty-four patients with MBC were treated with S-1 twice daily at a dose of 80 mg/m^2 for 4 weeks, followed by a 2-week rest interval at Keio University Hospital from January 2004 to January 2012, excluding the patients who were concurrentry treated with trastuzumab. Laser-captured microdissection was performed from the formalin-fixed, paraffin-embedded tumor sections at surgery and the expression of 5-FU-related enzyme including thymidylate synthase (TS), thymidine phosphorylase (TP) and dihydropyrimidine dehydrogenase (DPD) was evaluated by RT-PCR. Univariate and multivariate analyses of TTP and OS were conducted using Cox's proportional hazards regression models. The clinicopathological variables were compared using logistic regression where appropriate.
Results: The median follow-up was 25.6 months (range 0.4–81.5). The median age of the patients was 55 years (range 40–84). ER and HER2 were positive in 19 (58%) and 4 (12%) patients, respectively. The median number of metastatic site was 2 (1–4). The sites of metastatic disease were viscera, bone, and soft tissue in 21 (65.6%), 5 (15.6%) and 6 (18.8%), respectively. Twenty-one patients were treated by S-1 as first line chemo therapy. The therapeutic agents administered in the previous treatment included the following: taxanes (18 patients, 40.9%) and anthracyclines (10 patients, 22.7%). The overall response rate (ORR) was 29.5% and CBR was 45.5%. Response rate in triple negative type was slightly higher than those in luminal type and HER2 type (50% vs. 20%, p = 0.074). The median TTP was 11.4 months (3.9–19.0). Univariate analysis revealed that several clinicopathological variables, including TS expression, contributed to ORR and the TTP. Multivariate analysis indicated that low TS expression was the only independent predictive factor for TTP (HR = 4.651, 95% CI 1.734–12.475, p = 0.002). All hematological toxicities were grade 1 or 2. Leukopenia, anemia thrombocytopenia liver dysfunction and kidney dysfuction were found in 19 (43.2%), 4 (9.1%), 3 (6.8%), 12 (27.3%), 4 (9.1%), respectively. Non-hematological toxicities, there were much frequency of diarrhea, vomiting and loss of appetite.
Conclusion: This study demonstrated that TS can be a significant predicitve factor of S-1 in patients with MBC.
Disclosure of Interest: No significant relationships.

P167
Preoperative systemic therapy for locally advanced breast cancer: single center experience

D. Mizrak[1], P. Kubilay[2]*, B. Ozturk[2], H. Onur[1], H. Akbulut[1]. *[1]Medical Oncology, Ankara University, Ankara, Turkey, [2]Internal Medicine, Ankara University, Ankara, Turkey*

Goals: Preoperative therapy has been shown to improve survival, local control, and operability in locally advanced breast cancer. We aimed to investigate our pathologic response rates and breast conservation rates after different chemotherapy regimens.
Methods: Medical records of all breast cancer patients treated in Ankara University Department of Medical Oncology between January 2009 and December 2013 were evaluated retrospectively. A total of 1941 patients' records analyzed and 41 of them with locally advanced breast cancer, who underwent surgical tumor removal after neoadjuvant chemotherapy and with no sign of recurrence have been included in the study.
Results: Median age of patients was 44 year (28–74). Median follow up time was 36 months (6–60 months). Breast conservation rate was 12.2%. Twenty of 41 women have had HER2-positive tumors. Of these patients with HER2-positive tumors, 60% have received trastuzumab containing regimes (3 cycles of FEC followed by 3 or 4 cycles of decetaxel and trastuzumab). Pathologic complete remission (pCR) rate was 33.3% for this group. Forty percent of patients with HER-2 positive tumor have not received anti HER-2 therapy because the HER-2 status could not studied in their biopsy materials. No pCR was seen in these patients. In HER-2 negative patient group 90.4% received antracyclin containing regimes, most of them (73.6%) not followed by docetaxel. No pCR was seen in this taxan free group. Only 5 of 19 patients received docetaxel after antracyclin containing regimes, and pCR was seen in 20% in this group.
Conclusion: Our results suggest that antracyclin containing regimens followed by docetaxel is the best neoadjuvant therapy option for HER-2 negative locally advanced breast cancer. The reason of our very small patient population could be concerned about detection of breast cancers mostly at earlier stages as well as the surgeons choice for the surgery as a primary treatment.
Disclosure of Interest: No significant relationships.

P168
Time-to-failure in 1st-line endocrine therapy with ER+/HER2− metastatic breast cancer

S. Nishimura*, S. Akiyoshi, C. Koga, M. Oikawa, Y. Nskamura, M. Ishida, S. Ohno. *Breast Oncology, National Kyushu Cancer Center, Fukuoka City, Japan*

Goals: Endocrine therapy (ET) is an important treatment option for HR$^+$ metastatic breast cancer (MBC), and offers good prognosis as 1st-line therapy in patients with ER$^+$ MBC (Delpech et al. Breast cancer Res Treat 2012; 135: 619–27). However, the importance of duration of response to 1st-line ET with HR$^+$ MBC is unclear. We investigated whether time to failure (TTF) for 1st-line ET with ER$^+$, HER2$^-$ MBC after recurrence correlates with overall survival after recurrence.
Methods: Patients who were diagnosed with MBC at National Kyushu Cancer Center from 2000 to 2012, were retrospectively examined. 178 patients with ER$^+$/HER2$^-$ MBC were treated with ET as 1st-line therapy after recurrence. We excluded patients with synchronous and asynchronous contra lateral breast cancer, those

with local-recurrence only, and male. We evaluated association between TTF for 1st-line ET after recurrence with clinicopathological factors of main disease and prognosis. Positivity for ER and PgR were defined by immunohistochemically staining of >1% of tumor cell nuclei or ≥4.9 fmol/mg in enzyme immunoassays.

Results: Median follow-up period was 38.8 months (mo); range: 3.3–169. Patients were divided into 3 groups by their TTF for 1st-line ET after recurrence: <3 mo (n = 15), 3–6 mo (n = 40), and ≥6 mo (n = 123). Pathological (p)T stage, pN stage, histological grade, ER status and PgR status at surgery were not associated with 3 TTF groups (<3 mo, 3–6 mo, and ≥6 mo) for 1st-line ET after recurrence. However, median relapse-free survival periods were 49.5 mo for the group of <3 mo TTF for 1st-line ET after recurrence, 49.2 mo for the group of 3–6 mo TTF for 1st-line ET after recurrence, 76.2 mo for the group of ≥6 mo TTF for 1st-line ET after recurrence (P = 0.096). Patients with recurrence during adjuvant ET had the shortest TTF for 1st-line ET after recurrence (<3 mo) among 3 TTF groups for 1st-line ET after recurrence (P < 0.001). The median overall survival after diagnosis of metastatic disease was 23.1 mo for the group of <3 mo TTF for 1st-line ET after recurrence, 37.5 mo for the group of 3–6 mo TTF for 1st-line ET after recurrence, 78.1 mo for the group of ≥6 mo TTF for 1st-line ET after recurrence (P < 0.001). Multivariate analysis showed recurrence during adjuvant ET (P = 0.005) and shorter TTF on 1st-line ET after recurrence (P < 0.001) to be independent adverse prognostic factors in metastatic disease.

Conclusion: Recurrence during adjuvant ET was associated with shorter TTF for 1st-line ET after recurrence. And shorter TTF in 1st-line ET after recurrence was correlated with shorter overall survival after recurrence.

Disclosure of Interest: No significant relationships.

P169

Contralateral breast cancer: a clinico-pathological study of second primary in opposite breast

A. Shankar[1] *, S. Roy[2], A. Malik[1], R. Bhandari[1], K. Kishor[1]. [1]*Radiation Oncology, All India Institute of Medical Sciences, New Delhi, India,* [2]*Pediatrics, VMMC & Safdarjung Hospital, New Delhi, India*

Goals: Breast cancer is by far the most frequent cancer of women (23% of all cancers), ranking second overall when both sexes are considered together. Study of contralateral breast cancer is becoming an important public health issue because of the increased incidence of primary breast cancer and improved survival. The present communication is a study to evaluate the role of various clinico-pathological factors on the occurrence of contralateral breast cancer.

Methods: A detailed analysis was carried out with respect to age, menopausal status, family history, disease stage, surgery performed, histopathology, hormone receptor status, and use of chemotherapy or hormonal therapy. The diagnosis of contralateral breast cancer was confirmed on histopathology report. Relative risk with 95% CI was calculated for different risk factors of contralateral breast cancer development.

Results: Contralateral breast cancer was found in 24 (4.5%) out of 532 patients. Mean age of presentation was 43.2 years. Family history of breast cancer was found in 37.5% of the patients. There was statistically significant higher rate (83.3%) of contralateral breast cancer in patients in age group of 20–40 years with RR = 11.3 (95% CI: 1.4–89.4, p = 0.006) seen in 20–30 years and RR = 10.8 (95% CI: 1.5–79.6, p = 0.002) in 30–40 years as compared to older age of 60–70 years. Risk of development of contralateral breast cancer was higher in premenopausal women (RR = 8.6, 95% CI: 3.5–21.3, p ≤ 0.001). Women with family history of breast cancer had highest rate (20.9%) of CBC (RR = 5.4, 95% CI: 2.5–11.6, p ≤ 0.001). Use of hormonal therapy in hormone receptor positive patients was protective factor in occurrence of CBC but not significant (RR = 0.7, 95% CI: 0.3–1.5, p = 0.333).

Conclusion: Younger age, premenopausal status, and presence of family history were found to be significant risk factors for the development of contralateral breast cancer (CBC). Use of hormonal therapy in hormone receptor positive patients was protective factor in occurrence of CBC but not significant.

Disclosure of Interest: No significant relationships.

P170

Serum levels of CEA and CA 15-3 in different subtypes of recurrent breast cancer

D. Mizrak[1], B. Ozturk[2] *, P. Kubilay[2], H. Akbulut[1], H. Onur[1]. [1]*Medical Oncology, Ankara University, Ankara, Turkey,* [2]*Internal Medicine, Ankara University, Ankara, Turkey*

Goals: Breast cancer recurrence can be treated with curative intent, so screening for recurrence and early detection is important. But there is no consensus about the intensity of surveillance. Routine serum tumor marker studying is not recommended for surveillance because there is no detected improvement in overall survival. We investigated the importance of CEA and CA 15-3 level in different subtypes of recurrent breast cancer.

Methods: All recurrent breast cancer cases treated in Ankara University's Department of Medical Oncology in the last five years were retrospectively screened. A total of 231 recurrent cases with serum CEA and CA 15-3 levels studied in the recurrence are included in the study. We investigated serum CEA and CA 15-3 levels according to estrogen receptor (ER), progesterone receptor (PR), and HER2 status.

Results: The median age was 48 years (18–85 years). There was no significant difference in serum CEA and CA 15-3 levels according to the ER status, in ER positive patients serum CEA was high in 39.4% whereas it was high in 30.0% of ER negatives (p = 0.399), serum CA 15-3 was high in 47.9% of ER positives and high in 35.0% of ER-negatives (p = 0.142). We found no significance with respect to PR status, in PR positive patients serum CEA was high in 40.4% (p = 0.402) and serum CA 15-3 level was high in 46.2% (p = 0.201). In HER2 positive patients, serum CEA level was high in 50% of patients, whereas it was high in 34% of HER2 negative patients (p = 0.076). There was no difference in CA 15-3 levels according to HER2 status (p = 0.904). In non-triple negative patients, we found that serum CEA level was significantly high (41.0%) in recurrence when compared with triple negative patients (8.3%) (p = 0.026). But we found no significant difference for serum CA 15-3 levels for triple negative patients at recurrence (p = 0.233).

Conclusion: Serum CEA level can be an important surveillance parameter in non-triple negative patients.

Disclosure of Interest: No significant relationships.

P171

Efficacy and safety of eribulin as first- to third-line treatment with HER2(−) MBC (KBC-SG 1105)

S. Maeda[1] *, M. Saimura[2], S. Minami[3], K. Kurashita[4], R. Nishimura[5], Y. Kai[6], H. Yano[3], T. Tanaka[7], S. Mitsuyama[2], K. Tamura[7]. [1]*Surgery, National Nagasaki Medical Center, Omura, Japan,* [2]*Kitakyushu Municipal Medical Center, Kitakyushu, Japan,* [3]*Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan,* [4]*Urasoe General Hospital, Okinawa, Japan,* [5]*Breast and Endocrine Surgery, Kumamoto City Hospital, Kumamoto, Japan,* [6]*Ueo Breast Cancer Hospital, Oita, Japan,* [7]*Division of Medical Oncology, Hematology and Infectious Disease, Fukuoka Univercity, Fukuoka, Japan*

Goals: In Japan, eribulin is approved for use from first-line therapy in patients (pts) with advanced or metastatic breast cancer (MBC) previously treated with an anthracycline and taxane. This study

evaluated the efficacy and safety of eribulin as the first- to third-line treatment in patients with MBC.
Methods: This was a phase II, single-arm, open-label, multicenter study in pts with HER2-negative MBC who were previously treated with an anthracycline and taxane. The primary endpoint was the objective response rate (ORR) according to the RECIST criteria. The secondary endpoints were progression-free survival (PFS), the duration of response (DOR), overall survival (OS) and safety.
Results: Fifty-three pts were enrolled between December 2011 and November 2013, and 47 pts (for a median of 7.7 cycles) met inclusion criteria for analysis. The median numbers of prior chemotherapy regimens for MBC was one. The median dose intensity and relative dose intensity for up to 6 cycles was 0.8 mg/m^2/week and 86%, respectively. Patients with higher dose intensity had more response than those with lower dose intensity. The primary endpoint of ORR by independent review was 17.0% (95% CI, 7.6% to 30.8%). The distribution of responses was zero cases of CR (0%), 8 cases of PR (17%), 23 cases of SD (49%), 12 cases of PD (26%) and four cases of NE (8%). Median PFS was 149 days (95% CI, 105 days to 213 days). and median DOR was 451 days (95% CI, 213 days to 592 days). Median OS has not been reached. The most frequent treatment-related grade 3/4 toxicities were neutropenia (55%), leukopenia (36%) and anemia (9%).
Conclusion: Treatment with eribulin as the first- to third-line regimen for HER2-negative MBC is effective and safe practically. Dose intensity is important for PFS.
Disclosure of Interest: No significant relationships.

P172
Prognosis of hormone receptor positive recurrent breast cancer during endocrine therapy

S. Akiyoshi*, M. Oikawa, Y. Koi, C. Koga, S. Nishimura, Y. Nakamura, M. Ishida, S. Ohno. *Breast Oncology, National Kyushu Cancer Center, Fukuoka, Japan*

Goals: There are still lots of recurrence with hormone receptor positive breast cancer (HR+). More than half of recurrence of HR+ tumors occurs during post-operative endocrine therapy, and effective therapeutic strategy is necessary based on the concept of de novo and acquired resistance to endocrine therapy (ET) for patients with recurrent HR+ breast cancer. The aim of this study was to analyze the prognosis of patients with recurrent HR+ breast cancer, associated with recurrence free interval (RFI) and type of treatment.
Methods: We reviewed medical records and database of patients with recurrent breast cancer who were treated at National Kyushu Cancer Center. Among 1931 patients receiving surgery for Stage I–III breast cancer, recurrence was observed in 194 patients. Recurrence was diagnosed in 65 patients within 2 years (short RFI group), in 90 between 2 and 5 years (medium RFI group), and 39 beyond 5 years after operation (long RFI group). Clinicopathological characteristics, prognosis related to treatment for recurrence were compared among those groups.
Results: The median overall survival (OS) times after breast cancer recurrence were 2.5 years in short RFI group, 3.2 years in medium RFI group. The prognosis of long RFI group was good ($p = 0.004$). While medium RFI group had significantly larger tumors as compared to short RFI group ($p = 0.013$), there was no significant difference in those two groups for the other factors. As initial treatment to recurrence of short RFI group, twenty-five patients (51%) received ET and 24 (49%) were treated with chemotherapy (CT). In patients with recurrence of medium RFI group, ET and CT were given to 55 (77%) and 16 (23%), respectively. There were no difference in response rates to ET in these two groups, and clinical response was observed in 18 of 25 patients (72%) with recurrence in short RFI group, and 40 of 55 those (73%) in medium RFI group. The prognosis of patients with recurrent disease was significantly correlated to the sensitivity to the initial treatment ($p < 0.0001$). The median OS rates were 4.2 years for patients with response to ET, 2.4 years for those given CT, and 1.4 years for those with resistant to ET.
Conclusion: Our study showed that the prognosis of patients with recurrent breast cancer during postoperative ET may depend on the sensitivity to the following ET.
Disclosure of Interest: No significant relationships.

P173
Breast cancer in young females: recognition of age as a prognostic factor

M.M. Elsebaie[1]*, H. Alzawahry[2], A. Abdalsamie[2], S. Najeeb[3]. *[1]Radiotherapy, National Cancer Institute, Cairo, Egypt, [2]Medical Oncology, National Cancer Institute, Cairo, Egypt, [3]Surgical Oncology, National Cancer Institute, Cairo, Egypt*

Goals: Explore different prognostic factors that might significantly influence treatment out come in young females with breast cancer.
Methods: All cases with pathologically proven breast cancer referred to the breast cancer unit, National Cancer Institute, Cairo, Egypt, were reviewed between September 2013 till September 2014. Female patients younger than the age of forty were looked at and their different clinical, pathological and biological prognostic factors were analyzed and were correlated to their treatment outcome.
Results: We elicited an incidence of 3.8% of invasive breast cancer in young females (≤40 years). The mean age at time of presentation was 33 years (27–40). Locally advanced disease (T3 & T4) was diagnosed in 38% of our cases. The majority of our cases presented with clinically positive nodes (86%). Distant metastases were evident at time of diagnosis in 10% of cases. Estrogen and progesterone receptors were strongly positive in 62% of patients and Her-2neu was positive in only 14%. Modified radical mastectomy was the most appropriate surgical approach for 55% of our cases due to poor response to neo-adjuvant chemotherapy, 20%, or being operated outside our institution, 35%. Thirty-two percent of the study cohorts were surgically managed by breast conservative surgery. Adjuvant radiation therapy was given in about 80% of cases. All the cases were reviewed to explore prognostic factors that significantly may affect the treatment-outcome in this group of patients.
Conclusion: We do believe that younger age (≤40) at the time of diagnosis of breast cancer carries a poor prognosis in Egyptian females.
Disclosure of Interest: No significant relationships.

P174
IMRT-SIB for locally advanced inoperable breast cancer patients

I. Wziętek[1], S. Blamek[1], A. Namysł-Kaletka[1], R. Kulik[2], K. Trela-Janus[1]*, D. Gabryś[1]. *[1]Department of Radiotherapy, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, Gliwice, Poland, [2]Radiotherapy and Brachytherapy Planning Department, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, Gliwice, Poland*

Goals: Radiobiological and clinical data suggest that higher dose per fraction with shortening overall treatment time in breast cancer patients may enhance locoregional control. This, ethics approved, prospective study was designed to evaluate the technical feasibility, toxicity and early results of simultaneous integrated boost (SIB) for locally advanced, breast cancer patients.
Methods: Nineteen women (8 right; 11 left-sided) received radiotherapy with SIB applying various dose levels in 30 fractions. Doses were individualized according to the stage of the disease. The regional lymph nodes received 49.8–60 Gy, df 1.66–2 Gy, metastatic lymph nodes received 66–69.9 Gy, df 2.2–2.33 Gy, breast with chest wall was irradiated with a dose 49.8–60 Gy, the whole breast to

60 Gy, and the highest dose was delivered to the breast tumour 69.9 Gy. Early toxicity and results were prospectively recorded using CTCAE 4.03, QLQ 30, QLQ Br23, and Lent Soma scale. All patients underwent planning CT or FDG PET-CT. The majority (13 patients) were treated with the use of Clinac IMRT-SIB, 5 patients were treated with Tomo-SIB.

Results: The median age was 58 years (range 37–78). Median tumor size was 6 cm (range 1–12 cm). Almost all (13) patients presented with clinical stage IIIB of the disease, one patient with IIIA, three with IIIC. Two patients in stage IIA were not qualified to surgery, one was not suitable for resection due to medical conditions, the second did not agree for a surgery. All patients received chemotherapy, 11 patients FAC only, remaining various combinations with taxanes. Ten patients were treated with hormonal therapy, the majority of them (8 patients) were treated with tamoxifen. The mean dose to the ipsilateral lung was 16 Gy (range 12.9–20.7). The percentage of lung receiving >5 Gy was 74.9%, >10 Gy – 50%, >20 Gy – 24.5. The mean heart dose was 9.6 Gy (range 5.4–16.9) and V5 Gy was 64.4, V10 Gy – 28.6, V30 Gy – 4.9. There was significant decrease in WBC (median 6.4 vs. 5.1×10^3/ul; p 0.02), PLT (238 vs. 187×10^3/ul; p 0.01) before and after radiotherapy. RBC and Hb did not significantly decrease. The maximum Grade 3 early skin toxicity by the end of treatment was present only in two patients. No Grade 4 toxicities were observed. The maximum Grade 2 fatigue, Grade 1 dysphagia, Grade 1 pain with swallowing were recorded. The early skin toxicity resolved in all patients evaluated one month after finishing the treatment. There were no clinically relevant changes in patients quality of life.

Conclusion: This 6-week course of definitive radiotherapy using SIB technique showed to be feasible and was associated with acceptable early skin toxicity. Long-term follow-up data are needed to assess late toxicity and clinical outcomes.

Disclosure of Interest: No significant relationships.

P175

Intermittent high dose proton pump inhibitor enhances the antitumor effects of chemotherapy in MBC

B. Wang[1] *, J. Zhang[1], J. Wang[1], Z. Shao[2], S. Fais[3], X. Hu[1]. *[1]Department of Medical Oncology, Fudan University Shanghai Cancer Center, Shanghai, China, [2]Breast Surgery, Shanghai Cancer Center, Fudan University, Shanghai, China, [3]Department of Therapeutic Research and Medicines Evaluation, National Institute of Health, Roma, Italy*

Goals: Acidity is a hallmark of malignant tumor, representing a very efficient mechanism of chemoresistance. Proton pump inhibitors (PPI) at high dosage have been shown to sensitize chemoresistant human tumor cells and tumors to cytotoxic molecules. The aim of this study was to investigate the efficacy of PPI in improving the clinical outcome of cisplatin + docetaxel therapeutic regimen in patients with metastatic breast cancer.

Methods: Patients enrolled were randomly assigned to three arms: Arm A, docetaxel 75 mg/m^2 followed by cisplatin 75 mg/m^2 on d4, repeated every 21 days with a maximum of 6 cycles; Arm B, the same chemotherapy preceded by three days esomeprazole (ESOM) 80 mg p.o. bid, beginning on d1 repeated weekly. Weekly intermittent administration of ESOM (3 days on 4 days off) was maintained up to maximum 66 weeks; Arm C, the same as Arm B with the only difference being dose of ESOM at 100 mg p.o. bid. The primary endpoint was response rate. Secondary endpoints included time to progression (TTP), overall survival (OS), and safety profile.

Results: From Aug. 2009 to Aug. 2011, 94 patients were randomly assigned and underwent at least one injection of chemotherapy. Response rates for arm A, arm B and arm C were 46.9%, 71.0%, and 64.5%, respectively. After a median follow up of 40 months, median TTP for arm A (n = 33), arm B (n = 30), arm C (n = 31) were 8.7, 9.4, and 9.7 months, respectively. A significant difference was observed between patients who had taken PPI and who not with ORR (46.9% vs. 67.7%, p = 0.049) and median TTP (9.7 months vs. 8.7 months, p = 0.045). Exploratory analysis showed that among 15 patients with triple negative breast cancer (TNBC), this difference was bigger with median TTP of 10.7 and 5.8 months, respectively (p = 0.011). PPI combination showed a marked effect on OS as well, while with a borderline significance (29.9 vs. 19.2 months, p = 0.090). No additional toxicity was observed with PPI.

Conclusion: The results of this pilot clinical trial showed that intermittent high dose PPI enhance the antitumor effects of chemotherapy in MBC patients without evidence of additional toxicity, which requires urgent validation in a multicenter, randomized, phase III trial.

Disclosure of Interest: No significant relationships.

P176

The DETECT-study concept – circulating tumor cells (CTCs) in metastatic breast cancer

A. Schramm[1] *, V. Mueller[2], J. Huober[1], B. Rack[3], P.A. Fasching[4], F. Taran[5], A. Schneeweiss[6], B. Aktas[7], W. Janni[1], T. Fehm[8]. *[1]Gynecology and Obstetrics, University of Ulm, Ulm, Germany, [2]Gynecology and Obstetrics, University Hospital Hamburg-Eppendorf, Hamburg, Germany, [3]Hospital Ludwig-Maximilians-University Munich, Munich, Germany, [4]Friedrich-Alexander University of Erlangen-Nuremberg, Erlangen, Germany, [5]University Hospital Tübingen, Tuebingen, Germany, [6]Medical Oncology, National Center for Tumor Diseases (NCT), University of Heidelberg and German Cancer Research Center (DKFZ), Heidelberg, Germany, Heidelberg, Germany, [7]University Clinics Essen, Essen, Germany, [8]Heinrich-Heine University, Duesseldorf, Germany*

Introduction: The prognostic relevance of circulating tumor cells (CTC) has been repeatedly shown. The importance of CTC phenotypes for therapeutic decisions and specific treatment response predicted by Her2-phenotype and other cell markers of CTCs will be investigated within the DETECT Studies.

Study design and Methods: Approximately 2000 patients will be screened for CTCs. Patients with HER2-negative primary tumor and HER2 positive CTCs are recruited for the DETECT III trial. Patients are randomized to therapy of physicians' choice (chemotherapy or endocrine therapy) with or without additional HER2-targeted lapatinib therapy. DETECT IV offers an individualized treatment for patients with HER2-negative MBC and HER2-negative CTCs. Postmenopausal patients with hormone receptor-positive primary breast cancer are treated with everolimus + endocrine therapy. For women with triple negative MBC or hormone receptor positive MBC and need for chemotherapy, the trial has been extended to a treatment arm with eribulin (DETECT IVb).

Results: In DETECT V, patients with HER2-positive and hormone receptor-positive MBC are randomized to compare chemo- versus endocrine therapy in combination with dual HER2-targeted therapy (trastuzumab and pertuzumab).

Perspectives: Estimation of clinical efficiency of treatment in DIII and DIV is evaluated by PFS (primary object) and CTC-clearance. Primary object in DETECT V is to assess the safety of a dual HER2-targeted therapy defined by the presence of adverse events. Important translational research aim is the evaluation of an "endocrine responsiveness score", which is based on the expression of estrogen receptor (ER) and HER2 on CTCs for assessing endocrine therapy success.

Conclusion: In the DETECT trials, targeted therapy is based on molecular characterization of CTCs. Thus, efficacy of individualized therapy is investigated by the DETECT study concept and offers innovative strategies for new cancer therapy. The translational research program evaluates the association of presence and molecular characteristics of circulating tumor cells with treatment

response and prognosis for additional information regarding therapy decisions based on CTC detection.
Disclosure of Interest: No significant relationships.

P177
Sodium fluoride PET/CT – a superior imaging modality in confirmation of osseous metastatic disease?

E. Harrold[1] *, C. O'Leary[2], D. Collins[2], S. O'Reilly[2], J. Murphy[3], K. O'Reagan[3]. *[1]Medical Oncology, Cork University Hospital, Co. Cork, Ireland, [2]Medical Oncology, Cork University Hospital, Co Cork, Ireland, [3]Department of Radiology, Cork Univesrsity Hospital, Cork, Ireland*

Goals: Meticulous staging is a critical component of cancer management influencing treatment decision-making and predictive of survival outcomes. Technetium-99m methylene-diphosphonate bone scintigraphy (Tc-99 MDP BS) is currently the imaging modality of choice for diagnosis of bone metastases. However, although sensitive it is not specific and it is limited in assessment of lytic lesions. Several studies have shown NaF-18 PET/CT to have greater specificity, sensitivity and diagnositic accuracy for bone metastases than Tc-99m MDP BS, MDP SPECT and F-18 FDG PET. Na-F-18 PET/CT is available in our centre and has been used in a number of cases when bone scintography and other radiological investigations did not correlate with clinical suspicion of osseous metastatic involvement. We retrospectively reviewed all breast cancer patients who received NaF-18 PET/CT to assess for osseous metastatic disease over an 18 month period. We wanted to assess for correlation between Na-F-18 PET/CT and most recent comparator imaging modality in diagnosis of osseous metastatic disease.
Methods: We used a contemporaneously updated database of all patients who have received Na-F-18 PET/CT in our centre to identify patients eligible for inclusion. With exclusion of prostate cancer patients we had twelve patients who received Na-F-18 PET/CT over the last 18 months.
Results: Four patients who had negative or equivocal Tc-99 MDP BS had confirmation of osseous metastatic disease with Na-F PET/CT. Five patients who had equivocal bone scans had confirmation of the absence of osseous metastases on Na-F PET/CT. Three patients had confirmation of benign osseous disease by Na-F PET/CT.
Conclusion: Minimizing radiation exposure without compromising accuracy of imaging or patient care is critical. Confirmation of metastatic disease has prognostic implications but also impacts patient's quality of life from a symptomatic perspective. Initiation of bisphosphonates and radiotherapy referral depends on this confirmation. One third of our patients had bone disease undetectable on Tc-99 MDP BS illustrating the importance of clinical correlation in interpretation of radiological findings. This small case series is suggestive of superiority of Na-F-18 PET/CT compared with Tc-99 MDP BS and where available Na-F-18 PET/CT should be considered to evaluate for osseous metastatic disease.
Disclosure of Interest: No significant relationships.

The Breast 24S1 (2015) S87–S150

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Poster Abstracts II

Health politics/Guidelines

P180
A visual approach to improve early detection and patient reporting

C.E. Beaumont *. *Global Health Design, Worldwide Breast Cancer, Oxted, United Kingdom*

Goals: A high quality communication plan which includes strategies for difficult-to-reach populations is essential in order to achieve high coverage in cancer screening programmes such as breast cancer (Ullrich, 2011).

However, in low-to-medium developed countries, general screening programs are costly and require infrastructure that is often beyond available resources. Self-reporting of symptoms in these settings becomes paramount to early breast cancer detection. Sadly, most patients present symptoms beyond in situ, making treatment difficult.

With the goal to improve the recognition of symptoms and patient reporting, educating these populations presents major challenges. Low literacy rates, fear of cancer and the cultural taboos associated with breasts, create a hurdle that's difficult to overcome. Despite a large number of education campaigns being developed, none have yet to offer a multilingual, multicultural solution that leaps over these obstacles.

Methods: An action research method was used to design a breast cancer education campaign and test with a variety of viewers.

Three posters and an accompanying leaflet were created. The design method used visual metaphor to explain how the symptoms of breast cancer can look, how to feel for a cancerous lump and steps to take for further investigation.

These visuals were tested and improved for interpretation accuracy using viewer feedback, translated into several languages and then distributed to a range of populations with various screening access capabilities both online and in print. The effectiveness of these images as teaching aids were gathered through qualitative interviews and surveys.

Results: showed that the visual metaphor overcame literacy issues, as a majority of viewers were able to interpret the visuals accurately without the use of text.

Symptoms Image: 65% said the image made them feel more confident in their ability to recognize breast cancer. 89% said they would be better able to recognize the symptoms on themselves after viewing the image.

Anatomy Image: 86% had an accurate tactile knowledge (relating to BSE) after viewing the anatomy image, compared with 15% accurate tactile knowledge with the standard line drawing anatomy image. 97% said the image helped improve their understanding of what to feel for during BSE.

Health practitioners using these materials in the field reported the images were effective in communicating symptoms and teaching BSE to patients. This included reports of patients discovering symptoms during the education session, and patients reporting symptoms to a physican after viewing the images.

Conclusion: A visual approach to reducing breast cancer deaths through early self-reporting seems possible based on the positive results of patient interpretation and practitioner feedback. Further testing is needed to measure the rate of effectiveness with a controlled group to determine the potential of large-scale campaigns.

Disclosure of Interest: No significant relationships.

P181
Choosing wisely: utilization of advanced testing in early stage breast cancer at our institution

H. Ali[1] *, V. Dabak[1], H. Mccoy[2], C. Burmeister[2], W. Haykus[2], M. Paquette[2], L. Young[2]. *[1]Division of Hematology and Oncology, Henry Ford Hospital, Detroit, United States of America, [2]Henry Ford Hospital, Detroit, United States of America*

Goals: Advanced testing (AT), defined as the use of computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET) and radionuclide scanning (such as bone scans), is increasingly utilized in clinical practice and is a major contributor to rising health care spending. In an effort to reduce the cost of health care in the US the American College of Physicians (ACP) and many subspecialty groups such as the American society of clinical oncology (ASCO) have initiated the Choosing Wisely program. Each organization is asked to choose its top five goals for improvement. One of ASCO's top five goals is the reduction in the use of advanced testing in early breast cancer patients. In an effort to understand the patterns of use and drivers for use of AT in clinical practice we analyzed our institution's data collected as part of our participation in the Michigan Breast Oncology Quality initiative (MIBOQi) a statewide quality collaborative.

Methods: Data from all stage I and II patients treated at our institution from January 2006 until December 2011 was collected. Data for advanced testing was collected +/− 90 days from date of diagnosis. Cases in which advanced testing was used were reviewed and additional information regarding the reasons for ordering the tests were abstracted.

Results: A total of 1077 patients in the database met our eligibility criteria. 720 patients were in stage I and 357 patients were in stage II. 167 patients in stage I underwent AT and 201 patients in stage II. Staging was the express intent of AT in 30.6% of those tested in stage I and 78.8% in stage II. A correlation was found between stage, HR (hormone receptor) status, Her2 status and frequency of testing. Patients in clinical stage II were more likely to undergo AT, 56.3% for stage II vs 23.2% for stage I ($p < 0.0001$), patients who were HR positive were less likely to have AT, 30.4% vs 50.3% for

HR negative ($p < 0.0001$), and Her2 positive patients were more likely to have AT, 44.8% vs 32.6% for Her2 negative ($p = 0.0022$).
Conclusion: Although not universal, the use of AT in early stage breast cancer is a significant presence, a real world look into the data suggests that physicians are testing based on their perception of risk. Future research should focus on means to standardize this practice in a simple and reproduceable method to reduce practice variability and focus testing on high yield patients.
Disclosure of Interest: No significant relationships.

P182
NEPA, a new combination antiemetic, exhibits sustained efficacy over repeated chemotherapy cycles

M. Aapro[1]*, H. Rugo[2], G. Rizzi[3]. [1]*Medical Oncology, Institut Multidisciplinaire d'Oncologie, Clinique de Genolier, Genolier, Switzerland,* [2]*Comprehensive Cancer Center, University of San Francisco, San Francisco, United States of America,* [3]*Helsinn Healthcare SA, Lugano, Switzerland*

Goals: Breast cancer (BC) patients (pts) receiving anthracycline-cyclophosphamide (AC) chemotherapy (CT) are at high risk for developing chemotherapy-induced nausea and vomiting (CINV) due to the emetogenicity of the CT and also the predisposing risk factors of young age/female gender. Antiemetic guidelines recommend prophylactic co-administration of an NK_1 receptor antagonist (RA), a 5-HT_3 RA, and dexamethasone (DEX) in these pts. NEPA is the first fixed antiemetic combination and is comprised of a new NK_1 receptor antagonist (RA), netupitant (300 mg), and the pharmacologically/clinically distinct 5-HT_3 RA, palonosetron (PALO 0.50 mg). NEPA has been shown to be superior to oral PALO after a single cycle of AC (Aapro, Ann Oncol 2014). This analysis evaluates sustained efficacy over multiple cycles.
Methods: This was a multinational, randomized, double-blind study evaluating the efficacy/safety of single oral doses of NEPA versus oral PALO in chemotherapy-naive pts receiving multiple cycles of AC. All pts also received oral DEX 12 mg (NEPA) or 20 mg (PALO), only on Day 1. Overall (0–120 h) complete response (CR: no emesis, no rescue medication) rates for NEPA vs oral PALO were prospectively evaluated during each cycle. A post-hoc analysis also compared the probability that a pt would remain a complete responder over multiple cycles considering pts who experienced CINV in the prior cycle as failures.
Results: 1455 pts were randomized; 1286 participated in the multiple cycle extension. Treatment groups were comparable; 98% were females, 97% with BC. CR rates were higher for NEPA than oral PALO during each cycle ($p \leq 0.001$). The percent of pts with a CR in cycle 1 with sustained CR over cycles 2–4 was greater for NEPA than oral PALO ($p < 0.0001$). The table shows percent of pts with continuing CR over time.

Table: Percentage of patients with continuing CR over time

Time since first CT	NEPA + DEX	Oral PALO + DEX
Cycle 1	74.3% (N = 724)	66.6% (N = 725)
Cycle 2	68.5% (N = 485)	57.1% (N = 434)
Cycle 3	65.7% (N = 423)	52.7% (N = 348)
Cycle 4	63.6% (N = 375)	50.6% (N = 300)

N, number of patients at risk.

Conclusion: NEPA, a novel, fixed antiemetic combination offering guideline-consistent prophylaxis in a single dose, demonstrated improved sustained control of CINV over multiple cycles compared to oral PALO in this BC population at high risk for CINV.
Disclosure of Interest: I am a consultant for Helsinn Healthcare, Eisai Inc, and Merck.

P183
Perioperative factors associated with underlying depression in breast cancer patients

H. Do[1]*, J. Jeong[2], Y.S. Kim[3], J.W. Lee[4], B.H. Son[4], S.H. Ahn[4]. [1]*Nursing, Asan Medical Center, Seoul, Korea,* [2]*University of Ulsan College of Medicine, Ulsan, Korea,* [3]*Chosun University Hospital, Gwangju, Korea,* [4]*Asan Medical Center, Seoul, Korea*

Goals: The aims of this study were to determine the prevalence of severe, definite depression symptoms, as measured using the Center for Epidemiological Studies Depression Scale (CES-D), and the association between high CES-D scores (i.e., ≥25) and sociodemographic and perioperative factors during perioperative period.
Methods: Among 1690 consecutive breast cancer patients who were admitted for definitive breast surgery during the study period, 1499 patients were included in this study. Patients with a past medical history of psychiatric medication or support, a plan for elective surgery due to locoregional recurrence or any metastatic disease were excluded. The CES-D score was checked 1 day before definitive surgeries. The sociodemographic data and perioperative data were analyzed.
Results: The mean CES-D score was 18.5, with 24.1% (362/1499) and 56.7% (850/1499) having high CES-D scores of ≥25 and ≥16, respectively. Multivariate analysis revealed that the number of family members with any malignancy (≥2 vs 0), sedative medication (yes vs no) and postoperative numeric rating scale (NRS) scores (persistent, sever pain vs stably mild pain) were significant associated factors for severe, definite depression symptoms [CES-D score of ≥25: adjusted odds ratio (OR) = 1.56, 95% confidence interval (CI) = 1.10–2.21, P = 0.013; adjusted OR = 1.65, 95% CI = 1.00–2.71, P = 0.048; and adjusted OR = 2.14, 95% CI = 1.15–3.95, P = 0.016, respectively].

Table (abstract P183): Multivariate analysis of associated factors for higher CES-D scores (CES-D ≥25)

Variable	Univariate			Multivariate		
	OR	95% CI	P	Adjusted OR	95% CI	P
Age at diagnosis (45–59 years vs other)	1.29	1.01–1.64	0.035	1.28	1.00–1.64	0.055
Current smoker (yes vs no)	1.75	0.97–3.15	0.061	1.61	0.88–2.94	0.124
Education level (less than high school vs college or more)	1.34	0.98–1.84	0.069	1.34	0.97–1.87	0.080
Number of family members with any malignancy (≥2 vs <2)	1.42	1.01–1.99	0.043	1.56	1.10–2.21	0.013
Sedative medication (yes vs no)	1.75	1.08–2.84	0.023	1.65	1.00–2.71	0.048
Type of surgery, breast (mastectomy vs breast conserving surgery)	1.34	1.01–1.77	0.040	1.14	0.84–1.57	0.401
Type of surgery, axilla (axillary lymph node dissection vs sentinel lymph node biopsy)	1.42	1.09–1.85	0.009	1.25	0.93–1.67	0.137
Disease extent (invasive vs in situ)	1.17	0.78–1.77	0.450	1.37	0.79–2.35	0.262
Administration of ketorolac (yes vs no)	1.60	1.04–2.47	0.033	1.30	0.79–2.15	0.300
Postoperative NRS score (persistent, severe pain vs stably mild pain)	2.64	1.53–4.55	0.001	2.14	1.15–3.95	0.016

CES-D, Center for Epidemiological Studies Depression Scale; CI, confidence interval; NRS, numeric rating scale; OR, odds ratio.

Conclusion: During the perioperative period, underlying depression in breast cancer patients should be suspected preoperatively if they have family members with any malignancy, or a need for sedative medication, and postoperatively if they report persistent severe pain.
Disclosure of Interest: No significant relationships.

P184
Perceptions of the factors causing delay of breast cancer diagnosis

M.S. Tramonte, P.C.D.S. Silva, S.R. Chubaci, C.C.R.C. Cordoba, G.Z. Matthes, R.A.C. Vieira*. *Mastology and Reconstructive Surgery, Barretos Cancer Hospital, Barretos, Brazil*

Goals: Evaluate the main factors related to delay in breast cancer diagnosis in a large Public Oncologic Hospital at an inland city of São Paulo State, Brazil.
Methods: A prospective study was performed in breast cancer patients without treatment in the first visit to the Hospital. A specific questionnaire was performed after agreement to the informed consent document. The questionnaire evaluated the previous history of mammography, the clinical signs and symptoms, the time between the exams and the total time to begin the treatment. At the end of the questions, the nurse choose the main factor related to late diagnosis, which was considered as absent, related to the system of health, education and women's attitude. The analysis was dichotomized (absent/present) in diagnostic delay and early clinical stage (stage 0 and I). The chi-square method was used for analysis and a logistic regression was used to evaluate the main variables related to this conditions.
Results: 156 patients were selected for the study. They frequent had low schooling (58.9%), 40–69 years old (73.1%), did not know how to perform breast clinical examination (55.8%) and did not perform regular mammography (52.6%). 72.4% of the tumors are advanced (clinical stage II, III and IV) at the diagnosis. The median time between the onset of symptoms was 7.8 months (mean of 4 months). 23.7% of women did not have delay at diagnosis. The interval cancer represented 5.8% of the total. There was an association between delay in diagnosis and age. The system of health was the main factor related to late diagnosis in women below 40 year-old and the attitude of not perform the mammography was the main factor related in women over 70 year-old ($p < 0.001$). Evaluating exclusively the age 40–69 years old, 28.9% had no delay in diagnosis and the delay in diagnosis was due to the system of health in 34.2%, the adherence to mammography in 28.1% and the education in 8.8%. The adjusted logistic regression model showed that the odds ratio to delay in diagnosis was 3.08 to education, 5.46 to education and 5.67 to adherence.
Conclusion: The factors related to delay in diagnosis are multiple. These findings reflect the limitations of the local system of health organization. It is necessary to decrease the diagnosis time and increase the strategies of mammography adherence and breast cancer diagnosis.
Disclosure of Interest: No significant relationships.

Neoadjuvant (pre-operative) therapy

P190
PgR loss identifies breast cancer patients who underwent neoadjuvant chemotherapy with poor survival

S. Chen*, L. Huang, Z. Shao. *Breast Surgery, Shanghai Cancer Center, Shanghai, China*

Goals: The aim of this study was to investigate the potential of progesterone receptor (PgR) as a biomarker for differentiating estrogen receptor (ER)-positive patients who fail to achieve a pathological complete response to neoadjuvant chemotherapy (NCT) with different prognoses.
Methods: A total of 327 consecutive, locally advanced breast cancer patients with ER-positive disease were included in this study. According to their HER-2 and Ki-67 status, the patients were classified into the Luminal-A or Luminal-B subtype. We evaluated the clinical and pathological response to NCT and relapse or death occurring during follow-up according to PgR status in the different luminal subtypes. Survival analyses were performed using the Cox regression model. Statistically significant prognostic variables in the univariate analysis were tested in the multivariate model with forward selection. The distributions of survival curves were shown using the Kaplan–Meier method, and the differences were measured using the log-rank test.
Results: In the Luminal-B subtype, patients with PgR− tumors had a relatively higher pathological complete response (pCR) rate (29.5% vs. 4.7% pCR, $P < 0.001$) and Miller–Payne grades (45.5% vs. 23.5% of grade 4–5, $P = 0.033$) compared to PgR+ tumors. In Luminal-B patients with residual tumor after NCT, PgR loss was also independently correlated with poor relapse-free survival ($P = 0.017$; HR = 0.430; PgR− as a reference) and overall survival ($P = 0.013$; HR = 0.355; PgR− as a reference). However, in the Luminal-A subtype, there were no statistically significant differences between PgR+ and PgR− disease in response to NCT or survival. In addition, PgR had different prognostic values for patient survival with respect to HER-2 status. It was significantly correlated with RFS and OS in HER-2− Luminal-B patients ($P = 0.018$ and $P = 0.004$, respectively). However, in HER-2+ Luminal-B patients, there was no significant difference in either RFS or OS with respect to the PgR category ($P = 0.562$ and $P = 0.794$, respectively).
Conclusion: In summary, although Luminal-type patients are assumed to have a relatively good prognosis, different permutations and combinations of biomarkers are associated with variable tumor behavior, as we have described for the ER+/PR−/HER-2− subset. Our findings have demonstrated the prognostic value of PgR loss in the neoadjuvant setting, indicating that ER+/PgR− Luminal-B tumors require greater attention due to their high risk of relapse after primary treatment. Prospective approaches regarding tailored treatment strategies should be considered for this unique subset of Luminal-B tumors.
Disclosure of Interest: No significant relationships.

P191
Sentinel lymph node mapping in breast cancer after NAC: a single institution experience

W. Salamoun[1]*, G. Chahine[1], S. Khairallah[2], D. Abi Gerges[3]. [1]*Surgical Oncology, Middle East Institute of Health, Bsalim, Lebanon,* [2]*Pathology, Middle East Institute of Health, Bsalim, Lebanon,* [3]*Medical Oncology, Middle East Institute of Health, Bsalim, Lebanon*

Goals: Neoadjuvant chemotherapy (NAC) is the standard of care for patients with locally advanced breast cancer (LABC). Its use in operable breast cancer is gaining wider acceptance. Sentinel lymph

node biopsy (SLNB) is currently the most accurate staging procedure for the axilla. The aim of our study is to assess the accuracy of sentinel node biopsy after neoadjuvant chemotherapy both for operable and locally advanced breast cancer.

Methods: Between August 2004 and December 2013, we performed 67 SLNM after neoadjuvant chemotherapy. Patients received all chemotherapy cycles before surgery. The procedures were performed by a single surgeon, using dual technique (radioactive tracer and blue dye).

Results: All patients were diagnosed with true-cut biopsy and had clips placement before neoadjuvant chemotherapy. Histology of primary cancer: infiltrating ductal carcinoma (IDC): 44; infiltrating lobular carcinoma (ILC): 13; IDC and ILC: 4; others (colloid, tubular, papillary): 6. Mollecular subtypes: Luminal A and B: 41; triple negative: 14; HER-2 overexpression: 12. Patients were divided into 3 groups according to axillary status. Group 1: histologically positive axillary node(s) by fine needle aspiration (FNA): 19. Group 2: clinically palpable and/or radiologically suspicious nodes: 20. Group 3: unknown axillary status and NAC given for primary breast cancer: 28.

No patients progressed on chemotherapy. Identification rate: 94%. SLNB negative: 36 patients; SLNB positive: 27 patients; SLN not found: 4 patients. Group 1: SLN negative: 8/19, no axillary lymph node dissection (ALND) done; SLN positive: 9/19, ALND; SLN not found: 2/19, ALND. Group 2: SLN negative: 10/20, no ALND; SLN positive 9/20, ALND except 1 patient who received radiation therapy; SLN not found: 1/20, ALND. Group 3: SLN negative 18/28, no ALND; SLN positive 9/28 ALND; SLN not found: 1/28, ALND. 1 sentinel lymph node was removed in 22 patients, 2 in 21 patients, 3 in 15 patients, 4 in 4 patients, SLN not found in 4 patients. SLN positive: 27 patients; macrometastasis 21, micrometastasis 6. Completion ALND: no additional disease: 6 patients. Of 36 patients with SLN negative, 22 patients had no residual disease in the breast. Breast conserving surgery: 40 patients; nipple sparing mastectomy 20 patients, skin sparing mastectomy 5 patients, modified radical mastectomy 2 patients.

Conclusion: Sentinel lymph node mapping is an accurate procedure after neoadjuvant chemotherapy. It provides accurate staging and local control of the axilla, while preventing unnecessary complications of axillary node dissection.

Disclosure of Interest: No significant relationships.

P192

Study of neoadjuvant therapy with FEC followed by weekly nab-paclitaxel for breast cancer

S. Nakagawa[1]*, U. Toh[2], N. Iwakuma[2], M. Mishima[2], R. Takahashi[1], M. Furukawa[2], M. Yamaguchi[3], M. Tanaka[3], E. Ogo[4], Y. Akagi[2]. *[1]Breast Surgery, Clinical Research Institute, National Hospital Organization Kyushu Medical Center, Fukuoka, Japan, [2]Surgery, Kurume University School of Medicine, Kurume, Fukuoka, Japan, [3]Breast Surgery, Kurume General Hospital, Kurume, Japan, [4]Radiology, Kurume University School of Medicine, Kurume, Fukuoka, Japan*

Goals: Nanoparticle albumin-bound paclitaxel (nab-PTX, 130 nm) provides tumor selective localization, potential tumor uptake, and improved pharmacokinetics vs cremophor-paclitaxel, and nab-PTX has demonstrated clinical benefit in metastatic breast cancer in a randomized phase III trial vs paclitaxel (CA012) and in a randomized phase II trial vs docetaxel (CA024). This multicentic phase II study (KSCOG-BC07) was conducted to confirm efficacy and safety of nab-PTX in neoadjuvant chemotherapy setting for patients (pts) with operable breast cancer.

Methods: This is an open-label, multicentre, single-arm, phase II study (Registry number: UMIN000010504). Pts receive 4 cycles of FEC100 (500 mg/m^2 Fluorouracil+100 mg/m^2 Epirubicin+500 mg/m^2 Cyclophosphamide on day1 every 3 weeks) followed by 4 cycles of weekly nab-PTX (100 mg/m^2) administrating on days 1, 8 and 15. Trastuzumab (4 mg/kg for the initial dosing and 2 mg/kg for conccurent administration) was administrated for Her2 positive pts on days 1, 8, 15 and 22 and treatment repeated every 4 weeks. Primary objective is the pCR rate; main secondary objectives are the assessment of preserving operation rate, safety and response rate (RR).

Results: The study has been opened in 4/2013. 18 of planned 32 pts have been recruited so far and 9 pts has been evaluated for the first analysis. The primary endpoint of pCR rate was 44.4% (4/9), RR was 88.9% (8/9) and preserving surgery rate was 66.7%. The most frequent treatment-related grade 3/4 toxicities were neutropenia (65%), leukopenia (54%). No cardiac events have yet to be reported.

Conclusion: Neoadjuvant chemotherapy with FEC followed by weekly nab-PTX for operable breast cancer might be safe and feasible.

Disclosure of Interest: No significant relationships.

P193

Ki-67 as predictor of chemotherapy response in neoadjuvant chemotherapy for breast cancer

A.K. Mishra*, A. Kapoor, S. Tewari, S. Gond, R. Kumar. *Surgery, King George's Medical University, Lucknow, India*

Goals: Aims of study to evaluate changes in Ki-67 before and after neoadjuvant anthracycline based chemotherapy in breast cancer in Indian women as a pilot prospective study.

Background: The absence of Ki-67 in quiescent cells and its high levels in rapidly proliferating cells has created interest in its role in predicting whether a patient would benefit from primary systemic therapy.

Methods: Tru Cut biopsy specimens were collected from carcinoma breast patients admitted in department of surgery KGMU. Ki-67 levels were estimated at start and at end of chemotherapy.

Twenty-two patients of locally advanced breast cancer were enrolled in the study in one year period and received neoadjuvant chemotherapy (Docetaxel (75 mg/m^2), Adriamycin (50 mg/m^2), and Cyclophosphamide (500 mg/m^2) at 3 weekly intervals with peglated granulocyte stimulating factor coverage. These patients underwent repeat Ki-67 estimation from histopathology specimen after 6 cycles.

Results: Twenty patients received six cycles of chemotherapy, and proceeded to surgery. The complete clinical response rate was 20% (4/20). Thirteen patients (65%) achieved a partial response. All the 4 patients with complete clinical response also achieved a complete pathological response. Three patients (15%) were classified as having stable disease.

On comparison of Ki-67 index between the patients showing complete clinical response (CCR) and those showing partial response and stable disease, we found a significant fall in Ki-67 levels by the 6th cycle of chemotherapy in only those patients showing CCR.

CCR patients 4/20 had median Ki-67 at 1st cycle 34.6+18.2 which fell to 17.8+8.7 by 6th cycle (p value 0.01). In patients with stable disease Ki-67 changed from 35.3+20.3 to 22.65+10.2 by 6th cycle (p value 0.13) and in partial responders from 37.3+19.2 to 27.6+9.8 by 6th cycle (p value 0.11).

Conclusion: Our results confirm that subjects showing significant change in Ki-67 (over 50%) are associated with complete response and can reliably benefit from primary systemic therapy.

Disclosure of Interest: No significant relationships.

P194

Pathological response to NAC for locally advanced breast cancer using MRI and PET/CT

K. Higaki*, M. Fujihara, Y. Yoshimura, Y. Kajiwara, M. Kochi, M. Ito, S. Otani. *Breast Surgery, Hiroshima City Hospital, Hiroshima, Japan*

Goals: Neoadjuvant chemotherapy (NAC) is the favored treatment of choice among locally advanced breast cancer patients because it significantly increase the possibility of breast-conserving surgery. However, for non-responders, a prediction of response to NAC is essential. The purpose of this study was to determine US, magnetic resonance imaging (MRI), and positron emission tomography (PET/CT) of whether is useful for prediction of response to NAC. Neoadjuvant chemotherapy (NAC) is the favored treatment of choice among locally advanced breast cancer patients because it significantly increase the possibility of breast-conserving surgery. However, for non-responders, a prediction of response to NAC is essential. The purpose of this study was to determine US, magnetic resonance imaging (MRI), and positron emission tomography (PET/CT) of whether is useful for prediction of response to NAC.
Methods: US, MRI, and PET/CT before and after NAC was performed in 160 consecutive patients with stage II or III breast cancer. The women included in this report received four cycles of taxane with four additional cycles of doxorubicin and cyclophosphamide and 5-FU combination. The tumor size and consistence by erastography were measured with US. The MRI scans were performed on a 1.5 T scanner and dynamic contrast-enhanced fast spoiled gradient echo images T1WI was obtained after intravenous administration of GdDTPA contrast agent. PET/CT was acquired after injection of ^{18}FDG and quantified with standardized uptake value assessment (SUV). Pathologic no response (pNR) was defined in specimens that did not meet the criteria for a pathologic complete or partial response (pCR or pPR). The differences between US and MRI defined volumes, US defined consistence, SUV were tested before and after treatment. Response criteria in solid tumors (RECIST) measures were calculated before and after NAC in each patient and modality.
Results: pCR was obtained in 34 cases and pNR was in 88 cases. The sensitivity was determined by pCR+pPR cases: CR+PR cases ratio and the specificity was determined by pNR cases: PD+SD cases ratio. The sensitivity rate was 73.7% with US, 47.0% with MRI, and 49.0% with PET/CT. The specificity rate was 33.3% with US, 81.8% with MRI, and 88.2% with PET/CT.
Conclusion: US may be accurate in the sensitivity after NAC and MRI and PET-CT may be accurate in the specificity after NAC. Combination of US and PET/CT is useful for a prediction of response to NAC, however PET-CT is expensive and high radiation exposure in spite of the result. Thus, it appeared possible to be substituted MRI with PET/CT.
Disclosure of Interest: No significant relationships.

P195

Elevated lymphocyte-to-monocyte ratio predicts favorable prognosis in LABC following NCT

X. Ni*, Z. Shao. *Breast Surgery, Fudan University Shanghai Cancer Center, Fudan University, Shanghai, China*

Goals: Neoadjuvant chemotherapy (NCT) is a standard treatment option for locally advanced breast cancer. However, the lack of an efficient method to predict treatment response and patient prognosis hampers the clinical evaluation of patient eligibility for NCT. An elevated lymphocyte-to-monocyte ratio (LMR) has been reported to be associated with a favorable prognosis for certain hematologic malignancies and for nasopharyngeal carcinoma; however, this association has not been investigated in breast cancer. The purpose of this study was to evaluate whether pre-NCT LMR analysis could predict the prognosis of patients with locally advanced breast cancer.
Methods: A retrospective cohort of 542 locally advanced breast cancer patients (T3/T4 and/or N2/N3 disease) receiving NCT followed by radical surgery was recruited between May 2002 and August 2011 at the Fudan University Shanghai Cancer Center. Counts for pre-NCT peripheral absolute lymphocytes and monocytes were obtained and used to calculate the LMR.
Results: Univariate and multivariate analysis revealed that higher LMR levels (≥4.25) were significantly associated with favorable DFS (P = 0.009 and P = 0.011, respectively). Additionally, univariate analysis revealed that a higher lymphocyte count ($\geq 1.5\times10^9$/L) showed borderline significance for improved DFS (P = 0.054), while a lower monocyte count ($<0.4\times10^9$/L) was associated with a significantly better DFS (P = 0.010).
Conclusion: An elevated pre-NCT peripheral LMR level was a significantly favorable factor for locally advanced breast cancer patient prognosis. This easily obtained variable may serve as a valuable marker to predict the outcomes of locally advanced breast cancer.
Disclosure of Interest: No significant relationships.

P196

Predictive value of IHC4 score for response to neoadjuvant chemotherapy in breast cancer

S. Elsamany[1]*, S. Elmorsy[2], A. Alzahrani[3], A. Rasmy[4], W. Abozeed[5], A.A. Mohammed[6], M. Ateia[7], M.M. Abbas[8], M. Mashhour[9]. *[1]Medical Oncology, Oncology Center, Mansoura University, Mansoura, Egypt, [2]Pharmacology, Faculty of Medicine, Cairo University, Cairo, Egypt, [3]King Abdullah Medical City, Makkah, Saudi Arabia, [4]Oncology, King Fahed Specialist Hospital, Dammam, Saudi Arabia, [5]Mansoura University Hospital, Mansoura, Egypt, [6]Medical Oncology, Faculty of Medicine, Zagazig, Egypt, [7]Medical Oncology, National Cancer Institute, Cairo University, Cairo, Egypt, [8]Pathology, King Abdullah Medical City, Makkah, Saudi Arabia, [9]Pathology, King Fahed Specialist Hospital, Dammam, Saudi Arabia*

Goals: In hormonal receptors (HR)-positive breast cancer (BC) patients treated with adjuvant hormonal therapy, IHC4 score provided similar prognostic information to that of Oncotype DX-recurrence score. This study aims to explore the value of IHC4 in predicting pathological response after neoadjuvant chemotherapy in patients with HR-positive BC.
Methods: In this retrospective exploratory study, data of 68 HR-positive BC patients who received neoadjuvant chemotherapy was recorded. IHC4 score was calculated based on estrogen receptors, progesterone receptors, Ki-67 and HER2 status. Logistic and ordinal regression analyses in addition to likelihood ratio test were used to explore the association of IHC4 score and other clinico-pathological parameters with pathological complete response (pCR) and pathological stage after chemotherapy.
Results: Among our cohort, pCR was found in 29.4% of patients while pathological stages I, II, III were found in 11.8%, 26.5% and 32.4% of patients respectively. Taking the median value as the cut-off, lower IHC4 score was significantly associated with an increased likelihood of pCR (low; 41.2% vs. high; 17.6%, OR = 3.27, 95% CI=1.07–9.96, p = 0.037) and lower pathological stage (OR = 3.24, 95% CI = 1.33–7.88, p = 0.009). When IHC4 score was treated as a continuous variable, lower score was significantly associated with an increased probability of pCR (OR = 1.009, 95% CI = 1.001–1.018, p = 0.036) and lower pathological stage (OR = 1.009, 95% CI = 1.002–1.017, p = 0.011). In addition, lower clinical stage was associated with a better pCR rate that was of borderline significance (p = 0.056). When clinical stage and IHC4 score were incorporated together in a logistic model to assess their association with pCR, the likelihood ratio test gave a p-value of 0.004 after removal of the IHC4 score and 0.011 after

removal of the stage, indicating a more significant predictive value of IHC4 score.
Conclusion: This study suggests that IHC4 score may be utilized to predict pathological response to neoadjuvant chemotherapy in HR-positive BC patients. This finding needs to be validated in a larger cohort of patients.
Disclosure of Interest: No significant relationships.

P197
Phase II study of neoadjuvant weekly albumin-bound paclitaxel for node-positive breast cancer

A. Hattori[1]*, A. Hirano[1], K. Ogura[1], H. Inoue[1], F. Okubo[1], R. Miyamoto[2], N. Jibiki[2], M. Fujibayashi[1], T. Shimizu[1]. [1]*Tokyo Women's Medical University Medical Center East, Breast Surgery, Tokyo, Japan,* [2]*Tokyo Women's Medical University Yachiyo Medical Center, Breast Surgery, Chiba, Japan*

Goals: Conventional paclitaxel requires solvents such as polyoxyethylated castor oil; however, such solvents are associated with toxicity including peripheral neuropathy and hypersensitivity reaction. Therefore, nanoparticle albumin-bound paclitaxel (nab-PTX) requiring no solvent has been developed. Nab-PTX is effective in patients with metastatic breast cancer and as a neoadjuvant therapy. A comparison between weekly and triweekly nab-PTX suggested that weekly nab-PTX was superior in progression-free survival. However, the optimal dose of weekly nab-PTX is still unknown. Thus we planned a phase II neoadjuvant trial with epirubicin/cyclophosphamide (EC) followed by weekly nab-PTX +/− trastuzumab (T) (Trial registration; UMIN000007648).
Methods: The primary endpoint is the pathologic complete response (pCR) rate in the breast and axilla, and the secondary endpoints are the breast conserving rate, toxicities, feasibility and overall survival. pCR was defined as no evidence of residual invasive cancer, either in the breast or axilla. Patients with histologically diagnosed invasive breast cancer based on a core needle biopsy of the T1–4 N1–3 without previous operation or chemotherapy were included in this trial. Eligible patients were aged between 20 years and 70 years with a performance status of 0 to 2 and adequate organ functions. Patients received four cycles of EC (90 mg/m^2, 600 mg/m^2) every 3 weeks, followed by four cycles of nab-PTX (125 mg/m^2) on Days 1, 8 and 15 in a 28-day cycle. Fifteen cycles of T (2 mg/kg, loading 4 mg/kg) were added to the nab-PTX regimen in HER2-positive patients every week.
Results: Forty patients were enrolled in this study and 1 patient withdrew. The safety population consisted of 40 patients and primary endpoint analysis was performed on 39 patients. pCR were observed in 13 patients and the pCR rate was 33.3% (13/39) (95% CI, 20.1–49.0%). According to ER, PgR, HER2 status, the following 4 subtypes were classified: luminal (ER and/or PgR+, HER2-; n = 19), luminal-HER2 (ER and/or PgR+, HER2+; n = 5), HER2 (ER and PgR−, HER2+; n = 10) and triple negative (ER, PgR and HER2-; n = 5). The pCR rates were 5.3% in luminal type, 40.0% in luminal-HER2, 90% in HER2, and 20% in triple negative, respectively ($P < 0.0001$). Seventeen patients (43.6%) underwent breast conserving surgery. Grade 3 or 4 leukocytepenia was recorded in 55.0% (EC) and 44.7% (nab-PTX), and grade 3 or 4 neutropenia was recorded in 57.5% (EC) and 60.5% (nab-PTX). Febrile neutropenia occurred in 3 patients (7.5%) (EC). Peripheral neuropathy (nab-PTX) was recorded in 94.7% (grade 1: 76.3%, grade 2: 13.2%, grade 3: 5.3%).
Conclusion: EC followed by weekly nab-PTX (125 mg/m^2) +/− T was an effective treatment. In particular, patients with HER2 type had a significantly higher rate of pCR.
Disclosure of Interest: No significant relationships.

P198
Prognostic value of breast cancer subtypes: from phase 2 randomized trial of neoadjuvant therapy

V.F. Semiglazov[1]*, G.A. Dashyan[1], V.V. Semiglazov[2], O. Petrenko[1], A. Komyahov[1], R.M. Paltuev[3], D. Matzko[1]. [1]*Breast Cancer, N.N. Petrov Research Institute of Oncology, St. Petersburg, Russian Federation,* [2]*Clinical Oncology, 1st Pavlov Medical University, St. Petersburg, Russian Federation,* [3]*Breast Department, Railway Hospital, St. Petersburg, Russian Federation*

Goals: Previously the primary efficacy end point was already reported (Semiglasov V. et al., Cancer 2007; 110: 244–254). Here we present 10-year disease-free (DFS) and overall (OS) survival rates in both neoadjuvant therapy groups according to breast cancer subtypes using Kaplan–Meier method.
Methods: Eligible patients were randomly assigned to receive neoadjuvant endocrine therapy (anastrozole 1 mg/day or exemestane 25 mg/day for 3 months, 121 patients) or chemotherapy (doxorubicin 60 mg/m^2 with paclitaxel 200 mg/m^2 four 3-week cycles, 118 patients). Treatment of each patient after surgery was at the investigator's discretion. It was typically recommended that patients with objective response (OR) to neoadjuvant endocrine therapy receive tamoxifen for 5 years, and patients with OR to chemotherapy receive adjuvant chemotherapy (4–6 cycles). All patients are being followed for development of local recurrence, distant metastases and survival at 10 years postsurgery.
Results: Breast cancer subtypes were defined as luminal A [strong expression (Allred ≥6) ER/PR+, HER− and G1), luminal B (ER/PR+, HER− and G2–3), luminal B HER2+ using immunohistochemical staining.
Most patients (133, 55.6%) had a luminal A cancer (70 patients received endocrine therapy, 63 chemotherapy). Luminal B (HER2−) was identified in 75 patients (31.4%) (37 patients received endocrine therapy, 38 chemotherapy). Luminal B (HER2+) was identified in 31 patients (13%), (14 patients received endocrine therapy, 17 chemotherapy). Patients with HER2-positive cancer did not receive anti-HER2 therapy.
There was a trend towards higher overall rates of objective response (OR) and breast-conserving surgery (BCS) among patients with tumors expressing high levels of ER (luminal A) in the endocrine therapy group compared with the chemotherapy group (43% vs 24%; $p = 0.054$). The study showed that patients with luminal A breast cancer who received neoadjuvant endocrine therapy have tendency to improve 10 year DFS rates compared with chemotherapy (72.8% vs 53.9%; $p = 0.068$).
There was no significant difference in DFS and OS rates through 10 years of follow up in the luminal B group (including luminal HER2+) between 51 pts who received neoadjuvant endocrine therapy and 55 women who received chemotherapy (DFS, 41.0% vs 49.0%; OS, 49.0% vs 52.7%, correspondingly, $p > 0.5$).
Conclusion: Neoadjuvant endocrine therapy constitutes an effective treatment in a selective group of ER+ (luminal A) breast cancer patients compared to chemotherapy.
Disclosure of Interest: No significant relationships.

P199

Neoadjuvant systemic therapy for breast cancer: a survey of Australian and New Zealand specialists

N. Zdenkowski[1] *, P. Butow[2], G.B. Mann[3], S. Fewster[1], C. Beckmore[1], R. Isaacs[4], F.M. Boyle[2]. *[1]Trials Coordination Department, Australia and New Zealand Breast Cancer Trials Group, Waratah, Australia, [2]University of Sydney, Sydney, Australia, [3]University of Melbourne, Melbourne, Australia, [4]MidCentral Regional Cancer Treatment Service, Palmerston North, New Zealand*

Goals: To understand Australian and New Zealand (ANZ) breast cancer specialists' use of neoadjuvant systemic therapy (NAST) for women with operable breast cancer.
Methods: A cross-sectional survey was sent to members of major ANZ professional groups representing breast cancer specialists. The online survey included questions on referral patterns, patient selection, clinical workup, reasons for offering NAST and barriers to its use. Those that do not offer NAST for operable breast cancer were given an abbreviated survey about demographics, interest in NAST, and barriers to its use.
Results: Eligible responses were received from 207 clinicians from Australia and NZ: 112 surgeons (54%), 87 medical oncologists (42%), 6 radiation oncologists (3%) and 2 breast physicians (1%). One hundred and twenty, 81 and 6 responses were from metropolitan, regional and rural areas respectively. Fifty-two academics, 111 public and 44 private practitioners participated. There were equal numbers of males and females. Forty-five respondents (22%) reported not offering NAST, and 162 (78%) reported routinely offering NAST to selected women with operable breast cancer. A median of 9% of all operable patients were offered NAST. NAST was offered to all subtypes, but more frequently to women with HER2 positive and triple negative cancers. These subtypes were also more likely to be offered NAST for a smaller primary tumour size. Reasons for offering NAST were: to enable breast conserving surgery (80% of respondents); if a neoadjuvant clinical trial is available (73%); if adjuvant therapy is clearly indicated (58%); to plan definitive surgery (58%); to facilitate for immediate reconstruction (51%); to give time for genetic testing prior to making definitive local therapy decisions (51%); and to better estimate the effectiveness of systemic therapy (48%). Of 207 respondents, 45% and 58% indicated a preference to increase the number of patients who receive NAST as part of routine care and as part of a clinical trial respectively. Patient barriers were: desire for surgery as soon as possible (29% rated as highly important); lack of awareness about NAST (20%); concern about progression on NAST (13%); and disinterest in downstaging to lumpectomy (10%). Forty-three percent experienced system-related barriers to the use of NAST, including: lack of interest from other clinicians (22%), lack of clinical trials (15%); and insufficient evidence for the use of NAST (10%).
Conclusion: Australian and New Zealand clinicians are interested in NAST for operable breast cancer, and offer it for downstaging, research and surgical planning. Patient-related and institutional barriers that prevent the optimal uptake of this treatment approach will need to be systematically addressed.
Disclosure of Interest: No significant relationships.

P200

Neoadjuvant therapy in HER2+ breast cancer: Opti-HER Heart run-in phase safety data (SOLTI-1002)

J. Gavilá[1] *, M. Fernández-Abad[2], J.M. Pérez[3], Á.L. Guerrero[1], M. Oliveira[3], M. Llobet-Canela[4], A. Llombart[5]. *[1]Medical Oncology Service, Instituto Valenciano de Oncología, Valencia, Spain, [2]Centro Integral Oncológico Clara Campal, Madrid, Spain, [3]Hospital Universitari Vall d'Hebron, Barcelona, Spain, [4]Scientific Department, SOLTI, Barcelona, Spain, [5]Hospital Universitari Arnau de Vilanova, Valencia, Spain*

Goals: The Opti-HER Heart (NCT01669239) is a phase II trial that seeks to optimize the treatment of HER2+ breast cancer (BC) patients (pts), while minimizing cardiac risk by combining HER2 dual-blockade plus a taxane and a non-pegylated liposomal anthracycline. The trial included a safety run-in, in which the first 10 pts enrolled undergo intensified safety monitoring for cardiac and hematological adverse events (AE) during one year from study drugs first administration. Here we report these data.
Methods: Patients receive neoadjuvant therapy for six 21-day cycles. Regimen consists of: trastuzumab 4 mg/kg loading dose (LD) on Day (D) 1 of Cycle (C) 1, then 2 mg/kg on D8 and 15 and on D1, 8, and 15 of subsequent cycles; pertuzumab 840 mg LD on C1D1, then 420 mg on D1 of the following cycles; Myocet® 50 mg/m^2 on D1 of each cycle; and paclitaxel 80 mg/m^2 on D1, 8 and 15 of each cycle. Neutropenia is an expected AE for this regimen so prophylactic Granulocyte-Colony Stimulating Factor (G-CSF) administration is allowed. The primary objective is to evaluate cardiac safety measured by the incidence of: 1. symptomatic congestive heart failure or type A cardiac event; and 2. asymptomatic reduction of Left Ventricular Ejection Fraction (LVEF) value or type B cardiac event, assessed by clinical evaluation, ECG, and LVEF measurement.
Results: By September 2013, ten pts with primary HER2+ BC (stage I–IIIA) and adequate cardiac function were enrolled in the safety run-in phase. Median age was 47 years (22–67), median LVEF value at baseline was 66.5% (60–78), and baseline cardiovascular risk factors identified were hypertension (2 pts), diabetes mellitus (1 pt), hypercholesterolemia (1 pt) and smoking (1 pt). Nine pts completed all 6 cycles, whereas 4 needed to adjust or temporarily interrupt the treatment. No symptomatic cardiac events or asymptomatic LVEF decline was observed. Median LVEF value at the end of treatment was 64% (58–67). Three pts experienced treatment-related serious AE: one pt presented Grade (G) 3 asthenia and G3 nausea; and two pts developed G4 neutropenia. Most frequent non-serious AE (incidence ≥40%) suspected to be treatment related were asthenia, gastrointestinal disorders (i.e., abdominal pain, diarrhea, nausea), and skin and subcutaneous tissue disorders (i.e., alopecia, rash, nails disorders). Most of these side effects were manageable and mainly G1–2.
Conclusion: In the Opti-HER Heart trial run-in phase, no type A or type B cardiac events occurred, allowing continuation of recruitment of the remaining 73 pts, which is currently underway. Two cases of G4 neutropenia were reported, therefore, primary G-CSF prophylaxis is highly recommended for all patients recruited for the second stage of the trial.
Disclosure of Interest: Trastuzumab and pertuzumab are kindly provided by Roche and Myocet by Teva. The trial is supported by a grant from TEVA. For additional information, contact SOLTI Breast Cancer Research Group at depto.cientifico@gruposolti.org.

P201

Subcutaneous versus intravenous trastuzumab in early breast cancer: 2-year follow-up of HannaH

C. Jackisch[1]*, R. Hegg[2], D. Stroyakovskiy[3], J. Ahn[4], B. Melichar[5], S.C. Chen[6], A. Crepelle-Flechais[7], D. Heinzmann[8], M. Shing[9], X. Pivot[10]. [1]*Department of Obstetrics and Gynecology & Breast Cancer and Gynecology Cancer Center, Sana Klinikum Offenbach GmbH, Offenbach, Germany,* [2]*Department of Gynecology and Obstetrics, Hospital Pérola Byington, São Paulo, Brazil,* [3]*Chemotherapeutic Department, City Clinical Oncology Hospital 62, Moscow, Russian Federation,* [4]*Department of Medicine, Samsung Medical Center, Seoul, Korea,* [5]*Department of Oncology, Palacký University Medical School & Teaching Hospital, Olomouc, Czech Republic,* [6]*Department of Surgery, Chang Gung Memorial Hospital, Taipei, Taiwan,* [7]*Global Pharma Development, F. Hoffmann-La Roche Ltd, Basel, Switzerland,* [8]*Biostatistics, F. Hoffmann-La Roche Ltd, Basel, Switzerland,* [9]*Global Pharma Development, Genentech, Inc., South San Francisco, United States of America,* [10]*Chemotherapy–Oncology, CHU Jean Minjoz, Besançon, France*

Goals: To evaluate the secondary endpoints of event-free survival (EFS: time from randomisation to disease recurrence/progression or death), overall survival (OS: time from randomisation to death) and safety of subcutaneous (SC) trastuzumab (Herceptin® SC [H SC], F. Hoffmann-La Roche Ltd) versus intravenous (IV) trastuzumab (Herceptin® [H IV]) for HER2-positive early breast cancer after 2-year treatment-free follow-up in the phase III HannaH study (NCT00950300). The primary analysis reported non-inferior co-primary endpoints: pathological complete response (pCR) and trough serum concentration (C_{trough}).

Methods: N = 596 patients were randomised to receive 8 cycles of 3-weekly neoadjuvant H SC (600 mg fixed dose) or H IV (8 mg/kg loading/6 mg/kg maintenance doses) concurrently with docetaxel followed by 5-fluorouracil/epirubicin/cyclophosphamide (4 cycles each). Post-surgery, patients received 10 cycles of adjuvant H SC or H IV to complete 1 year of therapy. EFS and safety were also assessed across patient weight quartiles to investigate the appropriateness of the fixed dose.

Results: Median follow-up was 40.3 months with H SC (range 0.3–50.7) and 40.6 months with H IV (1.0–51.0). Three-year EFS rates in the intent-to-treat populations were 218/294 (74%) for H SC and 217/297 (73%) for H IV (unstratified hazard ratio [HR] 0.95, 95% confidence interval [CI] 0.69–1.30). EFS was similar between H SC and H IV groups and across weight quartiles. Three-year OS rates were 272/294 (93%) for H SC and 268/297 (90%) for H IV (unstratified HR 0.76, 95% CI 0.44–1.32). Safety information is shown in the table. Cardiac adverse event (AE) rates were similar between H SC and H IV, and also between different weight quartiles. Only a small number of new AEs were observed during the treatment-free follow-up period, and these were balanced between groups.

	Overall		Treatment-free follow-up	
	H SC	H IV	H SC	H IV
Safety population	297 patients	298 patients	297 patients	298 patients
≥1 AE (any grade), n (%)	290 (98)	282 (95)	7 (2)	7 (2)
≥1 grade 3–5 AE, n (%)	158 (53)	158 (53)	2 (<1)	3 (1)
≥1 serious AE (SAE), n (%)	65 (22)	43 (14)	2 (<1)	3 (1)
≥1 related SAE, n (%)	31 (10)	24 (8)	1 (<1)	0
AEs leading to death, n (%)	4 (1)	3 (1)	1 (<1)	2 (<1)

Conclusion: HannaH's long-term efficacy endpoints, EFS and OS, support the established non-inferiority of H SC relative to H IV per the co-primary endpoints, pCR and C_{trough}. The safety profile of H SC was consistent with the known H IV safety profile.

Disclosure of Interest: CJ: Consultant/ad board/research/travel (Amgen). BM: Consultant/ad board/research/travel (Roche/Novartis/GSK). AC: Employment/shares (Roche). DH: Employment/stock/royalties/equity (Roche). MS: Employment (Roche/Genentech). XP: Consultant/ad board (Roche).

P202

Phase 2 study of neoadjuvant anthracycline followed by nab-paclitaxel and trastuzumab

M. Iwamoto[1]*, S. Tanaka[2], K. Kimura[2], N. Matsunami[3], H. Morishima[3], K. Yoshidome[4], T. Nomura[5], T. Morimoto[5], D. Yamamoto[6], Y. Tsubota[6]. [1]*Breast Surgery, Osaka Medical College, Osaka, Japan,* [2]*Osaka Medical College, Osaka, Japan,* [3]*Osaka Rosai Hospital, Osaka, Japan,* [4]*Osaka Police Hospital, Osaka, Japan,* [5]*Yao Municipal Hospital, Osaka, Japan,* [6]*Kansai Medical University, Osaka, Japan*

Goals: Nab-paclitaxel (PTX) has been developed to reduce toxicities associated with PTX injection while maintaining or improving its chemotherapeutic effect. This phase II study has been designed to evaluate the activity and safety of nab-PTX q3wks as neoadjuvant treatment in HER2-positive operable breast cancer. Neoadjuvant setting of the combination of nab-PTX plus trastuzumab q3wks appears to be effective and safe in this population.

Methods: Stage I–IIIA patients were treated with neoadjuvant EC (epirubicin 90 mg/m^2, cyclophosphamide 600 mg/m^2) or FEC (5-fluorouracil 500 mg/m^2, epirubicin 100 mg/m^2, cyclophosphamide 500 mg/m^2) q3wks ×4, followed by nab-PTX (260 mg/m^2) plus trastuzumab q3wks ×4. Primary end point was pCR rate. Secondary end points included clinical response rate, disease free survival, pathological response (defined as pCR or minimal residual invasive disease only in the breast) rate, breast-conserving surgery rate, and safety.

Results: Forty-six patients were enrolled. Because one patient met the exclusion criteria because of co-existence of another malignant disease, forty-five patients were evaluable for analysis. Among them, one patient showed rapid disease progression during EC and surgery was performed. Therefore, forty-four patients were evaluable for safety of nab-PTX. Forty-nine percent of patients achieved pCR. pCR rate was 36% and 71% in estrogen receptor positive and negative patients, respectively. Two patients discontinued planned nab-PTX plus trastuzumab therapy (one case was due to disease progression as above, and another was administered only trastuzumab from 3 to 4 cycles due to prolonged neutropenia). Among all chemotherapy, the most frequent reasons for delay or dose reduction were hematologic toxicities, and only one case needed dose reduction for nab-PTX due to peripheral neuropathy.

Conclusion: Neoadjuvant setting of this combination appears to be effective and safe in HER2-positive breast cancer patients.

Disclosure of Interest: No significant relationships.

P203

Dual HER2 blockage with lapatinib and trastuzumab for Japanese patients with HER2+ breast cancer

H. Iwata[1]*, N. Yamamoto[2], N. Masuda[3], H. Bando[4], K. Kuroi[5], S. Ohno[6], H. Kasai[7], S. Morita[8], T. Sakurai[9], M. Toi[10], JBCRG-16 (Neo-LaTH) Study Group. [1]*Department of Breast Oncology, Aichi Cancer Center Hospital, Aichi, Japan,* [2]*Division of Breast Surgery, Chiba Cancer Center, Chiba, Japan,* [3]*Department of Surgery, Breast Oncology, National Hospital Organization Osaka National Hospital, Osaka, Japan,* [4]*Breast and Endocrine Surgery, Faculty of Medicine, University of Tsukuba, Ibaraki, Japan,* [5]*Department of Breast Surgery, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Tokyo, Japan,* [6]*Clinical Research Institute, National Hospital Organization Kyushu Cancer Center, Fukuoka, Japan,* [7]*Department of Experimental Therapeutics Institute for Advancement of Clinical and Translational Science, Kyoto University Hospital, Kyoto, Japan,* [8]*Department of Biomedical Statistics and Bioinformatics, Kyoto University Graduate School of Medicine, Kyoto, Japan,* [9]*Department of Diagnostic Pathology, Kyoto University Hospital, Kyoto, Japan,* [10]*Department of Surgery (breast Surgery), Graduate School of Medicine, Kyoto University, Kyoto, Japan*

Goals: The JBCRG-16 (Neo-LaTH) trial was conducted to evaluate the efficacy and safety of lapatinib (La) + trastuzumab (T) therapy followed by LaT + weekly paclitaxel (wP) in a neoadjuvant setting for primary HER2+ breast cancer (BC). We also aimed to verify the period of LaT therapy (6 vs 18 weeks [wks]) and the effect of add-on endocrine therapy in ER(+) patients (pts).

Methods: We recruited and randomized pts aged ≤70 years with central laboratory-confirmed HER2+ primary invasive BC (T1c–3, N0–1, M0, T ≤7 cm) into groups A and B (ER[−]), and C–E (ER[+]). Groups A, C and D received LaT for 6 wks; B and E for 18 wks. All groups received ongoing LaT plus wP for 12 wks following the initial LaT phase. La was administered at 1000 mg/day and 750 mg/day during the initial LaT periods and the LaT+wP period, respectively. Groups D and E received additional endocrine therapy. The primary endpoint was the comprehensive pathological complete response (CpCR) rate; safety, overall response rate (ORR) and breast conservation rate (BCR) were assessed as secondary endpoints.

Results: A total of 215 pts were enrolled between April 2012 and September 2013; 213 were included in the safety analysis sets (44, 48, 41, 40 and 40 pts in groups A, B, C, D and E, respectively) and one was excluded for the full analysis sets. Pts had a median age of 52.5 years (range 26–70); 65.3% were classified as T2, and 55.4% as N0. The relative dose intensities [mean (SD)] of La during the LaT period were 97.1% (7.2), 91.7% (17.4), 94.9% (15.5), 96.0% (12.3) and 90.4% (21.1) in groups A, B, C, D and E, respectively, and during the LaT+wP period were 81.7% (27.3), 72.7% (38.8), 80.5% (30.4), 86.0% (24.0) and 78.2% (34.2). Grade ≥3 adverse events were observed in 42.3% of pts; the most common were neutropenia (19%), diarrhea (12%), skin and subcutaneous disorders and elevated ALT (5% each), and paronychia (3%). In groups A, B, C, D and E, respectively, CpCR was achieved by 65.9%, 60.4%, 34.1%, 33.3% and 41.0%; ORRs evaluated by MRI or CT were 81.8%, 81.3%, 85.4%, 92.5% and 92.5%; and BCRs were 63.6%, 55.3%, 70.7%, 53.8% and 68.4%.

Conclusion: Safety and efficacy of LaT and LaT followed by wP for HER2+ BC were confirmed in Japanese pts, consistent with the results of the Neo-ALTTO study; the efficacy based on CpCR did not improve by alteration of LaT treatment period and/or addition of endocrine therapy.

Disclosure of Interest: Please refer to the file sent to the secretariat.

P204

Axillary nodal burden and chemotherapy influences PCR in advanced breast cancer treated with NACT

D. Mondal[1], A. Srivastava[2], P. Ranjan[2], D.N. Sharma[1], R. Das[1], L. Kashyap[1], K.P. Haresh[1], P.K. Julka[1]*, N. Manoharan[3], S. Gupta[1]. [1]*Department of Radiation Oncology, All India Institute of Medical Sciences, New Delhi, India,* [2]*Department of Surgery, All India Institute of Medical Sciences, New Delhi, India,* [3]*Department of Biostatistics, Dr. B.R. Ambedkar Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi, India*

Introduction: Pathological complete response (pCR) after neoadjuvant chemotherapy (NACT) in locally advanced breast cancer (LABC) is a surrogate marker for survival. A retrospective analysis of outcome to neoadjuvant chemotherapy being presented.

Aims and objectives: To analyse impact of NACT on pCR in LABC patients and correlating with different factors.

Methodology: Data of LABC patients treated with NACT with curative intent from 2010–2013 were collected and analysed retrospectively.

Statistical analysis: Correlation with different factor were tested with SPSS version 16. Chi square test was used to assess significance. P value of 0.05 or less was considered significant.

Results: 100 patients were retrieved. 1 patient was excluded from analysis for lack of information. 99 patients were finally analysed. 41, 54 and 5 patients were premenopausal, postmenopausal and perimenopausal respectively. 18, 22 and 44 patients had cT2, cT3 and cT4a tumor respectively. cN0, cN1, cN2 and cN3 disease were present in 30, 40, 22 and 3 patients respectively. 20 patients had oligometastases. 6, 11 and 3 patients had skeletal, visceral and both metastasis respectively. 96 patients had IDC. ER and PR were positive in 40 and 38 patients. 63 patients were Her2 negative, 32 positive and 4 were indeterminate. 20 patients were TNBC. DE was commonest chemotherapy followed by CEF (69 vs. 20). 73 patients received 6 cycles of NACT. Clinical response was assessed after each cycle. Poor responders were operated after 3 cycles. US guided biopsy was performed for axillary node. Axillary node positive and negative patients underwent ALND and SLNB respectively. SLN negative patients received no further axillary treatment. Positive SLNB patients underwent ALND. Poor responders were directly taken for ALND without evaluating for SLNB. 18 patients showed clinical CR in both breast and axilla. 36 patients did not show any response. BCS, radical mastectomy, MRM or mastectomy was performed in 22, 36, 28 and 13 patients respectively. SLNB was done in 38 patients. 24 patients were node negative. Minimum 3 and 10 nodes were removed for adequate SLNB or ALND. 75 patients underwent ALND. 53 patients showed axillary nodal disease. 40, 10 and 26 patients showed pCR in both breast and axilla, breast only and axilla only, respectively. 23 patients showed residual disease both in breast and axilla. 23 patients out of 40 with cN1 disease showed CR (statistically significant, P = 0.019). Among cN1 patients DE showed significantly better response (P = 0.001). No significant association was seen with other variables.

Conclusion: cN1 axillary disease group showed more pCR compared to N0, N2 or N3 group and DE regimen showed better response in this group. DE is the current standard NACT regimen in our institute.

Disclosure of Interest: No significant relationships.

P205

The relationship between dose intensity and pathological effect of nab-paclitaxel as neoadjuvant

H. Inoue[1]*, A. Hirano[1], A. Hattori[1], N. Jibiki[2], K. Ogura[1], R. Miyamoto[2], F. Okubo[1], Y. Naritaka[3], M. Fujibayashi[4], T. Shimizu[1]. *[1]Breast Surgery, Tokyo Women's Medical University Medical Center East, Tokyo, Japan, [2]Breast Surgery, Tokyo Women's Medical University Yachiyo Medical Center, Tokyo, Japan, [3]Surgery, Tokyo Women's Medical University Medical Center East, Tokyo, Japan, [4]Surgical Pathology, Tokyo Women's Medical University Medical Center East, Tokyo, Japan*

Goals: Although anthracycline followed by weekly paclitaxel (PTX) is a standard chemotherapy in the neoadjuvant setting of breast cancer, peripheral neuropathy is a problem for patients treated with weekly PTX. Since nanoparticle albumin-bound (nab)-PTX contains neither polyoxyethylene castor oil nor ethanol, reduction or rapid recovery of neuropathy is expected. Therefore we planned a phase II neoadjuvant trial with epirubicin (E)/cyclophosphamide (C) followed by weekly nab-PTX +/− trastuzumab (T). Forty patients were enrolled in this trial and their neoadjuvant chemotherapy (NAC) and operations were finished in 2013. In this trial, delay and dose-reduction of nab-PTX were frequently observed. Thus, we assessed the relationship between relative dose intensity (RDI) of weekly nab-PTX and the pathological effect of NAC.
Methods: Women from 20 to 70 years old with node-positive breast cancer were enrolled in this trial between 2011 and 2013. Patients received four cycles of E (90 mg/m^2) and C (600 mg/m^2) every 3 weeks, followed by four cycles of nab-PTX (125 mg/m^2) on Days 1, 8 and 15 in a 28-day cycle. Fifteen cycles of T (2 mg/kg, loading 4 mg/kg) were added to the nab-PTX regimen in HER2-positive patients every week. Adverse events were assessed according to NCI-CTCAE version 4.0. Administration of nab-PTX was delayed for 1 week if grade 2 hematological or grade 1 non-hematological toxicities except for nausea, vomiting and alopecia were observed. Furthermore, dose of nab-PTX was reduced if toxicity did not improve after 2 weeks delay. The relationship between RDI and pathological complete response (pCR) in patients who received nab-PTX was analyzed.
Results: Thirty-seven patients who received at least one administration of nab-PTX were analyzed, and the median age was 56 years (range 31–68 years). Fifteen patients (40.5%) were positive HER2. Fourteen patients (37.8%) achieved pCR. The median total dose of nab-PTX was 1500 (350–1500) mg/m^2. Thirty-one patients (83.8%) received 4 complete cycles of nab-PTX. The median dose intensity (DI) was 80.6 mg/m^2/week (planned DI:93.8), and the median-delivered RDI was 86%. The median total dose was 1450 mg/m^2 in patients with pCR, whereas in those with non-pCR the median total dose was 1500 mg/m^2 (P = 0.5375). In patients with pCR, the median RDI was 80%, whereas in those with non-pCR the median RDI was 92% (P = 0.1775). Among patients with HER2 positive, the median RDI in the pCR-group was 83% whereas in the non-pCR group the median RDI was 97% (P = 0.0673).
Conclusion: In this trial, the median RDI of weekly nab-PTX was low (86%) because administration was delayed and dose reduction was carried out in many patients. However, the tendency was seen that the RDI in the pCR group was lower than that in the non-pCR group, suggesting that the same pathological effect would be obtained in HER2 positive patients even if the dose intensity of nab-PTX were reduced.
Disclosure of Interest: No significant relationships.

P206

Ipsilateral breast cancer recurrence in conservative treatment for locally advanced breast cancer

G.F.A. Carrara[1], C.S. Neto[1], L.F. Abrão-Machado[2], J.S. Nunes[3], M.A.A.K. Folgueira[4], M.M. Brentani[4], R.A.C. Vieira[1]*. *[1]Postgraduate Course In Oncology, Barretos Cancer Hospital, Barretos, Brazil, [2]Pathology, Barretos Cancer Hospital, Barretos, Brazil, [3]Clinical Oncology, Barretos Cancer Hospital, Barretos, Brazil, [4]Oncology, USP School of Medicine, São Paulo, Brazil*

Goals: Evaluate the clinical and pathologic factors related to local and regional recurrence in locally advanced breast cancer (LABC) in women submitted to neoadjuvant chemotherapy (NC) and conservative surgery.
Methods: A retrospective study was performed in patients with LABC submitted to NC and conservative treatment during 01/2006 to 06/2011. The main regimen proposed was AC-T (4 AC + 4 T). From the 421 women evaluated 97 underwent to a breast conservative surgery. We evaluated the clinical, pathologic, immunohistochemistry and surgical factors that would contribute to locoregional recurrence (LRR) and local recurrence (LR). The chi-square and logistic regression were used for association analysis. A Kaplan–Meier curve and a Cox model were used to evaluate the main factors related to free recurrence survival.
Results: 88.7% were clinical stage III, 76.3% had T3 and T4 tumors, 79.4% N1 and N2 axilla, 92.8% invasive ductal carcinoma and 94.8% Nottingham grade II and III. Immunohistochemistry evaluation demonstrated that 37.6% were luminal A/B1, 18.3% triple negative, 31.2% luminal B2 and 12.9% Her2 tumors. The AC-T regime was performed in 92.7% of the women. The pathologic complete response was present in 25.8% of the tumors. 97.9% had free margins and concentric tumor decrease was present in 55.7% of the patients. Adjuvant radiotherapy was performed in 96.9% of the patients, but adjuvant trastuzumab was performed only 2.1% of the patients. The mean follow up was 53.9 months and the 5-year actuarial global survival was 83.4%. The LRR and LR was 15.5% and 7.2% respectively. The chi-square and univariate logistic regression analysis showed the clinical stage T-TNM (0.015), histologic grade (0.02) and necrosis (0.008) was related to LRR, but the presence of necrosis was the main factor in multivariate analysis (OR = 0.09; IC 0.01–0.73; p = 0.02). The only factor related to decrease of LR was necrosis (p = 0.04). The main factor related to LRR free survival and LR free survival was the molecular subtype, as Her2 tumors had decrease of free survival with the odds ratio of 3.06 and 3.27 respectively.
Conclusion: Her2 tumors had a higher risk of locorregional and local disease free of recurrence. More studies are necessary to evaluate this condition in the trastuzumab era with a large number of patients.
Disclosure of Interest: No significant relationships.

P207

Prognostic significance of biomarker discordance after neoadjuvant chemotherapy in breast cancer

A. Matsumoto[1]*, H. Jinno[2], T. Ando[1], T. Fujii[1], T. Nakamura[1], J. Saito[1], M. Takahashi[2], T. Hayashida[2], Y. Kitagawa[2]. *[1]Department of Surgery, Inagi Municipal Hospital, Tokyo, Japan, [2]Department of Surgery, Keio University School of Medicine, Tokyo, Japan*

Goals: Neoadjuvant chemotherapy (NAC) was reported to change the status of biomarker including estrogen receptor (ER), progesterone receptor (PgR), HER2 and Ki-67. However, the impact of these changes on response to treatment and long-term outcomes still remains to be elucidated. The objectives of this study is to evaluate the frequency of biomarker status changes after NAC in patients with residual disease and their relationship with response to treatment and prognosis.

Methods: From a prospective database of 196 patients receiving NAC from January 2005 to June 2014, 156 patients (79.6%) with non-pCR were analyzed. Patients were treated with sequential anthracycline and taxane. ER, PgR, HER2 and Ki-67 were assessed in both core needle biopsy (CNB) performed prior to NAC and surgical samples. Pathological response criteria were classified as grade 0, 1, 2, or 3: grade 0 includes almost no change in cancer cells; grade 1 includes slight or marked changes in less than two thirds of the area; grade 2 includes marked changes in more than two thirds of the area; grade 3 includes necrosis or disappearance of all tumor cells.
Results: The median age at diagnosis was 50.0 years and the median tumor size was 3.2 cm. Clinical nodal status was positive in 57.7% of patients before NAC. The rate of pathological response grade 0, 1 and 2 were 5.8%, 65.4% and 28.8%, respectively. Before receiving NAC, ER, PgR and HER2 were positive in 73.7%, 67.9% and 11.5% of patients. Changes in ER, PgR and HER2 status between CNB and surgical samples were 10.9% (3.8% gain; 7.1% loss), 17.9% (1.9% gain; 16.0% loss) and 5.3% (2.0% gain; 3.3% loss), respectively. After NAC, Ki-67 expression decreased in 77.8% of patients (CNB sample: 24.7%, surgical sample: 5.0%; $p < 0.001$). In the ER-discordant group, clinical complete response rate (41.2% vs. 15.1%; $p = 0.016$) and grade 2 rate of pathological response (61.1% vs. 30%, $p = 0.033$) was significantly higher than in the ER-concordant group, whereas discordance in PgR and HER2 status was not significantly correlated with clinical and pathological response. Although there was no correlation between Ki-67 of CNB samples and disease-free survival (DFS), patients with high (>14%) Ki-67 of surgical samples had significantly shorter DFS when compared with low (<14%) Ki-67 (28.5 months vs. 41.3 months, $p = 0.003$). After a median follow-up of 49.4 months, patients with a loss in hormone receptor (HR) status had a trend toward a worse DFS compared with the concordant HR-positive group (32.5 months vs. 39.0 months; $p = 0.08$).
Conclusion: This study suggested that changes in biomarker status caused by NAC might have a prognostic value in breast cancer patients without pCR.
Disclosure of Interest: No significant relationships.

P208

Pathological complete response (PCR) rates after sequential CT in locally advanced BC

I. Bozovic-Spasojevic[1] *, S. Milosevic[1], S. Susnjar[2], Z. Neskovic-Konstantinovic[2]. *[1]Daily Chemotherapy Hospital, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia, [2]Medical Oncology Department, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia*

Goals: Pathological complete response (pCR) has predicted long term survival in several neoadjuvant studies and in the recent meta-analysis (Cortazar, Lancet 2014). Hence, we conducted a single institutional study, aiming to analyze the percentage of pCR in breast cancer (BC) patients (pts) treated with neoadjuvant chemotherapy (CT) regiments.
Methods: Consecutive breast cancer patients treated with neoadjuvant CT at the Institute for Oncology and Radiology of Serbia between January 2013 and April 2014, were selected for the analysis. Pts who were treated with sequential CT: 3–4 cycles of antracycline-based CT (AC/FAC/FEC) and taxane-based CT (12 weekly paclitaxel or 3–4 cycles of 3 weekly docetaxel) with or without trastuzumab according to HER2 status, were eligible for the analysis. pCR was defined as no invasive tumor cells and no in situ residuals in breast and axillary lymph nodes (von Minckwitz, JCO 2012).
Results: We identified 112 patients with a median age of 47 years (range 21–74). 57 patients had IIIB, 34 IIIA and 21 IIB UICC TNM clinical stages; the commonest histological type on core biopsy was ductal invasive carcinoma seen in 56 pts, 32 had lobular invasive carcinoma and 24 had other BC histology; grade 2 tumors had 84 pts and grade 3 28 pts. Tumors stained positive for ER (ER+/PR+/−) in 78 and for HER2 in 39 pts. Up to 1st of May 2014, 46 pts completed CT and were operated; 6 of them had breast conserving surgery, 2 pts had skin sparing mastectomy and the rest of the patients had radical mastectomy. 14 pts achieved pCR, defined as ypT0 ypN0; 10 pts were HER2+ and were treated with 4 cycles of neoadjuvant trastuzumab (TR) plus CT, 1 pt HER2+ER+ (treated with neoTR plus CT), 2 pts ER+ (CT) and 1 HER2−/ER− (CT). Of the partial responders there was no change in histological type; grade was available on excision in 30 pts and was different between core biopsy and final excision in 11 pts, 3 upgrades and 8 downgrades. Out of 32 stained paired pre and post tumor samples, one tumor change profile from ER weak positive to negative (Allred score 4 to 0); two changed profile from PR negative to weak positive (Allred 0 to 4 and 5 respectively) whereas one changed from weak positive to negative (Allred score 3 to 0); three HER2+ tumors (two IHC3+ and one CISH positive) changed profile to HER2 negative (all IHC 1+).
Conclusion: In our single institutional-study rate of pCR after sequential anthacicline-taxane based neoadjuvant CT with/without trastuzumab, within all BC pts was 30%. Implications of changes in histological grade and receptor status following neoadjuvant CT should be further explored.
Disclosure of Interest: No significant relationships.

P209

Metabolic signature predicts progression and response after taxane–anthracycline neoadjuvant regimen

I. Dale[1] *, A. Roscher[2], A. Lopes Carvalho[3], E. Guimarães Do Turco[4], R.A. Da Costa Vieira[3]. *[1]Gynecology Department, Federal University of São Paulo, São Paulo, Brazil, [2]Children's Research Center, Ludwig-Maximilians Universität München, München, Germany, [3]Barretos Cancer Hospital, Barretos Cancer Hospital, Barretos, Brazil, [4]Surgery, Federal University of Sao Paulo, São Paulo, Brazil*

Goals: To identify predictive blood metabolites signatures of complete pathologic response (pCR) defined as no histopathologic evidence of any residual invasive and/or noninvasive residual in breast or nodes (ypT0/ypN0), along with signatures able to predict stable disease and/or progression (SDPR) defined here as any response less than 30% reduction in the initial tumor volume in response to neoadjuvant treatment for stage III breast cancer.
Methods: In this prospective, NIH registered, neoadjunvant taxane/anthracyclin-based protocol, we applied a targeted, quantitative mass spectrometry approach (Biocrates, Innsbruck, Austria) to measure the absolute micromolar concentrations of metabolites in plasma samples from 59 stage III breast cancer patients prior to chemotherapy and compared the results with the final tumor volume after chemotherapy. For the detection of discriminative metabolites, training and validation sets were assembled. Blinded-created data was then imported to ROC Curve Explorer & Tester (ROCCET, available at http://www.roccet.ca/ROCCET) for the computer-assisted generation of uni and multivariate Receiver Operating Characteristic (ROC) curves.
Results: Complete pathologic response (pCR) and stable disease/progression (SDPR), were observed in 11% (7/59) and in 32% (19/59) of patients respectively. After training and validation sets, two predictive metabolites combinations for pCR have emerged with good discriminative characteristics, the first one with sensitivity=100.00%, specificity= 83.8, PPV= 44.44% and NPV= 100.00% in addition to a second one with sensitivity=100.00%, specificity= 89.66, PPV= 57.14% and NPV= 100.00%. The third metabolites combination was able to predict SDPR with sensitivity=100.00%, specificity= 93.10%, PPV= 84.62% and NPV= 100.00%. The identified metabolites are mainly related to glutaminolysis, glycolysis, ether lipids, biogenic amines and

mitochondrial function. Finally, taking into consideration the cancer-intrinsic subtypes of breast cancer our findings were able to discriminate HER2 Tumors (LumB-HER2 and HER2) from patients with Triple Negatives and Luminals A/B with Sensitivity= 86.36%, Specificity= 76.92%, Positive predictive value= 61.29%, Negative predictive value = 93.02%, p-value = 0.002 (1000 permutations).
Conclusion: Women harboring tumors fated to reach complete pathologic response or stable disease/progression seems to retain, in blood, specific and quantifiable metabolic changes that might help in the prediction of chemotherapy response as well as in the identification of intrinsic subtypes.
Disclosure of Interest: No significant relationships.

P210

Older women with triple negative breast cancer are less likely to get neoadjuvant chemotherapy

N.M. Foley*, C. Murphy, M. Jinih, N. Relihan, Z. Khan, A. Khan, H.P. Redmond. *Department of Surgery, Cork University Hospital, Cork, Ireland*

Goals: Triple negative breast cancer (TNBC) conveys a significant negative prognosis. These breast cancers affect women of all ages and tend to be aggressive, yet younger women are more likely to receive neoadjuvant chemotherapy. It is now recommended that all patients with TNBCs over 5 mm receive neoadjuvant chemotherapy.
Methods: A prospective database of all breast cancers diagnosed in the Southern breast cancer centre has been maintained since 2010. We interrogated this database and isolated the triple negative tumours diagnosed between 2010 and 2014. The database was consolidated with the TNM stage of the tumour, the use of neoadjuvant therapies and survival status of the patients.
Results: 119 triple negative breast cancers have been diagnosed between 2010 and 2014 with an average age of 58 years (range 27–91). 55% of our cohort are aged over 55, and 8% of our cohort are aged over 80 years. 29% (n = 35) of TNBCs have had or are receiving neoadjuvant chemotherapy [average age 49 years (range 27–77)]. 71.5% of patients receiving neoadjuvant chemotherapy are aged under 55 years. Two of our patients are currently receiving metronomic chemotherapy.
Conclusion: TNBC is a poor prognosticator in breast cancer. We are seeing a significantly increased incidence in older women. These patients present a therapeutic dilemma as comorbid conditions and ageism can limit the use of neoadjuvant chemotherapy. With the use of metronomic chemotherapy we may see increased utilisation of neoadjuvant chemotherapy in older patients.
Disclosure of Interest: No significant relationships.

P211

Phase 2 neoadjuvant trial: myocet (M), cyclophosphamide (C) +/− trastuzumab (T) and paclitaxel (P) +/− T

B. Pistilli[1], G. Benedetti[1]*, D. Rossi[2], A.M. Baldelli[2], C. Magalotti[3], V. Casadei[2], L. Foghini[1], M. Staffolani[1], G. Fiorentini[2], L. Latini[1]. [1]*Oncology, Oncology Unit Macerata Hospital, Macerata, Italy,* [2]*oncology Unit Ospedali Riuniti Marche Nord, Pesaro, Italy,* [3]*Surgery Department – S.M. Misericordia Hospital, Senology Unit, Urbino, Italy*

Goals: M is a non-pegylated liposomal doxorubicin exhibiting reduced cardiotoxicity as compared to doxorubicin. Combination of M and C has demonstrated efficacy in first line treatment of metastatic BC, however few data are available in neoadjuvant setting, especially in combination with T. The aims of the study were activity, in terms of pathological complete response (pCR; ie, no remaining invasive tumor in breast and lymphnodes) and safety of a sequential schedule of M and C +/− T followed by weekly P +/− T.
Methods: Estrogen receptor (ER), progesterone receptor (PgR), HER2+ (defined as 3+ overexpression by immunoistochemical testing or HER2 amplification by fluorescent in situ hybridisation) and Ki67 index were assessed in core needle biopsies at baseline and in residual tumour after chemotherapy. Patients with stage II/III BC received 4 cycles of MC (myocet 60 mg/m^2, cyclophosphamide 600 mg/m^2 on day 1 every 3 weeks), followed by 12 weekly doses of P (paclitaxel 80 mg/m^2); all patients with HER2+ disease received T in combination with chemotherapy (trastuzumab loading dose of 8 mg/kg followed by 3 cycles of 6 mg/kg alongside MC; 2 mg/kg per week with the following 12 P administrations).
Results: 68 patients were enrolled, median age 55 years (range 34–72). Tumour characteristics were: stage IIA 11 patients, IIB 16, IIIA 22, IIIB 18 (5 inflammatory BC), IIIC 1; ER+ and PgR+/− 36 patients, triple negative 12, HER2+ 20 (ER+ and/or PgR+ 11); Ki67 ≤15% in 12 (17.6%). To date, 58 patients were evaluable for pathological response: pCR was obtained in 16 (27.6%). The rate of pCR in HER2+ and HER2− BC was 63.1% (12/19) and 10.2% (4/39), respectively. Clinical response was evaluable in 62: CR in 28 (45.2%) and PR in 24 (38.7%). Conservative surgery was performed in 20 out of 61 patients (32.8%). The most frequently observed grade 3–4 AEs were: grade 3 neutropenia 5 patients (8.1%), grade 3 paresthesia 3 (4.8%), grade 3 vomiting 3 (4.8%). Only 1 patient experienced an asymptomatic decrease of ejection fraction lower than 50%.
Conclusion: The use of M in this sequential regimen resulted to be active, despite of the high rate of patients with ER+ disease and with locally advanced cancer. Consistently with previous data, pCR was higher in patients with HER2+ BC.
Disclosure of Interest: No significant relationships.

P212

The effect of neoadjuvant chemotherapy on histologic grade and molecular markers in breast cancer

L. Amaadour[1]*, N. Benaicha[2], C. Nejjari[2], H. Fatemi[3], S. Arifi[1], N. Mellas[1]. [1]*Medical Oncology, Hassan II University Hospital, Fez, Morocco,* [2]*Laboratory of Epidemiology, Faculty of Medicine, Fez, Morocco,* [3]*Pathology, Hassan II University Hospital, Fez, Morocco*

Goals: Histological and immunohistochemical findings may vary in cases of breast cancer. Possible changes in tumor estrogen receptor (ER), progesterone receptor (PR) Scarf bloom Richardson (SBR) grade and human epidermal growth factor receptor 2 (HER2) between the core biopsy and surgical excision specimens performed before and after neoadjuvant chemotherapy (NAC) are controversial and pose a challenge when a clinical decision is needed. The aim of this study was to compare histologic profiles (SBR grade, ER, PR and HER2) of primary breast carcinomas before and after neoadjuvant chemotherapy (NAC).
Methods: We retrospectively analysed the SBR grade and immunohistochemical results of ER, PR and HER2 between the core biopsy and surgical excision specimens in 102 patients with locally advanced breast cancer (stage II or III) treated with NAC at the department of medical oncology of Hassan II University Hospital of Fez Morocco between January 2009 and December 2013. Statistical analysis was carried out using Fisher's exact test, McNemar's test, Spearman's correlation and the Kappa index with linear weighting. Significance was defined at $p < 0.05$.
Results: All patients were females, with mean age of 48.6 years (range: 30–74 years). Of the 102 carcinomas studied, 69.8% (71/102) were of ductal histologic type and 31.2% (31/102) were lobular. After initial diagnosis biopsy, the patients were given a neoadjuvant chemotherapeutic regimen of 60 mg/m^2 adriamycin and 600 mg/m^2 cyclophosphamide (4 cycles) every 21 days, followed by 4 cycles of triweekly paclitaxel (175 mg/m^2) or docetaxel (100 mg/m^2) combined with trastuzumab in Her2-positive tumors, followed by mastectomy within 3 weeks after the last chemotherapy cycle. After

NAC, 34.9% of patients had SBR grade change, and 85.7% of patients decreased one grade. The rates of changes in the expression of ER, PR and HER2 were 42.4% (45/102), 55.4% (68/102) and 26.6% (21/102), respectively. Only the SBR grade had significant difference between before and after neoadjuvant chemotherapy (P = 0.049).
Conclusion: Profiles for ER, PR and HER2 were not significantly different in primary breast carcinomas before and after neoadjuvant chemotherapy. Until more comparable studies are being published, it seems prudent to reevaluate immunohistochemical markers after neoadjuvant chemotherapy, since the findings will guide the strategy for implementation of adjuvant systemic treatment.
Disclosure of Interest: No significant relationships.

P213
Neoadjuvant nab-paclitaxel followed by FEC for operable breast cancer: KBC-SG 1103 trial

Y. Yamamoto[1]*, K. Anan[2], M. Tanaka[3], S. Maeda[4], H. Ueo[5], Y. Sagara[6], S. Ohno[7], H. Iwase[8], S. Mitsuyama[9], K. Tamura[10]. *[1]Molecular-targeting Therapy for Breast Cancer, Kumamoto University Hospital, Kumamoto, Japan, [2]Department of Surgery, Municipal Medical Center, Kitakyushu, Kitakyusyu, Japan, [3]Breast Surgery, Kurume General Hospital, Kurume, Japan, [4]Department of Surgery, National Hospital Organization Nagasaki Medical Center, Nagasaki, Japan, [5]Department of Breast Surgery, Ueo Breast Surgery, Ohita, Japan, [6]Department of Breast Oncology, Sagara Hospital, Kagoshima, Japan, [7]Clinical Research Institute, National Hospital Organization Kyushu Cancer Center, Fukuoka, Japan, [8]Department of Breast and Endocrine Surgery, Faculty of Postgraduate Medical and Pharmaceutical Sciences, Kumamoto University, Kumamoto, Japan, [9]Kitakyushu Municipal Medical Center, Kitakyushu, Japan, [10]Division of Medical Oncology, Hematology and Infectious Disease, Fukuoka University, Fukuoka, Japan*

Goals: The aim of this study was to evaluate the efficacy and safety profile of neoadjuvant chemotherapy (NAC) with sequential nab-paclitaxel (nP) followed by 5-fluorouracil/epirubicin/cyclophosphamide (FEC) for operable breast cancer.
Methods: Patients were treated with 4 cycles of 260 mg/m^2 nP every 3 weeks followed by FEC100 given every 3 weeks. Concurrent treatment with triweekly trastuzumab and nP was used in HER2-positive cases. Primary endpoint was pathological complete response (pCR) rate in the breast and axilla tumors. Secondary endpoints included objective response (OR), breast conservation (BCS) and pCR rates according to tumor subtype and safety.
Results: Between Dec 2011 and Jun 2012, a total of 41 patients were enrolled, and 38 were eligible and evaluable for response and safety. Twenty-nine patients (76.3%) completed 8 cycles of NAC. The median relative dose intensity was 94.0% for nP and 83.7% for epirubicin, respectively. Adverse events (AEs) were generally mild with grade 1 to 2. The nP gave rise to grade 3 AEs were elevation of AST/ALT (15.8%), sensory neuropathy (7.9%), muscle pain (5.3%) and arthralgia (5.3%). Febrile neutropenia was not observed with nP, while it developed in 31.4% patients with FEC. The overall pCR rate was 31.6% (12 of 38, 95% CI: 19.1–47.5%). The pCR rates according to subtypes were 6.3% (1 of 16) in Luminal/HER2−, 33.3% (4 of 12) in triple-negative, 60% (3 of 5) in Luminal-HER2+ and 80% (4 of 5) in HER2-enriched patients. ORR and BCS rates were 86.8% (33 of 38) and 65.8% (25 of 38), respectively.
Conclusion: Neoadjuvant nab-paclitaxel followed by FEC was feasible and had high activity. Further confirmatory studies are needed.
Disclosure of Interest: No significant relationships.

P214
Pathologic complete response after neoadjuvant chemotherapy in breast cancer molecular subtypes

E. Sari[1]*, S. Aksoy[2], M. Dogan[3], M. Altinbas[1], N. Zengin[3], Y. Ozisik[2], K. Altundag[2]. *[1]Medical Oncology, Diskapi Yildirim Beyazit Research Hospital, Ankara, Turkey, [2]Medical Oncology, Hacettepe University, Institude of Oncology, Ankara, Turkey, [3]Medical Oncology, Numune Research Hospital, Ankara, Turkey*

Goals: Our aim is to ascess the effect of molecular subtypes on attainig pathologic complete response (pCR) in breast cancer patients receiving neoadjuvant chemotherapy and also to investigate the impact of pCR on survival.
Methods: A total of 310 stage II and III breast cancer patients who received neoadjuvant chemotherapy were investigated retrospectively. Patients were classified according to 4 molecular subtypes. Pathologic complete response is defined as the absence of invasive tumor both in breast and axillary lymph nodes.
Results: In the study group, the molecular subtypes were classified as 51.7% HR+/Her2−, 18.8% HR+/Her2+, 13.4% HR-/Her2+ and 16.4% triple negative. pCR was achieved in 72 (23.2%) patients. Clinical stage at diagnosis was 18.4% Stage IIA, 27.7% Stage IIB, 24.2% Stage IIIA, 20.3% Stage IIIB, 6.8% Stage IIIC. As neoadjuvant chemotheraphy, 64.8% of the patients received both antracyclines and taxanes, 29% received only antracyclines, 5.5% received only taxanes. Among patients receiving only antracyclines as neoadjuvant treatment, 64.4% also received taxanes as adjuvant treatment. Among patients receiving only taxanes as neoadjuvant treatment, 41% also received antracyclines as adjuvant treatment. 71.3% of Her2+ patients received neoadjuvant trastuzumab containing regimens and 14.7% received trastuzumab at only adjuvant setting. The pCR rate was significantly different between the molecular subtypes (9.1% in HR+/Her2−, 26.8% in HR+/Her2+, 51.3% in HR-/Her2+, 40.8% in triple negatives; P < 0.001). Overall survival (OS) of the patients who achieved a pCR was significantly better than those who did not achieve pCR (P = 0.038).
Conclusion: The molecular subtypes of breast cancer patients might affect pCR rates in favor of HR-/Her2+ and triple negative subtypes. The patients achieveing pCR with neoadjuvant chemotherapy also have significantly higher OS. However, we need further prospective randomized trials in this issue.
Disclosure of Interest: No significant relationships.

P215
Phase II study with S-1 + low dose docetaxel (N-1 study) for operable breast cancer patients

Y. Tadokoro*, M. Morimoto, M. Nakagawa, H. Takechi, A. Tangoku. *Department of Thoracic, Endocrine Surgery and Oncology, Tokushima University Graduate School, Tokushima, Japan*

Goals: We have reported the efficacy of S-1 combined with low dose docetaxel (S-1+DOC) in ASCO 2011 (abstract No. 1075). It showed good objective response rate (ORR) and complete response (CR) could be realized within three months (4 cycles). But this therapy was difficult to keep compliance, because S-1 is oral medicine. To improve pathological CR (pCR) rate, we planed new protocol of primary chemotherapy.
Methods: Patients with operable breast cancer (stage II–III) were treated with i.v. docetaxel (40 mg/m^2) on day1 and oral S-1 (80 mg as FT/m^2/day) on day1 to 14 every 3 weeks for 4 cycles. According to the RECIST criteria, patients with CR were underwent operation, partial response were continued more 4 cycles of S-1+DOC. Stable disease or progressive disease cases were added EC or trastuzumab and paclitaxel (HT) according to their HER2 status. Supportive therapy was provided for typical adverse events. Primary endpoint is a pCR rate. Secondary endpoints are ORR, breast conservation rate and safety.

Results: Between May 2009 and October 2013, 70 patients were entry. After 4 cycles of S-1+DOC, CR was noted in 4 cases, PR in 49 cases, SD in 14 cases, and PD in 3 cases. 9 cases of SD and 2 cases of PD underwent EC, 5 cases of SD and 1 case of PD underwent HT. Among 70 assessable patients, 32.9% achieved pCR. ORR was 80.0%. According to subtype, pCR rate is 20.0% in Luminal A type, 40.0% in Luminal HER2 type, 54.5% in HER2 type, 42.8% in Basal type. Breast conservation rate was 82.9%, although the patients who could continue S-1 more than 80% was 72.9%. Adverse events over grade 3 were leucopenia, neutropenia, anemia, peripheral sensory neuropathy, muscle pain, nausea, vomiting, diarrhea, anorexia, constipation, and nail change. Grade 3, 4 of neutropenia was noted in 50.0%.
Conclusion: S-1+DOC switching therapy showed prior response to previous protocol with EC followed by taxane. Compliance of S-1 intake by supportive care is a key to establish the best response. The results suggested S-1 combined with low dose docetaxel could become an effective chemotherapy for Luminal type patients.
Disclosure of Interest: No significant relationships.

P216
Neoadjuvant chemotherapy of TCH: a phase II trial of Kyushu Breast Cancer Study Group

K. Mashino[1]*, S. Mitsuyama[2], N. Masuda[3], T. Kawasoe[4], M. Yamaguchi[5], S. Wakamatsu[6], K. Taketani[7], Y. Yamamoto[8], M. Tanaka[5], K. Tamura[9]. *[1]Surgery, Oita Prefectural Hospital, Oita City, Japan, [2]Surgery, Kitakyushu Municipal Medical Center, Kitakyushu, Japan, [3]Department of Surgery, Breast Oncology, National Hospital Organization Osaka National Hospital, Osaka, Japan, [4]Breast Surgery, Japanese Red Cross Kumamoto Hospital, Kumamoto, Japan, [5]Breast Surgery, Kurume General Hospital, Kurume, Japan, [6]Medical Oncology, Kitakyushu Municipal Medical Center, Kitakyushu, Japan, [7]Iizuka Hospital, Iizuka, Japan, [8]Molecular Targeting Therapy for Breast Cancer, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan, [9]Division of Medical Oncology, Hematology and Infectious Disease, Fukuoka Univercity, Fukuoka, Japan*

Goals: To evaluate the safety and efficacy of neoadjuvant chemotherapy of trastuzumab with carboplatin and docetaxel in HER2+ breast cancer.
Methods: Patients with HER2+ BCs, stage I–III (T1b–3, N0–2), non-inflammatory, operable breast cancer received trastuzumab 8 mg/kg (day 1), followed by 6 mg/kg tri-weekly, plus docetaxel 75 mg/m^2, and carboplatin (area under curve, 6) every three weeks for six cycles before surgery. The primary endpoint constituted pathological complete response (pCR) rate, determined from surgical specimens. We studied estrogen receptor, progesterone receptor, HER2, and Ki-67 immunohistochemically in surgical resected sections. In addition, we studied adverse events of this therapy, including bone marrow suppression, cardiotoxcity, and other events.
Results: Thirty-one patients were enrolled. Surgery was performed in fifteen patients and the resected samples were examined at this stage. Most patients had clinical T2/T3 tumors (63%) or clinical N1/2 nodes (50%). Expression of estrogen receptor was shown in fourteen patients (93%). Thirteen patients (81%) completed six cycles of therapy, two (13%) completed five cycles, and one withdrew for toxicity. A complete or partial objective clinical response occurred in 100% of patients (53% and 47%, respectively). Surgery was breast conservative in 66% of the all patients. In an intent-to-treat analysis, tumor and nodal pCR were seen in 60%. Treatment was generally well tolerated. Grade 3/4 non-hematological toxicity was uncommon. Grade 3/4 neutropenia and febrile neutropenia were observed in 93% and 44%, respectively. 31% of patients were treated with G-CSF and 44% received antibiotic therapy. No symptomatic cardiac dysfunction occurred. LVEF decreased from 71% to 61% in only one patient.
Conclusion: Neoadjuvant chemotherapy with trastuzumab plus docetaxel and carboplatin achieved promising efficacy, with a high pCR rate and favorable tolerability in operable HER-2+ BCs.
Disclosure of Interest: No significant relationships.

P217
Bevacizumab could increase the PCR rate in HER-2 negative breast cancer: a meta-analysis

L.X. Ma*, W.J. Huang, L. Liu. *Cancer Center, West China Hospital, Sichuan University, Chengdu, China*

Goals: Neoadjuvant therapy is administered to breast cancer patients as an induction process before surgery or radical radiotherapy to reduce tumor size. HER-2 negative breast cancer lack effective standard target monoantibodies in this treatment regimen. Bevacizumab has a controversial role in the treatment of breast cancer for its failure in OS detection in HER-2 negative breast cancer as well as the special triple negative group. Thus, we conduct a meta-analysis to evaluate the value of adding bevacizumab in neoadjuvant regimen.
Methods: Potentially eligible studies were retrieved using PubMed and Medline. Basic clinical characteristics of patients and statistical data with pCR data were collected. Then a meta-analysis model was established to investigate the correlation between administration of bevacizumab in neoadjuvant therapy and pCR rate in patients with HER-2 negative breast cancer.
Results: Seven eligible studies and 5500 patients were yielded in our meta-analysis. The pooled ORs to predict the pCR for both "breast" and "breast plus lymph node" are similar and the mathematic value for two settings were 1.47 [1.20, 1.80], (I2=0%, P = 0.0002) and 1.42 [1.26, 1.61], (I2=14%, P < 0.0001), respectively. In subgroup analysis, we emphasize the patients with triple-negative breast cancer. In the criterion of "lesions in breast" the pooled ORs is 1.48 [1.21, 1.81], (I2=0%, P = 0.0001) and regarding to the evaluation criterion of "lesions in breast and lymph nodes", the pooled ORs is 1.43 [1.16, 1.75], (I2=0%, P = 0.0006). Both standards are effective for prediction patient pCR after administration ($p < 0.05$) of bevacizumab as a component for neoadjuvant chemotherapy.
Conclusion: According to our pooled results, we recommend bevacizumab addition as a neoadjuvant chemotherapy component, for induction use of limited cycle, as the pCR could be improved significantly and patients may avoid long-term adverse event and long-term invalid survival improvement.
Disclosure of Interest: No significant relationships.

P218
Primary dose-dense epirubicin/cyclophosphamide→docetaxel in breast cancer: preliminary results

V. Cocciolone[1]*, K. Cannita[1], G. Bruera[1], A. Bafile[2], G. Coletti[3], V. Resta[2], A. Ciccozzi[4], A. Dalmas[3], C. Ficorella[1], E. Ricevuto[1]. *[1]Medical Oncology, S. Salvatore Hospital, University of L'Aquila, L'Aquila, Italy, [2]Breast Unit, S. Salvator Hospital, L' Aquila, L'Aquila, Italy, [3]Pathological Anatomy, S. Salvator Hospital, L' Aquila, L'Aquila, Italy, [4]Breast Radiology, S. Salvator Hospital, L' Aquila, L'Aquila, Italy*

Goals: Neoadjuvant dose-dense (dd) anthracycline/taxane chemotherapy increases activity and shortens time to surgery compared to conventional schedules in breast cancer (BC). Pathologic complete response (pCR) strongly correlates with improved survival. Proper docetaxel (D) dose and schedule sequential to dd epirubicin/cyclophosphamide (EC) is not clear. A phase I/II study was planned to define recommended dose (RD) of dd D following dd EC and to evaluate safety and activity.
Methods: Thirty-two operable (14)/locally-advanced (17)/inflammatory (1) BC patients (pts) were enrolled. Tumor features: ER and/or PR+, 21; HER2+, 16; triple negative, 4. Schedule:

E(90 mg/m^2)–C(600 mg/m^2) q14. An inter-patient approach was planned to evaluate D RD, designing a dose de-escalation from 65 mg/m^2 to 60, 55 and 50 mg/m^2 if a limiting toxicity occurred. Trastuzumab (T) (4 mg/kg) was added in HER2+ pts. Pegylated G-CSF was scheduled d2. Dose-limiting toxicities (DLTs): G4 haematological; G3 non-haematological; any toxicity resulting in >2 weeks delay; limiting left ventricular ejection fraction (LVEF) reduction, arrhythmia, symptomatic heart failure. pCR was defined as absence of invasive tumor on breast and nodes.

Results: 60 mg/m^2 was D RD in combination with T in HER2+ pts (DLTs: G3 asthenia, 2 pts; G2 asthenia for >2 weeks, 1 patient, all in the first cohort); 65 mg/m^2 was D RD in HER2− pts (DLTs: G3 hand–foot syndrome, 1 patient in the first cohort; G2 anemia for >2 weeks, 1 patient in the second cohort). Median received dose-intensities: E, 45 mg/m^2/w; D, 29.5 and 30.04 mg/m^2/w, in HER2+ and HER2−, respectively. Cumulative G3–4 adverse events: neutropenia 19%, vomiting 3%, asthenia 19%, myalgia 7%. No severe cardiac toxicity occurred; mean LVEF was 65% at baseline, 63% after EC, 65% and 60% in HER2+ and HER2− group, respectively, at treatment completion. pCR rate was: 5.6% (5/32 pts) in the ITT analysis, 16.7% (5/30 pts) in the as-treated analysis (HER2+, 26.7%; triple negative, 25%; ER+/HER2−, 8.3%), 18.8% (6/32 pts) in the whole population treated with sequential EC and taxanes, as one of two pts with allergic reaction to D who continued with nab-paclitaxel achieved a pCR (HER2+, 31.3%; triple negative, 25%; ER+/HER2−, 7.7%).

Conclusion: dd E(90 mg/m^2) C(600 mg/m^2)→D(60 mg/m^2) and (65 mg/m^2) with or without T, respectively, can be recommended as a safe and active neoadjuvant regimen in BC.

Disclosure of Interest: No significant relationships.

Predictive and prognostic factors

P221

The influence of breast cancer subtype on the prognosis of young breast cancer patients

L. Tang*, H. Yang, X. Jin, Z. Shao, G. Di. *Breast Surgery Department, Shanghai Cancer Center, Shanghai, China*

Goals: The prognoses of young breast cancer patients are poor. The purpose of this study is to evaluate the different characteristics and prognosis among different subtype groups of young breast cancer patients.

Methods: The study included 4670 operable young breast cancer patients in Shanghai Cancer Center, Fudan University between 2003 and 2012. Among them, 1360 patients were <40 years old (y) and 3110 were 40–50 y. The characteristics, overall survival (OS) and disease-free survival (DFS) were compared.

Results: The median follow-up was 54.1 months. Median age was 35.2 y and 46.0 y in the <40 y group and 40–50 y group. Eighty (5.9%) <40 y patients had a family history in comparison with 40–50 y patients ($P < 0.05$). More grade III tumors (38.9% vs 25.2%, $P < 0.01$) and more lymph-vascular invasions (30.4% vs 25.4%, $P < 0.01$) were presented in <40 y group when compared with 40–50 y group. More patients <40 y presented Luminal B (25.3% vs. 17.5%, $P < 0.01$) and triple negative (16.7% vs. 13.4%, $P < 0.05$) breast cancer while less of them presented Luminal A tumor (48.5% vs. 59.2%, $P < 0.01$). The percentage of HER2 positive patients was similar in each group (9.0% vs. 9.9%, $P > 0.05$). In younger group, the 5-year disease-free-survival and 5-year overall-survival were 72% and 87%. Younger patients with tumors classified as Luminal A and Luminal B type were at increased risk of poor DFS ($P = 0.03$, HR = 1.69, 95% CI=1.05–2.72; $P < 0.01$, HR = 3.61, 95% CI=2.50–5.22) when compared with the elderly. Additionally, patients <40 y with Luminal B tumor had a two point five fold higher risk of death compared with older counterparts (HR = 2.54, 95% CI=1.35–4.79, $P < 0.01$) while there was no such significant risk in Luminal A subgroup ($P > 0.05$). On the other hand, in HER2 positive and triple negative subgroup, there was no significant age-related risk for DFS or OS between the younger and the elder groups. In a multivariate analysis, young age was an independent predictive factor for DFS ($P < 0.05$) but not for OS ($P > 0.05$). Lymph node positivity ($P < 0.01$) and higher T stage ($P < 0.05$) were the predictive factors for DFS and OS of younger patients. Furthermore, Luminal B subtype was a risk factor for relapse disease (HR = 1.09, 95% CI=1.01 to 1.19, $P < 0.05$) in younger patients with Luminal subtype tumor.

Conclusion: Characteristics of breast cancer are more aggressive in Chinese young breast cancer patients. Luminal B subtype may have a negative effect on young patients' prognoses which should be validated further.

Disclosure of Interest: No significant relationships.

P222

Tumor-infiltrating lymphocytes predict prognosis in early breast cancer

Y. Mao[1]*, Q. Qu[2], J. Wu[1], X. Chen[1], O. Huang[1], K. Shen[1].
[1]*Comprehensive Breast Health Center, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China,* [2]*Department of Oncology, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China*

Goals: The role of tumor-infiltrating lymphocytes (TIL) in the prognosis of breast cancer (BC) patients has not been fully evaluated. The present study aimed to retrospectively investigate the association between TIL and survival outcomes in breast cancer and also identify this association by a meta-analysis of published researches.

Methods: Clinical data from 120 patients with primary breast cancer, who underwent surgery at Ruijin Hospital, Shanghai, were retrospectively analyzed for hematoxylin-eosin staining of TIL measured by tissue microarray. For meta-analysis, Ovid MEDLINE and EMBASE were searched to identify studies reporting the prognostic significance of TIL for BC patients. Random or fixed effect models were adopted to estimate the summary odds ratio (OR), and the publication bias was evaluated using a funnel plot and Egger's, Begger's test. The primary outcome measures were overall survival (OS), cancer-specific survival (CS) and disease-free survival (DFS).

Results: In our retrospective study, patients with high level of TIL in stroma had significantly better DFS (HR, 0.337; 95% CI, 0.129–0.876) and OS (HR, 0.210; 95% CI, 0.056–0.792), however, patients with TIL in tumor bed had no survival benefit. For meta-analysis, a total of 35 published studies including 24,421 patients were identified. Studies were subdivided into those considering the associations between BC survival and generalized TILs (n = 7) and TIL subsets (n = 28) according to different locations. Pooled analysis revealed that high generalized TILs infiltrated in tumor was associated with good DFS (HR, 0.92; 95% CI, 0.86–0.99) and OS (HR, 0.81; 95% CI, 0.67–0.99). Similar results were found in triple negative breast cancer (TNBC). For TIL subsets, CD8+ lymphocytes infiltration was a statistically significant prognostic markers for DFS (HR, 0.72; 95% CI, 0.58–0.90) and BCSS (HR, 0.75; 95% CI, 0.65–0.87), especially in both sites, While FOXP3+ lymphocytes infiltration indicated poor OS (HR, 1.56; 95% CI, 1.03–2.34) and BCSS (HR, 1.24; 95% CI, 1.10–1.39), especially in tumor center. Furthermore, patients with high CD3+, CD20+ or low PD-1+ cells infiltration may indicate increased OS.

Conclusion: Overall, high TIL could be a good prognostic marker for BC. TIL subsets play different roles in the prognosis of breast cancer. Since limited data reported TIL in specific BC subtype, further prospective studies are needed to increase the robustness of the analyses.

Disclosure of Interest: No significant relationships.

P223
Image-guided sentinel lymph node detection using near-infrared fluorescence in breast cancer

U. Toh*, N. Iwakuma, M. Mishima, M. Furukawa, Y. Akagi. *Surgery, Kurume University School of Medicine, Kurume, Fukuoka, Japan*

Goals: To evaluate the usefulness of color charge coupled device (CCD) camera system (HyperEye medical system:HEMS), for the intraoperative detection of sentinel lymph nodes (SLN) in breast cancer (BC) patients.
Methods: Intraoperative detection of SLN was performed using conventional blue dye technique combined with HEMS for mapping of SLNs. Indigo carmine (blue dye) mixed with Indocyanine green (ICG) was injected via the subareolar plexus, the search of SLN was guided by HEMs for stained lymphatic channels leading to stained LNs. All bright LNs with lighting near-infrared fluorescence and LNs at the end of a lymphatic channel are removed and designated as SLNs.
Results: SLN identification was successful in 140 of 144 patients (detection rate: 97.3%). There were four false-negative cases in 144 patients (2.8%). After a median follow-up of 2.5 years none of the patients presented with axillary recurrence. No severe adverse events were observed.
Conclusion: HEMS provides color imaging and that recognizes the lymphatic mapping and the location of SLN without the problem of a limited irradiation. This technique might be safety and effective in SLN identification.
Disclosure of Interest: No significant relationships.

P224
Prognostic impact of SNPs in or near the ZNF423 and CTSO genes in early breast cancer patients

Y. Hato*. *Oncology, Immunology & Surgery, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan*

Goals: Selective estrogen receptor modulators (SERMs) can reduce the occurrence of breast cancer in high-risk women by 50%. Recently, a genome-wide association study identified SNPs in or near the ZNF423 (rs8060157) and CTSO (rs10030044) genes that were associated with breast cancer risk during SERM therapy and these SNPs were reported to be involved in estrogen-dependent induction of BRCA1 expression (Ingle JN. et al. Cancer Discovery 2013). We investigated whether these SNPs are associated with prognosis in breast cancer patients.
Methods: A total of 588 breast carcinomas collected between 1983 and 2003 were available for polymorphism assay. TaqMan pre-designed SNP genotyping assays for ZNF423 rs8060157 and CTSO rs10030044 were used. The effects of several variables on survival were tested by Cox proportional hazards regression analysis.
Results: Estrogen receptor (ER)-positive breast cancer patients receiving adjuvant endocrine therapy with the genotype GG at CTSO rs10030044 showed significantly shorter disease-free survival (DFS) and overall survival (OS) ($P = 0.0024$ and $P = 0.0003$, respectively). On the other hand, this genotype were not associated with prognosis in ER-negative breast cancer patients. Multivariate Cox regression analysis revealed that the GG genotype at CTSO rs10030044 was an independent poor prognostic factor in ER-positive breast cancer patients receiving adjuvant endocrine therapy (OS: RR = 1.86; 95% CI, 1.18 to 2.85). The SNP, ZNF423 rs8060157, was not associated with prognosis in this study.
Conclusion: We show that the genotype GG at CTSO rs10030044 is an independent factor indicating poor prognosis in ER-positive breast cancer patients receiving adjuvant endocrine therapy.
Disclosure of Interest: No significant relationships.

P225
Necessity of axillary lymph node dissection – future prospects in sentinel lymph-node positive cases

H. Tanaka*, S. Umeda, S. Murakami, M. Ishikawa, A. Uchiyama. *Surgery, JCHO Kyushu Hospital, Kitakyushu, Fukuoka, Japan*

Goals: Sentinel lymph node biopsy (SLNB) has been established as a standard therapy for clinical axillary lymph node-negative breast cancer patients. Even if the sentinel lymph nodes (SLN) are metastasized, the necessity of axillary lymph node dissection (ALND) is still being discussed, because compared with SLNB false-negative rate (7–10%), axillary lymph node recurrence rate is extremely low (1% or less). In Japan, Breast Cancer Clinical Guidelines were updated in April 2014, and recommendation of ALND has been changed for SLN positive patients. ALND could be omitted in SLN micro-metastases cases, in addition, we should consider the omission of ALND also in SLN macro-metastasis cases. There is room still for further research into the indication of ALND for SLN positive patients. Our goal is to determine the necessity of ALND in SLN positive patients.
Methods: We assessed 653 patients with primary breast cancer who underwent SLNB in our department from January, 2008 to June, 2014. We assigned SLN positive patients to two groups, with ALND and without ALND. We reviewed and weighed relapse free survival (RFS) and overall survival (OS), furthermore, patients performed ALND were classified by the number of positive SLNs, and we also examined positive non-SLNs number of axilla in each case.
Results: We performed ALND for all 77 patients with positive SLNs. In case of two or more SLNs metastasis, positive rate of non-SLNs was 54%. On the other hand, in case of only one SLN metastasis, positive rate of non-SLNs was no more than 11%. This percentage favorably compared with SLNB false negative rate (7–10%, in general) relatively. For all patients admitted SLN metastasis, post-operative therapy was performed as pN1 cases. In patients with four or more LN metastasis or performed breast-conserving surgery, we added radiation therapy. With a median follow-up of 28 months, compared SLNB followed by ALND group with SLN alone group, there was no significant difference in the local recurrence rate, including axillary lymph nodes metastasis.
Conclusion: In SLNs positive cases, we can consider the possibility that ALND could be omitted, only on the condition that the number of positive nodes is one, the tumor size is T1–T2, and furthermore, the appropriate adjuvant radiation and systemic therapy as pN1 cases are performed after surgery. On the other hand, ALND still remains quite important for patients with multi-positive SLNs.
Disclosure of Interest: No significant relationships.

P226
LSD1 is associated with poor prognosis in basal-like breast cancer

S. Nagasawa*, K. Tsugawa. *Breast Surgery, St. Marianna University School of Medicine, Kawasaki, Japan*

Goals: LSD1, a lysine-specific histone demethylase, is overexpressed in several types of cancers and linked to poor outcomes. In breast cancer, the significance of LSD1 overexpression is not clear. We have performed an in silico analysis to assess the relationship of LSD1 expression to clinical outcome. We demonstrate that LSD1 overexpression is a poor prognostic factor in breast cancer, especially in basal-like breast cancer. This link is also observed in samples of triple negative breast cancer. We propose therefore that high expression levels of the demethylase LSD1 is a potential prognostic factor of poor outcome in basal-like breast cancer.
Methods: In order to validate whether LSD1 is overexpressed in each intrinsic molecular subtypes of breast cancer, we have analyzed LSD1 mRNA expression data from The Cancer Genome Atlas (TCGA),

N = 504. To investigate the correlation between LSD1 level and the clinical outcome, we have analyzed the Kaplan–Meier of KM-plot (www.kmplot.com) of recurrence free survival (RFS) to evaluate whether LSD1 overexpression is a prognostic factor in each intrinsic subtype of breast cancer, N = 3455. We have checked the impact of expression of LSD1 protein product on prognosis in triple negative breast cancer (TNBC), given the similarity in clinical features to basal-like breast cancer. We used samples from 32 patients at St. Marianna University hospital with clinical information, diagnosed and treated between 2007 and 2011. The median follow-up period is 1279 days. For measurement of protein expression, the percentage of positive cells was determined by counting about 500 cells within five high-resolution fields. Immunohistochemical staining (IHC score) was evaluated using the semi-quantitative Remmele scoring system, which links the IHC staining intensity (SI) with the percentage of positive cells (PP). High-LSD1 is defined as above average IHC score = 5. For survival analysis, Kaplan–Meier prot was performed using Graphpad prism. Differences were considered to be significant when the p-value was <0.05.

Results: Bioinformatic analysis indicates that basal-like breast cancers show a significantly higher amount of LSD1 transcript than the other subtypes ($p < 0.0001$). The KM-plot analysis indicates that cancer with high LSD1 transcripts shows a trend to shorter recurrence free survival (RFS) when all subtypes of breast cancer are pooled (HR 1.14, P = 0.024). However, in basal-like breast cancer, there is a clear link to poor outcome with a hazard ratio of 1.39 (P = 0.014). 11 to 32 samples had high level of LSD1 protein (IHC score >5, see methods), which correlate with shorter recurrence free survival, showing a hazard ratio of 3.619 (p = 0.0027).

Conclusion: This study shows that LSD1 is a potential prognostic factor of poor outcome in basal-like breast cancer, and high expression levels of the LSD1 is a prognostic factor of poor clinical outcome with a hazard ratio of 3.688 in our cohort.

Disclosure of Interest: No significant relationships.

P227

Use of systemic inflammatory markers to prognosticate the outcome of breast cancer patients

Z.J. Lee[1]*, W.P. Lee[2], C. Kam[3], S.K. Lim[2]. [1]*Department of General Surgery, Singhealth, Singapore, Singapore,* [2]*Breast Service, General Surgery, Changi General Hospital, Singapore, Singapore,* [3]*Clinical Trials and Research Unit, Changi General Hospital, Singapore, Singapore*

Goals: Carcinoma have been postulated to enhance chronic inflammation leading to tumour growth, invasion, metastases and hence, poorer outcomes. With the aid of hematological investigations, this study aims to establish an association between systemic inflammation and disease free survival in invasive breast cancer patients.

Methods: A retrospective review of a prospectively collected database of 332 patients with invasive breast cancer was performed from 1st January 2006 to 31st January 2009. The neutrophil and lymphocyte ratio (NLR), which is derived by dividing the absolute neutrophil counts divided by the absolute lymphocyte counts, was compared against the patient's disease free survival and disease specific survival.

Results: A cut off value of 2.6 was decided as the optimum value according to the Receiver Operating Characteristics (ROC) curve. Patients with NLR >2.6 showed significantly lower 5 year disease free survival (5-year disease free survival, 74% vs 87%; p 0.038) and disease specific 5 year overall survival (5-year overall survival, 86% vs 95%; p 0.027). Cox proportional multivariate hazard model for disease specific survival revealed that NLR >2.6 was independently correlated with poor prognosis with hazard ratio of 3.09 (95% CI, 1.24–7.69; p0.015) and similarly, the hazard ratio for patients with recurrence with NLR >2.6 was 2.08 (95% CI, 1.09–3.97; p 0.027). Our results show that elevated NLR of >2.6 at initial clinical presentation was an independent factor for poorer 5 year disease free survival and disease specific survival in breast cancer patients.

Conclusion: We conclude that higher NLR is related to poorer 5 year disease free survival and 5 year overall survival. While the use of inflammatory markers is validated in other oncological studies such as gastric and colorectal cancers, there is a paucity of similar studies in breast cancer. This significant association sets the stage for preoperative haematological investigation to take a more significant role in the prognostication of patients with invasive breast cancers.

Disclosure of Interest: No significant relationships.

P228

Mammographic density and disease-free survival in [HR+, HER2−] locally advanced breast cancer

K. Rojas[1]*, R. Flores[2], C. Flores[3], J. Pinto[3], H.L. Gomez[1], C. Castaneda[1]. [1]*Oncology Medical, Instituto Nacional de Enfermedades Neoplasicas, Lima, Peru,* [2]*Radiodiagnostic, Instituto Nacional de Enfermedades Neoplasicas, Lima, Peru,* [3]*Division De Investigación, Oncosalud-AUNA, Lima, Peru*

Goals: Breast density is one of the strongest and most consistent risk factors for breast cancer and has been evaluated as prognostic factor. We evaluate the influence of breast density in the disease-free survival (DFS) in [HR+, HER2−] breast cancer treated with neoadjuvant chemotherapy (NAC).

Methods: We evaluated retrospectively 267 patients with [HR+, HER2−] breast cancer diagnosed and treated with NAC at Instituto Nacional de Enfermedades Neoplásicas (2000–2011). Patients were categorized using ACR BI-RADS breast density composition categories. Main clinicopathological variables were evaluated. In addition, Ki-67 proliferative index (PI) was measured and cases were grouped as Low PI (Ki-67 <14%) and High PI (Ki-67 ≥14%). Five-year rates for disease-free survival were estimated using the Kaplan–Meier method and the Cox model was used for multivariate analysis.

Results: The median age was 50.8 years (range 24–77); according to body mass index, 112 (41.9%) had overweight; 141 were post-menopausal (52.8%); 210 were in clinical stage III (78.7%); 157 had histological grade I/II (60.4%). Only 14 (7.2%) had pathologic complete response. In regard to Ki-67 PI, 132 were Low PI (49.4%) and 135 were high PI (50.6%). According to mammogram density, 47 were BI-RADS I (17.8%); 57 BIRADS II (21.6%); 92 BI-RADS III (34.8%) and 68 BI-RADS IV (25.8%). Mammogram density was associated with menopausal status (premenopausal were more likely to have dense breast; P < 0.001) and body mass index (patients with <30 kg/m^2 were more likely to have dense breast; P = 0.001). In the univariate analysis, tumor size (≤5 cm, 78.5% vs >5 cm, 56.6%; P = 0.04), nodal status (negative, 82.2% vs positive, 59.2%; P = 0.026) and mammographic density (BI-RADS I–III, 66% vs BI-RADS IV, 50.6%; P = 0.019) were significantly related to DFS. In the multivariate analysis, tumor size (HR = 4.5 for >5 cm; P = 0.006) and breast density (HR = 1.7 for BI-RADS IV; P = 0.024) were independent prognostic factors.

Conclusion: Breast density is a prognostic factor that should be evaluated in the subset of patients [HR+, HER2−] breast cancer patients treated with neoadjuvant chemotherapy.

Disclosure of Interest: No significant relationships.

P229

An elevated preoperative plasma fibrinogen level is related with poor prognosis in breast cancer

S. Krenn-Pilko[1]*, U. Langsenlehner[1], E. Thurner[1], T. Stojakovic[1], M. Pichler[2], A. Gerger[3], K.S. Kapp[1], T. Langsenlehner[1]. [1]*Department of Therapeutic Radiology and Oncology, Medical University of Graz, Graz, Austria,* [2]*Department of Experimental Therapeutics, MD Anderson Cancer Center, Texas, United States of America,* [3]*Division of Clinical Oncology, Department of Internal Medicine, Graz, Austria*

Goals: Plasma fibrinogen plays an important role in the pathophysiology of tumor cell invasion and metastases. High plasma fibrinogen levels have been associated with poor prognosis in different cancer types. In the present study, we evaluated the prognostic significance of the preoperative plasma fibrinogen level in a large cohort of breast cancer patients.
Methods: Data from 520 consecutive non-metastatic breast cancer patients, treated between 1999 and 2004, were evaluated. Disease-specific survival (DSS), overall survival (OS), and distant metastasis-free survival (DMFS) were assessed using Kaplan Meier curves. To evaluate the independent prognostic significance of fibrinogen, multivariable Cox regression models were applied for the three end points.
Results: Applying using receiver operating curve (ROC) analysis, the optimal cut-off level for the plasma fibrinogen was 375 mg dl^{-1}, respectively. Univariate analysis revealed a significant association between the elevated plasma fibrinogen and DSS (hazard ratio (HR) 1.70, 95% CI 1.07–2.76, p = 0.026) that remained significant in multivariate analysis (HR 1.71, 95% CI 1.02–2.85; p = 0.042). An increased fibrinogen level was also significantly associated with decreased OS in univariate (HR 1.71, 95% CI1.11–2.64, p = 0.015) and multivariate analysis (HR 1.62, 95% CI 1.01–2.61; p = 0.048). Furthermore, univariate analysis showed a significant impact of increased fibrinogen on DMFS (HR 1.65, 95% CI 1.10–2.48, p = 0.014). In patients with Luminal A tumors, plasma fibrinogen was associated with DSS in univariate (HR 2.54, 95% CI 1.13–5.73, p = 0.024) and multivariate analysis (HR 3.02, 95% CI 1.22–7.46, p = 0.017).
Conclusion: An elevated preoperative plasma fibrinogen level may represent an independent prognostic marker for survival in breast cancer patients.
Disclosure of Interest: No significant relationships.

P230

Endometrial carcinoma in breast cancer patients

L. Leitzin[1]*, O. Lavie[2], N. Sikorsky[1], M. Steiner[1]. [1]*Oncology Department, Lin Medical Center, Haifa, Israel,* [2]*Gyneco-oncology Unit, Carmel Hospital, Haifa, Israel*

Goals: The files of 88 patients data registered with endometrial and breast cancer diagnosis were analyzed. Patients were then divided into two groups: Group I, 58/88 (66%), included patients in whom breast cancer was the first primary tumor and endometrial cancer was diagnosed latter. Group II, 30/88 (34%), included patients in whom endometrial cancer was the first primary tumor and breast cancer was diagnosed latter. The two groups were compared as for clinical features.
Methods: Median age of Group I patients at breast cancer diagnosis was 68 years (47–88). Median age of Group II patients at endometrial cancer diagnosis was 63 years (46–83).
Results: Median time from diagnosis of breast cancer to diagnosis of endometrial cancer in Group I was 72 months (3–510). Median time from diagnosis of endometrial cancer to diagnosis of breast cancer in Group II was 63 months (1–459). Endometrial cancer was diagnosed in earlier stage in Group II patients than in patients followed for breast cancer (Group I). Stage I disease was found in 96% and 74% respectively. 25 Group I patients (59%) had tamoxifen therapy. In 8 endometrial cancer was diagnosed while taking tamoxifen for 9–90 months (median 40). In 17 patients endometrial cancer was diagnosed at median 51 months (0–236) after stopping of tamoxifen which was taken during 6–122 months (median 56). Endometrial cancer (stage I) was diagnosed in earlier stage in tamoxifen treated patients (78% vs 67%). Total endometrial cancer related events (recurrence or death) were more common in Group I than in Group II patients (14% vs 3%). In Group I, the total endometrial cancer event was 12% in tamoxifen treated patients and 17% in patients who had no tamoxifen.
Conclusion: We conclude that in patient suffering from both breast and endometrial cancer, endometrial cancer tends to present with more advanced stage when diagnosed as second primary after breast cancer diagnosis and treatment. Endometrial cancer prognosis is worse in this group unrelated to tamoxifen use for breast cancer treatment.
Disclosure of Interest: No significant relationships.

P231

Luminal subtypes vs. early Ki-67 response and Oncotype DX® in early breast cancer: WSG-ADAPT study

O. Gluz[1]*, U. Nitz[2], M. Christgen[3], H. Kreipe[3], R.E. Kates[4], S. Kuemmel[5], M. Braun[6], C. Schumacher[7], R. Wuerstlein[8], N. Harbeck[8]. [1]*Medical Science, West German Study Group, Moenchengladbach, Germany,* [2]*Breast Center Niederrhein, Ev. Hospital Bethesda, Moenchengladbach, Germany,* [3]*Pathology, Medical School Hannover, Hannover, Germany,* [4]*Statistics, West German Study Group, Moenchengladbach, Germany,* [5]*Clinics Essen-Mitte, Essen, Germany,* [6]*Rotkreuz Clinics Munich, Munich, Germany,* [7]*St. Elisabeth Hospital, Cologne, Germany,* [8]*Breast Center, University Hospital Munich – Grosshadern, Munich, Germany*

Goals: WSG-ADAPT aims to optimize early breast cancer (eBC) therapy within distinct subtypes of BC based on individual early proliferation response. Endocrine sensitivity combined with OncotypeDX® is used to guide chemotherapy decision within the HR+/HER2− subtype.
Methods: WSG-ADAPT (target n = 4950) analyzes biomarker changes after 3 weeks of subtype-specific therapy. For the HR+/HER2− subtype, preoperative ET is given for 3 weeks prior to surgery/biopsy [aromatase inhibitors (AI) in postmenopausal, tamoxifen (Tam) in premenopausal women]. Overall, n = 1760 patients (HR+/HER2−, pN0–1) with Recurrence Score (RS) 0–11 or RS 12–25 and post-Tx Ki67 <10% are treated by ET alone. Other RS 12–25 and all RS ≥26 patients are included in phase III CTx design (n = 2200). Aim of the present analysis is a first prospective comparison of local and central pathology to OncotypeDX® on core biopsies. Measures of concordance included gamma statistic and Spearman (rank) correlations.
Results: Within ADAPT HR+/HER2−, 2058 patients from 79 centers have been enrolled as of 11/2014. For quality assurance, a correlative analysis in the first n = 800 patients with complete baseline documentation was performed. For histological grade, concordance was only 63.5% on diagnostic core biopsies ($\gamma = 0.70$). Remarkably, 72% of centrally G3 tumors were assessed as G1–G2 by the local lab. Central grade was more strongly associated with RS than local grade (rank correlation 0.40 vs. 0.24). For Ki67, the rank correlation of local with central measurements was 0.64; central Ki67 had a slightly higher correlation with RS than local Ki67 (0.48 vs. 0.41). Defining "luminal B-type" as Ki67 >20% and/or PR <20%, local IHC has 26% discordance with central luminal B vs. A; including G3 in the definition, discordance is also 26%. The ADAPT design (no adjuvant chemotherapy if RS 12–25/postendocrine Ki67 <10% or RS 0–11) would spare 46% of chemotherapy indications based on locally assessed luminal B with or without the G3 criterion.

Conclusion: The present analysis confirms our prior observations regarding discordance of prognostic tools in HR+/HER2− eBC. Further quality control in pathology is a prerequisite for conclusive statements on the role of single markers (grade, Ki67, PR, and genomic signatures) in intermediate-risk eBC. Combining RS with individual early response to endocrine therapy could spare adjuvant chemotherapy in a substantial subset of luminal B eBC.
Disclosure of Interest: No significant relationships.

P232
Evaluation of OSNA assay for intraoperative detection of nodal metastasis in early breast cancer

W.P. Lee*, S.K. Lim, A.M.E. Bravo, A.Y. Chok, F.S. Sabado, Y.X. Koh, J. Seah, S.M. Tan. *General Surgery, Changi General Hospital, Singapore, Singapore*

Goals: Intraoperative assessment and identification of nodal metastasis in sentinel lymph node allows for the immediate decision by surgeons to proceed with axillary lymph node dissection.
The one-step nucleic acid amplification (OSNA) method is a molecular assay based on the cytokeratin 19 (CK19) mRNA expressions and has demonstrated good concordance rate compared to conventional pathological examination in multiple studies. Intra-operative use of OSNA, with its short processing time to identify sentinel lymph node metastasis, may confer this advantage of intraoperative decision for ALND, hence reducing the need for a second surgery.
Our aim is to establish the validity of the OSNA assay in the intraoperative detection of SLN metastasis in breast cancer patients in our institution.
Methods: Consecutive patients with early breast cancer and clinically negative lymph nodes were recruited for this study. Routine sentinel lymph node identification was performed with methylene blue dye and the identified nodes were cut in 4 upon retrieval. Alternate pieces were assayed for CK19 mRNA expression with OSNA and conventional histopathological examination with a result of 2 pieces analysed with each method.
The sensitivity, specificity, positive and negative predictive value of the OSNA technique was calculated and compared.
Results: Forty-seven patients were enrolled with 64 lymph nodes examined. Data analysis showed the OSNA assay of CK 19 mRNA expression has an overall sensitivity and specificity of 88.9% and 90.9% respectively. The positive predictive value was 61.5% whereas the negative predictive value was calculated to be 98.0%. The results from this pilot study were comparable to other validation studies.
Only one patient had false negative result while 5 others had false positive results with the OSNA assay.
Conclusion: We conclude that the OSNA assay is a reliable tool in detecting presence of nodal metastasis intra-operatively with high sensitivity and specificity in our institution. Hence, adopting the use of OSNA in breast cancer surgery will guide surgeons in their decision to proceed with axillary lymph node dissection in the same setting.
Disclosure of Interest: No significant relationships.

P233
CD146/Akt/NF-κB/latexin is a novel pathway involved in suppressing breast tumor growth

A. Ouhtit*, A. Fernando, Z. Abd Elmageed, I. Gupta, S. Shanmuganathan. *Genetics, Sultan Qaboos University, Muscat, Oman*

Goals: Despite the association between CD146 expression and development of melanoma, the expression patterns and the role of CD146 in normal and metastatic breast tissues are still controversial. Neither, the molecular mechanisms underpinning this suppression are known, nor has the ligand for CD146 been identified. We hypothesize that CD146 acts as a tumor suppressor in BC.
Methods: We developed tetracycline (tet-on) CD146 system in both MCF-7 and MDA-231 BC founder cell lines, and were structurally and functionally validated using time course RT-PCR, western blot analyses, immunohistochemistry and fluorescent microscopy and, siRNA inhibition respectively. To identify the main players involved in CD146-signaling pathway suppressing BC cell invasion, pharmacological approach combined with luciferase assay was performed.
Results: In functional experiments, induction of CD146 inhibited BC cell migration and invasion in vitro as well as tumor growth and progression in mouse breast xenograft model. Latexin (LXN: a variant of Tissue Inhibitor of Metalloproteinases), was identified by expression profiling as a novel transcriptional target of CD146-signaling, an association validated by quantitative PCR and immunoblotting experiments in a range of breast and melanoma cancer cells. To further validate our finding in vivo, immunohistochemical analysis of breast tumor tissues from both human and mouse (tet-inducible system) breast tissues showed that while, the expression of both CD146 and LXN were highly expressed in the early stages of BC (normal and benign tissues), it was lost in advanced stages (malignant and metastatic tissues). However, siRNA inhibition of CD146 in the SKMel-28 melanoma cell line increased LXN expression, suggesting that while LXN is a positive transcriptional target of CD146 in BC cells, it is negatively regulated in melanoma cells. Furthermore, using invasion assay, the functional relevance of LXN to CD146-suppressed metastasis was demonstrated by selective suppression of LXN in CD146-expressing BC inducible cells using RNAi. Pharmacological and molecular approaches revealed that the activation of NFκB via Akt pathway couples CD146 to the transcription of LXN in BC cells CD146-inducible cells.
Conclusion: Our findings support the hypothesis that CD146 is a breast tumor suppressor gene. Our study is the first report to provide a functional molecular link of a novel transcriptional target of CD146, LXN, to cancer via a unique axis that underpin CD146-suppressed BC progression. LXN is a potential target for guiding the development of novel therapeutic strategies for BC.
Disclosure of Interest: No significant relationships.

P234
BRIP-1, a novel marker of breast tumor malignancy in the Omani population

I. Gupta[1]*, A. Ouhtit[1], M. Al Riyami[2], A. Al Ajmi[3]. [1]*Genetics, Sultan Qaboos University, Muscat, Oman,* [2]*Pathology, Sultan Qaboos University, Muscat, Oman,* [3]*Surgery, Sultan Qaboos University, Muscat, Oman*

Goals: The rationale of the present investigation is based on the following observations: (1) in Oman, a significantly increasing number of younger females (25–40 years) present to the clinic with advanced stage of breast cancer (BC); (2) in Oman, the rate of consanguinity is significantly high (~50%); (3) The pathologic and clinical heterogeneity of BC reflects the complex molecular basis of the disease which is partially responsible for therapeutic failures; and (4) the transition from normal/benign to malignant phenotype of breast tumor requires the involvement of a subset of specific genes. In addition to increasing our understanding of the signaling pathways that underpin tumor malignancy and progression, validation of the identified genes might establish new biomarkers for diagnosis of BC and/or candidate genes to guide the design of appropriate targeted-therapies in Omani patients.
Methods: RNA was extracted from 40 malignant and 40 normal/benign breast tumor tissues and analyzed by Microarray Gene Expression Profiling. The differential expression of the

identified gene was structurally validated by RT-PCR using the remaining RNA of the same samples previously examined by microarray. Pathway analysis was carried out to predict the major functional pathways.
Results: Among a number of differentially expressed genes, BRIP1 showing a 5-fold up-regulation was identified as a potential gene that might underpin the transition to the malignant phenotype. The differential expression of BRIP-1 was structurally validated by RT-PCR.
Conclusion: Ongoing sequencing of these genes using DNA extracted from the same samples will ultimately identify any genetic alteration that can affect the normal function of these genes. Cell migration/invasion assays will validate further the physiological relevance of BRIP-1 in tumor malignancy, and perhaps other novel gene(s) specific to BC in the Omani population. This study discovered, BRIP-1 as a novel potential marker for BC malignancy, and might be considered as a biomarker for early diagnosis of BC and/or a target to pave the way towards the design of anti-BC therapeutic strategies.
Disclosure of Interest: No significant relationships.

P235
Prognostic and predictive value of tumor-infiltrating lymphocytes in triple negative breast cancer

E. Kim[1] *, J. Kwon[1], W. Byon[1], B.J. Song[2], C. Park[1]. [1]*Breast-thyroid Cancer Center, Department of Surgery, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea,* [2]*Department of Surgery, Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, Korea*

Goals: Previous preclinical and clinical data suggest that increased lymphocytic infiltration would be associated with good prognosis and benefit from immunogenic chemotherapy especially in triple negative breast cancer (TNBC). We investigated a single-center experience of TNBC and relationship with lymphocytic infiltration.
Methods: From January 2004 to December 2012, at department of surgery, Kangbuk Samsung Hospital, Sungkyunkwan University, School of Medicine, we retrospectively reviewed 897 breast cancer patients-clinical outcomes, clinicopathological characteristics, breast cancer subtypes. And we reviewed lymphocytic infiltration of TNBC specimens by two pathologists. Statistical analysis of risk factors associated with recurrence was performed.
Results: A total of 897 patients, 76 were TNBC (8.47%). Mean age of TNBC patients were 50.95 (SD10.42) years, mean follow-up periods was 40.06 months. We reviewed 49 slides, and there were 8 recurrent breast cancer patients (16.32%), and 4 patients were expired (8.16%). There were 9 lymphocytic predominant breast cancers (LPBC) – carcinomas with either intratumoral lymphocytes in >60% of tumor cell nests. 1 patient of LPBC was recurred and 8 were not. In multivariate logistic regression, the odds ratio of lymphocytic infiltration was 0.59 ($p = 0.643$).
Conclusion: In a single-center experience of TNBC, the lymphocytic infiltration in tumor cell nest might be good trend on the prognosis but there was not statistically significant. Further study with more patients will be needed.
Disclosure of Interest: No significant relationships.

P236
Intraoperative predictive model for non-SLN metastasis using total tumor load assessed by OSNA

J.I. Sánchez-Méndez[1] *, C. Martí Álvarez[2], A. Román Guindo[2], L. Paz Ramírez[3], L. Yébenes Gregorio[4], G. Steinberg Contreras[2], S. Serrano Velayos[2], A. Rychlik[2], J. De Santiago García[1], D. Hardisson[4]. [1]*Breast Unit – Gynaecologist, Hospital Universitario La Paz – IdiPaz, Madrid, Spain,* [2]*Breast Unit – Gynaecologist, Hospital Universitario La Paz, Madrid, Spain,* [3]*Universidad Autónoma de Madrid, Madrid, Spain,* [4]*Breast Unit – Pathologist, Hospital Universitario La Paz – IdiPaz, Madrid, Spain*

Goals: The aim of this study is to develope an intraoperative prediction model of non sentinel lymph node (SLN) axillary metastasis in breast cancer patients with macrometastasis in SLN.
Methods: The study included patients with clinically and ultrasonographically node-negative, cT1–3 invasive breast cancer, who had undergone intraoperative sentinel lymph node evaluation by one step nucleic acid amplification (OSNA) with a result of macrometastasis. A logistic regression model, "La Paz Score", modified from previously published "Teramoto Score", including tumor size, number of affected SLN, total tumor load (TTL) of cytokeratin 19 (CK19) mRNA, histopathological and molecular phenotype of the tumor was developed to predict intraoperatively the likehood of non-SLN axillary metastasis. The discriminating ability of some variables and logistic regression models, was assessed by plotting the ROC curve and computing the area under the curve (AUC) and corresponding 95% confidence interval (CI). All statistical analyses were performed with the statistical language R version 3.0.1.
Results: Ninety patients were recruited. The size of tumors ranged from 5 to 100 mm, with median (IQR) of 19.5 (12.75). TTL values (expressed as 10^3 copies/uL) ranged from 5.34 to 8401, with median (IQR) of 44.5 (219.5). The number of positive SLN were 1 (64.4%), 2 (27.8%) and 3 (7.8%). Sixty-five cases (72.2%) were ductal invasive carcinomas, 23 (25.6%) cases were lobular invasive, and 2 (2.2%) other histologic subtypes. Regarding the phenotypic molecular type 57.8% were luminal A, 38.9% luminal B, and 3.3% basal type. There is no Her2 positive tumors. In 60 patients (66.7%) there were no more axillary metastasis, and in 30 patients (33.3%) there were at least one non-SLN axillary metastasis. **The negative predictive value of our model is 90.24%**, with a sensitivity of 86.67%, a specificity of 61.67% and a predictive positive value of 53.06%.

Model	AUC	[CI]
Teramoto Score	0.56	[0.44 to 0.68]
La Paz Score	0.79	[0.69 to 0.89]

Conclusion: We showed that a predictive model with five variables may significantly improve the discrimination ability of the score proposed by Teramoto ($p = 0.001$). This logistic regression model including the (log10) TTL, tumor size, number of positive SLN, histology and molecular subtype provided a reasonable discrimination ability (AUC = 0.79). However, this should be validated in a new sample of larger size.
Disclosure of Interest: No significant relationships.

P237
The impact of body composition change on neo-adjuvant chemotherapy for breast cancer patients

T. Iwase *, T. Sangai, E. Ishigami, J. Sakakibara, K. Fujisaki, N. Shiina, H. Fujimoto, M. Sakakibara, T. Nagashima, M. Miyazaki. *General Surgery, Chiba University Hospital, Chiba, Japan*

Goals: Studies have reported that obesity decreases the chemotherapeutic efficacy of neo-adjuvant chemotherapy (NAC)

on breast cancer. However, the relationship between actual body composition and therapy outcome is still unknown. Therefore, we set out to clarify the effect of body composition on NAC.

Methods: A total of 172 cases with advanced breast cancer who underwent surgery after NAC between January 2004 and December 2012 were retrospectively analyzed. Abdominal circumference (AC), Subcutaneous fat area (SFA), visceral fat area (VFA), and skeletal muscle area (SMA) were calculated using computed tomography volume analyzing software, SYNAPSE VINCENT® (FUJIFILM Co., Ltd. Tokyo, Japan). VFA/SFA ratio was used for evaluating visceral obesity. The relationships between those body composition parameters, pathological complete remission (pCR) and survival prognosis were analyzed.

Results: Firstly, AC, SFA, and VFA were significantly correlated to body mass index (BMI) in body composition analysis ($p < 0.05$, AC; $r = 0.82$. SFA; $r = 0.71$, VFA; $r = 0.78$). AC, SFA, and VFA were significantly increased after menopause, while SMA was significantly decreased ($p < 0.05$). In addition, VFA/SFA ratio was significantly increased after menopause, despite no significant change in BMI. Secondly, a total of 46 cases achieved pCR. However, body composition parameters were not associated with pCR. Lastly, survival analysis demonstrated high VFA group (>100 cm^2) was significantly had worse DDFS compared to the low VFA group ($p < 0.05$). Moreover, that difference was more significant in postmenopausal group. Multivariate analysis demonstrated VFA pCR, and subtypes were independent prognostic factors for DDFS.

Conclusion: Present study suggests that increased visceral fat after menopause significantly relates to the worse outcome after NAC. It is highly probable to give an appropriate intervention to those high-risk cases improve the outcome.

Disclosure of Interest: No significant relationships.

P238

EndoPredict-based treatment decision can reduce chemotherapy usage in ER+, HER2− breast cancer

G. Schlake[1] *, R. Kronenwett[2], F. Tiecke[1], K. Kastrup[3], N. Bleuel[1], C. Petry[2], S. Wilhelms[3], P. Tönnies[4], W. Schlake[1]. *[1]Pathologie, Institut für Pathologie und Molekularpathologie, Gelsenkirchen, Germany, [2]Research and Development, Sividon Diagnostics GmbH, Cologne, Germany, [3]Klinik für Frauenheilkunde und Geburtshilfe-Brustzentrum am St. Elisabeth-Krankenhaus, Dorsten, Germany, [4]Frauenklinik/Brustzentrum am Krankenhaus Bethanien, Moers, Germany*

Goals: EndoPredict (EP) is a prognostic gene expression test for patients with estrogen receptor (ER) positive, HER2 negative primary breast cancer. It can be performed locally by the pathologist. The aim of this retrospective study was to evaluate whether treatment according to the EP result instead of the classical risk parameters alone would have an impact on chemotherapy usage in a German breast center.

Methods: All patients with ER+, HER2− primary breast cancer with up to 3 positive lymph nodes admitted to one hospital between January 2008 and June 2011 were screened. All intermediate-risk patients according to German S3 Guideline (2008) who were eligible for chemotherapy were included in this study. Archived tumor tissue was retrospectively analyzed with EP by the local pathologist and the molecular-clinico-pathological EPclin score was calculated using gene expression values, tumor size and nodal status. Risk classification into low or high risk by the EPclin score was compared with the original therapy decision that the tumor board had made before EP became available.

Results: 82 patients were included in this study (age: 37–75, median: 62). 58 were node negative, 24 had 1 to 3 positive lymph nodes. 50% had actually received adjuvant chemotherapy in addition to endocrine therapy. Using EP, 68% of patients were classified as low and 32% as high risk. Therefore, treatment according to the EP result would have reduced total adjuvant chemotherapy usage by 18%. 27% of patients who had received chemotherapy would not receive it if treated according to EP, 9% had not received chemotherapy and were classified as high risk by EP. In 64% of patients no change of risk classification was observed. Interestingly, re-classification by EP was particularly found in patients with small tumors: 34 of the 36 patients with change of risk classification had T1a/b or T1c tumors. These results suggest that EP would not only have reduced over-treatment but also under-treatment, especially of small tumors. Assuming direct costs for chemotherapy ranging from € 11,296 (Blank et al., 2014) to € 19,263 (Hornberger et al., 2012) a treatment following the EP result would have saved € 255–1,713 per patient in this single center cohort. The cost of EP was assumed to be € 1,800.

Conclusion: Our study suggests that EP applied in patients with intermediate risk according to classical guidelines can help reducing chemotherapy usage without impairment of outcome.

Disclosure of Interest: GS and WS have received honoraria from Sividon Diagnostics GmbH for lectures and advisory boards concerning EP. GS and WS have received research support from Sividon Diagnostics. RK and CP are shareholders and employees of Sividon Diagnostics GmbH.

P239

Clinical significance of CA 15-3 and CEA in detection of breast cancer recurrence

C.W. Mok[1] *, S.K. Lim[1], J. Seah[1], J.W. Kam[2], S.M. Tan[1]. *[1]Breast Service, General Surgery, Changi General Hospital, Singapore, Singapore, [2]Clinical Trials and Research Unit, Changi General Hospital, Singapore, Singapore*

Goals: The most widely used tumour markers in breast cancer are CA 15-3 and CEA. Current literature does not recommend the use of both tumour markers in detecting disease recurrence mainly due to a lack of specificity. This cohort study therefore aims to investigate the value of CA 15-3 and CEA in breast cancer surveillance and detection of disease recurrence.

Methods: Consecutive patients with available serum CA 15-3 and CEA level at initial diagnosis of recurrence in a prospectively collected database over 15 years (1998–2013) were reviewed. A second group of patients with no recurrence who were matched in terms of demographic and tumour characteristics were included as a control. Patients with metastatic disease at presentation or those without surveillance tumour markers performed were excluded from the study. Statistical analysis was performed using SPSS Version 20.

Results: A total of 137 patients (67 patients with recurrence and control group of 70 patients) were selected from a prospectively collected database over a 15-year period. ROC curve were plotted for both CA 15-3 and CEA which showed high discriminatory power in detecting recurrence with an AUC of 0.856 and 0.901 for CA 15-3 and CEA respectively ($p = 0.001$). Elevation of CA 15-3 and CEA above the normal upper limit of 25 U/ml and 5 ug/L respectively have been shown to be highly predictive of recurrence. CA 15-3 has a specificity of 97.1% and sensitivity of 71.6% ($p = 0.001$) whereas CEA was also statistically significant ($p = 0.001$) with specificity of 95.7% and sensitivity of 67.2%. Combined measurement of CA 15-3 and CEA level were shown to be statistically significant ($p = 0.001$) with improved specificity of 91.8%, sensitivity of 94.2% as well as PPV and NPV at 0.93. Logistic regression analysis was performed to investigate the interaction between tumour characteristics and disease recurrence. In univariate analysis, elevation of tumour markers above normal upper limit ($p = 0.01$), size of tumour ($p = 0.05$), axillary lymph node involvement ($p = 0.004$) as well as histological grade ($p = 0.003$) have been shown to be highly significant factors in predicting recurrence.

In multivariate analysis, both CA 15-3 and CEA remained as highly signifcant predictors (p = 0.01) as patients with at least one tumour marker value above the upper normal limit was 1677 times more likely to develop recurrence compared to patients with either one or both tumour markers level below the upper normal limit.
Conclusion: CA 15-3 and CEA were found to be highly discriminatory in detecting disease recurrence. Elevations of serum CA 15-3 and CEA level above the normal upper limit may prove to be helpful in detecting relapse in the absence of clinically evident recurrence.
Disclosure of Interest: No significant relationships.

P240
Impact of modified 2013 ASCO/CAP guidelines on HER2 testing in breast cancer

Z. Varga*, A. Noske. *University Hospital Zurich, Institute of Surgical Pathology, Zurich, Switzerland*

Goals: The world-wide used scoring criteria, the ASCO/CAP Guidelines for HER2 testing in breast cancer after being revised in 2008 for the first time, underwent a second modification in October 2013. Changes in current scoring include changes in cut-offs: 10% strong membranous staining for score 3+ on immunohistochemistry (previously 30%) and allowing using the ratio of >2 or absolute gene copy number (<6) alone or in combination with each other by in-situ hybridisation technology (previously >2.2 and average copy number of >6). We addressed the question in this study, which impact the modified cut-offs had on overall HER2 positivity in a single institution.
Methods: We retrospectively analysed all diagnostic breast cancer cases for one year (October 2013 to October 2014) at the Institute of Surgical Pathology University Hospital Zürich. The cohort included 625 consecutive cases, which underwent double HER2 testing by immunohistochemistry (IHC) and fluorescent in situ hybridisation (FISH), using the modified 2013 ASCO/CAP guidelines. Results were compared with HER2 test results on 1522 consecutive diagnostic breast cancer cases from two previous years (2011–2012), using the 2008 ASCO/CAP Guidelines, also tested with IHC and FISH in each case.
Results: Between October 2013 and October 2014, overall HER2 positivity was 15.5% (98 of 625 cases were either 3+ on IHC or amplified by FISH. 79 of 625 cases (13%) were 3+ on IHC, 96 of 625 cases (15.3%) were amplified by FISH. In the cohort of 625 cases, 33 (5.3%) were equivocal. In the earlier group of 1522 cases, 5 (0.3%) were equivocal. 30 of 33 equivocal cases (91%) in 2013–2014 were score 1+ or 2+ on IHC. In 21 equivocal cases, there was a repeated IHC/FISH testing: 5 of 21 cases (24%) became amplified by FISH, 2 of 21 cases (12%) were 3+ on IHC. In 2011–2012, overall HER2 positivity (IHC or FISH) was 13.7% (210 of 1522 cases). 184 of 1522 cases (12%) were 3+ on IHC, 181 of 1522 cases (12%) were amplified by FISH. Equivocal cases (n = 5) on FIDH were all 2+ on IHC.
Conclusion: Applying the modified ASCO/CAP Guidelines from 2013 resulted in an increase (1.8%) in overall HER2 positivity rate in comparison to overall positivity rate using the 2008 ASCO/CAP guidelines. The increased positivity rate was mainly due to more FISH positive cases (3.2% more than until 2013). The high rate of equivocal cases (5.3%) did not contribute to the increase in overall HER2 positivity, but resulted in delay of the definitive diagnosis on HER2 status.
Disclosure of Interest: No significant relationships.

P241
Usefulness of the 21-gene assay to guide adjuvant chemotherapy decision-making: Geneva experience

A. Bodmer[1]*, A. Hugli[2], S. Diebold Berger[3], L. Favet[2], M. Guetty Alberto[2], B. Exquis[2]. *[1]Medical Oncology, Geneva University Hospital, Geneva, Switzerland, [2]Membre du réseau SONGE, Geneva, Switzerland, [3]Laboratory Weintraub Viollier, Geneva, Switzerland*

Goals: To evaluate the impact of Oncotype DX recurrence score (RS) on recommendation for adjuvant chemotherapy in estrogen-receptor positive (ER+), HER2 negative, early breast cancer (EBC) with (N+) or without (N0) minimal lymph node involvement.
Methods: Local prospective observational study, in which Oncotype DX™ was considered for pre and postmenopausal patients with luminal A/B EBC. Patients had to be considered at intermediate risk of recurrence, with favourable prognostic factors combined with at least one of the following unfavourable characteristics: tumor size (T) >2 cm, tumor grading (G) 2 or 3, Ki67 ≥20% or presence of N+. This access program was open to all Geneva medical oncologists or breast surgeons. An application form with patient clinical and pathological data and initial treatment recommendation had to be sent to a panel of breast cancer specialists, consisting of 4 medical oncologists and one pathologist. The panel was asked to evaluate the recurrence risk and validate or not the Oncotype DX™ indication. Therapeutic decisions were compared between pre and post RS: the percentage of chemotherapy (CT) was compared using a Mc Nemar test. This comparison was stratified by histology, T, N, PR, Ki67 and RS. The differences in percentage of CT between pre and post were assessed with a 95% confidence using exact method and accounting for repeated measurement.
Results: Oncotype DX™ was performed in 60 patients. On the basis of the RS, 31 (51.7%), 24 (40%) and 5 (8.3%) tumours were classified as low, intermediate and high risk of reccurence. Before knowledge of RS, adjuvant CT was recommended by medical oncologist in 38 of 60 patients (63.3%), in 17 of 31 (54.8%), 17 of 24 (70.8%) and 4 of 5 (80.0%) patients with respectively low, intermediate and high RS. Initial treatment recommendation was revised in 28 (46.7%) patients after knowledge of the RS. The shift was predominantly from adjuvant combined chemo-endocrine (CTHT) to endocrine therapy (HT) alone (25/28 89.2%). Among the 38 recommended CT in pre-test, 25 have been avoided (25/38 65.8%), but for three patients (13.6%) the treatment plan post-test changed with an initial HT recommendation to a combined CTHT. After RS result, adjuvant CT was required for 16 patients, including 13 for which CT was already proposed in pre-test. The difference between CT recommendation in pre (63.3%) and in post-test (26.7%) was statistically significant (p = 0.0001). The overall reduction of recommended adjuvant CT after the RS result is 57.9% (22/38).
Conclusion: Our results confirm that RS has an impact on physicians' adjuvant decision-making in N0/N+ ER+ EBC, in 46.7% of time, with mainly a reduction of chemotherapy use. These results, although slightly higher, are congruent with other published data. However the small sample size of our cohort and the large heterogeneity of patients are a limitation. But this situation may reflect "daily life" in clinical practice.
Disclosure of Interest: No significant relationships.

P242
The St.Gallen classification does not add prognostic information to traditional markers

M. Sundquist[1]*, L. Brudin[2], D. Lager[1], G. Tejler[1]. *[1]Department of Surgery, Breast Unit, Kalmar, Sweden, [2]Department of Physiology, Kalmar, Sweden*

Goals: Microarray-based gene expression studies have identified a number of subtypes of breast cancer with different behaviour,

prognosis and response to therapies. In 2011, the St. Gallen International Breast Cancer Conference suggested a surrogate definition of identified intrinsic subtypes of breast cancer which was further developed in 2013 resulting in the following groups: Luminal A, Luminal B (HER2 negative), Luminal B (HER2 positive), HER2 positive (non-luminal) and Triple negative (ductal). The surrogate classification is increasingly used as a prognostic and therapy predictive tool. Our aim is to compare the prognostic strength of the St. Gallen surrogate classification (SGSC) to that of the classical prognostic markers grade, node status and size, as summarized in the Nottingham Prognostic Index (NPI).

Methods: Tumour characteristics, grade, nodal status, size, ER, PR, HER2, proliferation marker and clinical data from 1046 pts diagnosed with breast cancer in Kalmar County with median 10 years of follow up were collected. The relationships between distant recurrence/disease specific mortality and NPI and SGSC respectively were calculated and Cox regressions performed for the NPI parameters and the SGSC subtypes with and without adding nodal stage data to the SGSC.

Results: The NPI identified 5 subgroups with highly significant successively increasing risk of distant recurrence and breast cancer mortality, hazard ratios (HR) 2–3 by step. The SGSC did not discriminate prognostic groups as well as NPI. Of the 108 pts with grade 1, N0 tumours only 1 had distant recurrence. They all fell within the excellent NPI group. In the SGSC however, 33 of them were assigned the Luminal B or Triple negative subtype. Further, of the 403 grade 3 tumours, 32 were classified as Luminal A. Twenty-five per cent of those had distant recurrence. When NPI was applied to each SGSC subtype we found that NPI stratified pts in each of the Luminal A, Luminal B Her2+/− and Triple Negative types in subgroups with significantly different prognosis. HR ranged from 1.7 to 2.3 in the four groups; $p < 0.001$ to 0.005. Only for the HER2+ Non-Luminal subtype there was no significant prognostic information gained from the NPI.

Conclusion: The St. Gallen surrogate classification does not stratify patients according to the risk of distant recurrence and breast cancer death as effective as traditional prognostic factors, grade, nodal status and size, as summarized in the NPI.

Disclosure of Interest: No significant relationships.

P243

Basal-like breast carcinomas: prognostic and predictive factors

S.S. Todorov*, E. Bosenko. *Pathology, Rostov Oncological Institute, Rostov-on-Don, Russian Federation*

Goals: Basal-like breast carcinomas are tripple-negative malignant tumors. They characterise by the absence of hormone receptors (estrogen, progesteron), HER-2/neu, so called tripple-negative cancers. It remains the important problem in this breast cancer group – how to treat it, are there the specific targets in this tumor? The aim of our study was the comparative morphological, immunohistochemical investigation of basal-like tumors for understanding rate of malignancy, type of growth, variants of duration and development of these tumors.

Methods: Morphological, immunohistochemical investigation of 85 basal-like breast cancers diagnosed by biopsy and sectoral resection of the breast. For immunohistochemical investigation we have used the following antibodies by Ventana: vimentin, TGF-b, E-cadherin, Ki-67.

Results: Basal-like breast tumors (BBT) are the multivariable group of cancers. According to morphological and immunohistochemical features of these tumors we devided it into several subgroups. The first one, BBT characterised by intense expression of vimentin, high proliferative index Ki-67 (more than 60%), absence of E-cadherin protein, good diffuse TGF-b expression in the tumor cells. In the second group there were middle to intense expression of vimentin, low proliferative index Ki-67 (no more than 10–15% of the tumor cells), good expression of E-cadherin protein, focal TGF-b expression. The next one BBT group have demonstrated the predominance of vimentin, E-cadherin and low expression of TGF-b, Ki-67 (range 15–20%).

Conclusion: We consider BBT are the variable type of the tumors with different capacity to growth, transdifferentiation, proliferation activity. The different biological behavior of the tumors explain by the existence of 3 BBT groups: (1) high proliferative, transdifferentiation type of BBT; (2) low proliferative and high "interconnection" type of BBT; (3) low proliferative type of BBT. These data can give information about these tumors, described markers can serve as predictive and prognostic factors of BBT.

Disclosure of Interest: No significant relationships.

P244

Clinical and prognostic significance of menopausal status in triple negative breast cancer

M. Nakano[1]*, M. Fujisue[1], R. Tashima[2], Y. Okumura[1], Y. Nishiyama[1], T. Ohsako[1], Y. Toyozumi[3], N. Arima[3], R. Nishimura[1]. [1]*Breast and Endocrine Surgery, Kumamoto City Hospital, Kumamoto, Japan,* [2]*Surgery, Kumamoto City Hospital, Kumamoto, Japan,* [3]*Pathology, Kumamoto City Hospital, Kumamoto, Japan*

Goals: Triple negative breast cancer (TNBC) has a poor prognosis due to its heterogeneity and lack of effective targeted therapies. However, some studies have reported that there are racial differences of TNBC prevalence and prognosis. Moreover, it was reported that Japanese patients with TNBC is different from that of other races, especially with relation to menopausal status. The aim of this study is to evaluate the menopausal status as a prognostic marker and to analyze the correlation between menopausal status and clinicopathological parameters in patients with TNBC.

Methods: We retrospectively analyzed the clinicopathological characteristics and outcomes of 398 stage I–III primary TNBC patients, who were treated at our institution between 1990 and 2014. The factors investigated included the effect of menopausal status on disease-free interval (DFI) and overall survival (OS), and the influence of the Ki-67 index value and nuclear grade (NG) on the prognosis of TNBC patients. Most of the TNBC patients were treated with adjuvant chemotherapy (i.e. anthracycline +/− taxanes). Multivariate analysis was performed to identify the prognostic factors for DFI and OS. The median follow-up period was 6.2 years after initial surgery.

Results: Out of 398 TNBC patients, 101 patients were premenopausal and 297 were postmenopausal. The Ki-67 index value in premenopausal TNBC patients was significantly higher than that in postmenopausal TNBC patients ($p = 0.0015$). Postmenopausal TNBC patients had significantly better DFI than premenopausal patients ($p = 0.007$). In cases with a high Ki-67 index value (≥50%), the postmenopausal patients had a significantly longer DFI than that of premenopausal patients ($p = 0.0343$). However, there was no difference in DFI between pre and postmenopausal status in cases with lower Ki-67 index value (<50%). The DFI of premenopausal patients was significantly worse than the postmenopausal patients with a lower NG (1/2). On the other hand, there was no difference in DFI between pre and postmenopausal patients with a higher NG (3). Multivariate analysis revealed that menopausal status, NG, tumor size and lymph node metastasis were significant prognostic factors for recurrence of TNBC.

Conclusion: In this study, we found that the characteristics of premenopausal TNBC were different from that of postmenopausal TNBC. Therefore, the menopausal status may be an important prognostic factor in patients with TNBC.

Disclosure of Interest: No significant relationships.

P245

Neutrophil to lymphocyte ratio predicts lymph node metastasis in triple negative breast cancer

A. Philip[1]*, K. Pavithran[2], M. Jose[2], J. Wesley[2], P. Renjini[2], D.K. Vijaykumar[3], M. Dinesh[4], J. Annie[5], N. Seethalakshmi[5], N. Smitha[5]. [1]*Medical Oncology, Amrita Institute of Medical Sciences, Cochin, India,* [2]*Amrita Institute of Medical Sciences, Cochin, India,* [3]*Surgical Oncology, Amrita Institute of Medical Sciences, Cochin, India,* [4]*Radiotherapy, Amrita Institute of Medical Sciences, Cochin, India,* [5]*Pathology, Amrita Institute of Medical Sciences, Cochin, India*

Goals: The aim of the study was to investigate the value of pre treatment neutrophil to lymphocyte Ratio (NLR) as a prognostic marker in triple negative breast cancer (TNBC) and to see its bearing on the clinical and pathological Lymph node status.
Methods: This was a retrospective analysis of cases of TNBC treated at our centre from 2004 to 2011. The case files were retrieved and the pretreatment complete blood count was recorded from which the NLR was calculated as the percentage of neutrophils divided by the percentage of lymphocytes. The association between pretreatment NLR with the stage of the disease, clinical and pathological Lymph node status and disease-specific survival, was analyzed. A cutoff value of 1.85 was used for the NLR group stratification [High NLR (>1.85) and Low NLR (<1.85)], based on the receiver operating characteristic (ROC) curve derived from our data. The frequency distributions between the variables and the NLR groups were compared using the Chi Square test. Survival analysis, stratified by the two NLR groups, was used to test the prognostic significance of NLR.
Results: A total of 208 patients were eligible for the analysis. The median age of the study population was 50 years. The median follow up period was 48 months (2–122 months). At the time of analysis, 65% of our study population was alive and well. There was no significant correlation between the NLR and the disease specific survival (Mean disease specific survival of 61.5 vs 54 months in the low and high NLR groups respectively; $p = 0.326$). The NLR was found to have a strong correlation with the clinical stage at presentation (87% early stage disease in the low NLR group vs 44% early stage in the high NLR group; $p < 0.01$). The pathological lymph node status also showed significant correlation with the NLR (75% cases were node positive in the high NLR group compared to 36% in the low NLR group; $p < 0.01$).
Conclusion: Based on our study, we conclude that the pretreatment neutrophil to lymphocyte ratio is strongly associated with lymph node metastasis and clinical stage in triple negative breast cancer patients. It is not useful as a prognostic marker, as it does not seem to have any bearing on the disease specific survival.
Disclosure of Interest: No significant relationships.

P246

Risk assessment by St.Gallen 2013 recommendation and Oncotype DX®: results from the WSG PlanB trial

U. Nitz[1]*, O. Gluz[2], H. Kreipe[3], M. Christgen[3], R.E. Kates[4], M. Clemens[5], S. Kraemer[6], B. Aktas[7], S. Kuemmel[8], N. Harbeck[9]. [1]*Breast Center Niederrhein, Ev. Hospital Bethesda, Moenchengladbach, Germany,* [2]*Medical Science, West German Study Group, Moenchengladbach, Germany,* [3]*Pathology, Medical School Hannover, Hannover, Germany,* [4]*Statistics, West German Study Group, Moenchengladbach, Germany,* [5]*Mutterhaus der Borromäerinnen, Trier, Germany,* [6]*University Clinics Cologne, Cologne, Germany,* [7]*University Clinics Essen, Essen, Germany,* [8]*Clinics Essen-Mitte, Essen, Germany,* [9]*Breast Center, University Hospital Munich – Grosshadern, Munich, Germany*

Goals: In HR+, HER2− early breast cancer (BC), the 2013 St. Gallen Consensus recommends adjuvant chemotherapy (CT) for patients with pN >2, recurrence score (RS) >25, G3, or high Ki-67/low PR. Here, we present early outcome data from PlanB for prospective evaluation of these different risk assessment tools.
Methods: The WSG-PlanB trial compares 6 × TC vs. 4×EC plus Doc in pN+ or high risk N0 HER2− BC defined by St. Gallen 2007 (pT >2, G2–3, age <35 years old, high uPA/PAI). After an early amendment (August, 2009), HR+ patients with pN0–1 and RS ≤11 were selected to forgo CT, receiving only endocrine therapy. Luminal B (semiquantitative Ki-67 >20% or PR <20% or G3) subtype was centrally assessed by an independent trial pathologist. Aim of present analysis is to compare the adjuvant CT indication based on St. Gallen 2013 or RS.
Results: From April 2009 to December 2011, 3,198 patients were recruited; of these, 2,449 were randomized for the CT question. Median age was 56 years; 84.1% were HR+ (local pathology), 60.8% pN0. The central tumor bank population reported here included 3,071 cases. RS was available in n = 2,568 (RS 0–11: 18%, 11–25: 60.4%, >25: 11.6%). In 348 patients (14.6% of pN0–1 patients after amendment), CT was omitted based on RS ≤11. 37.1% of HR+ pN0–1 patients had luminal-A tumors. 96.4% of them had RS <25. Within the luminal-B (62.9%) subgroup, 70.1% had RS <25. After 35 months median follow-up, 3-year EFS in the no-CT group was 98.3%. In the central HR+ population, EFS was substantially shorter in patients with RS >25 than in others (3 y EFS: 92% vs. 98% in both RS 12–25 and RS 0–11; $p < 0.001$). This prognostic impact was mostly attributable to luminal-B tumors. pN status, Ki-67, local and central grade, tumor size, and RS were univariate prognostic factors for EFS. In multivariate analysis, only central G3, pN status, and RS (fractionally ranked) remained significant predictors for poor EFS.
Conclusion: As shown for the first time by a prospective trial, patients with RS 0–11 treated by ET alone have an excellent 3 y EFS. Using the 2013 St. Gallen Criteria central review identified about 1/3 of CT candidates as low risk. Highest clinical utility of RS was observed in the luminal-B subgroup. The excellent outcome of patients with RS 12–25 receiving CT suggests potential CT overtreatment in this group. This issue is addressed by the ongoing WSG-ADAPT trial.
Disclosure of Interest: No significant relationships.

P247

A laboratory comparison of the 21-gene assay and PAM50-ROR

M. Alvarado[1]*, C. Prasad[2], M. Rothney[3], D. Cherbavaz[3], A.P. Sing[3], F. Baehner[3], C. Svedman[3], C. Markopoulos[4]. [1]*USCF Comprehensive Cancer Center, University of California San Francisco, San Francisco, United States of America,* [2]*Marin Medical Laboratories, Greenbrae, United States of America,* [3]*Genomic Health Inc., Redwood City, United States of America,* [4]*Athens University Medical School, Athens, Greece*

Goals: The 21-gene Recurrence Score® assay is validated in patients (pts) with ER+ early stage invasive breast cancer (EBC) and predicts 10-yr distant recurrence risk and chemotherapy (CT) benefit. The Prosigna® assay (ROR) which uses 46 of the PAM50 genes, was validated in post-menopausal pts with ER+ EBC and is a prognostic assay only. Despite differences in platforms and methods used for development and validation, it is frequently believed that the assay results are interchangeable. We performed a study comparing results from the two assays obtained from the same tumor blocks.
Methods: 70 sequential BC tumors from Marin Medical Laboratories with sufficient tumor material were selected to be tested with the standard 21-gene assay. Samples were sent to an independent lab where Prosigna ROR and intrinsic subtype analysis was performed with the operators blinded to Recurrence Score results. Descriptive statistics were used to compare results from the two assays.
Results: Of the 70 patients evaluated, 18 were excluded: 3 for low RNA signal in the Prosigna assay, 4 were ER(−) by RT-PCR, 6 were node-positive and 5 were pre-menopausal. Correlation between the two assays in the remaining 52 post-menopausal patients

with node-negative disease was poor (Spearman correlation 0.08, 95% CI −0.20, 0.35). Risk group assignment (low/intermediate/high) between Recurrence Score and ROR was in agreement in 54% (28/52) with 4 of 7 high ROR scores having low Recurrence Score results. Prosigna classified 38 luminal A, 12 luminal B, 2 HER2 enriched and 0 basal. In both the luminal A and B groups there was a wide range of Recurrence Score results. Correlation in the overall population (including node positive and pre-menopausal women) was also poor (Spearman correlation 0.19, 95% CI −0.07, 0.4 [n = 63]).

Conclusion: Consistent with prior comparisons between the Oncotype DX and other genomic assays, there are substantial differences in the way patients are risk stratified and it cannot be assumed that the assay results are interchangeable. These results suggest that there is only a modest agreement between Recurrence Score results and ROR, with almost half of N(−), ER+ pts classified differently, including ~57% of high ROR pts being classified as low risk by the Recurrence Score with minimal if any benefit from chemotherapy expected.

Disclosure of Interest: 1. M. Alvarado: Advisory Board Member – BMS; Genentech; Genomic Health + Honoraria – Genentech; Genomic Health. 2. C. Prasad: no significant relationships. 3. C. Markopoulos: Honoraria – Genomic Health. 4. Other authors: Genomic Health employees.

P248

The 21-gene breast cancer assay: a roadmap of clinical evidence

T. Bayt[1] *, E. Burke[2], M. Rothney[1], A.P. Sing[1]. [1]*Medical Affairs, Genomic Health, Redwood City, United States of America,* [2]*Genomic Health, Redwood City, United States of America*

Goals: There are an increasing number of commercially available genomic assays available for clinical practice. Assays are developed and validated through a variety of approaches, resulting in varying levels of evidence supporting their ability to guide treatment decisions. By establishing consistent standards for clinical evidence, clinicians can evaluate these assays based on the same criteria.

Methods: Peer-reviewed articles, presentations, and oncology guidelines were reviewed to identify studies that generated clinical evidence on the validation and utility of the 21-gene invasive breast cancer assay.

Results: The 21-gene assay was analytically validated for accuracy, precision, and reproducibility using 447 samples from three independent studies. Robust clinical validation was established in two prospectively-designed studies of 1319 patient samples which demonstrated prognosis (n = 668) and prediction of chemotherapy benefit (n = 651). These findings were consistent in four confirmation and eight supportive studies. Additional studies have shown an association of the assay result with local- and late- (>5 yr) recurrence. Clinical utility has been established through international studies with standardized methodologies; use of the assay changes treatment recommendations in ~30% of patients and results in a decrease in chemotherapy use. Worldwide market analyses demonstrate that the assay is cost-effective or -saving.

Conclusion: Rigorous analytical and clinical validation of the 21-gene assay resulted in subsequent studies that confirmed the robust performance in the node-negative and -positive setting with respect to both prognosis and prediction of chemotherapy benefit. Clinical utility studies have consistently shown that the assay provides actionable information to individualize treatment based on tumor biology. Assay development and consistency of findings has led to the inclusion by payers and international guideline committees as standard of care for patients with ER+, HER2−, early stage, invasive breast cancer and has led to the incorporation into the NCCN®, ASCO®, St. Gallen, and ESMO® guidelines and to recommendation by NICE. With the rapid increase of genomic assays now being used for clinical management of disease, there is a burden of proof to demonstrate rigorous development, analytical validation, clinical validation, and clinical utility of genomic assays.

Disclosure of Interest: All authors are employees of Genomic Health, Inc. and own stock in the company.

P249

The prognostic role of ^{18}F-fluorodeoxyglucose PET/CT in operable invasive breast carcinoma

S.O. Hwang[1] *, J.K. Kang[1], J.O. Baek[1], J. Lee[1], W.W. Kim[1], S.W. Lee[2], J.H. Jung[1], H.Y. Park[1]. [1]*Surgery, Kyungpook National University, School of Medicine, Daegu, Korea,* [2]*Nuclear Medicine, Kyungpook National University, School of Medicine, Daegu, Korea*

Goals: We evaluated whether ^{18}F-fluorodeoxyglucose (FDG) uptake on tumor or axillary lymph node (ALN) in preoperative PET/CT could be prognostic factor in patients who had curative surgery for invasive breast carcinoma.

Methods: Retrospectively, we reviewed 455 consecutive patients with breast carcinoma had operation in our institute between 2008 and 2009, and 244 patients who conducted preoperative ^{18}F-FDG PET/CT and curative surgery were enrolled. We searched age, sex, menopausal state, ^{18}F-FDG uptake on primary tumor and ALN, tumor size, lymph node metastasis, stage, hormone receptor expression, c-erb2 expression, p53 expression, histological grade, and lymphovascular invasion. We also investigated the recurrence and survival after surgery. Finally, 5-year-disease-free survival rate (DFSR) were calculated by Kaplan–Meier survival analysis, and the factors related with recurrence and survival were investigated by Cox proportional hazard model.

Results: Mean follow-up time was 62.7±13.0 months (range, 7.9–82.8). Twenty-two (9.0%) patients recurred, and seven (2.9%) patients died from breast cancer. 5-year-DFSR was about 93.2%, and 5-year-overall-survival rate was about 97.5%. The recurrence was mostly regional (4.5%) or distant (4.1%) metastasis. In 124 (84.8%) patients, there was ^{18}F-FDG uptake in tumor. Fifty-four patients (22.1%) had ^{18}F-FDG uptake in axillary lymph node. In receiver operating characteristics curve about ^{18}F-FDG uptake on tumor and recurrence, the cut-off value of the maximum standardized uptake (SUVmax) value of tumor for recurrence was 3.0. There was significant difference in recurrence according to ^{18}F-FDG uptake on tumor (p = 0.009). ^{18}F-FDG uptake on ALN also showed significant relation with DFSR (p = 0.005). The ^{18}F-FDG uptakes on tumor (p = 0.034, OR 4.150, 95% CI 1.114–15.454) or ALN (p = 0.023, OR 3.133, 95% CI 1.170–8.388) were independent significant risk factors of DFSR.

Conclusion: Over 3.0 of SUVmax on tumor or ^{18}F-FDG uptake on ALN in preoperative PET/CT are risk factors of recurrence after the curative operation for invasive breast carcinoma.

Disclosure of Interest: No significant relationships.

P250

Clinicopathological analysis of the p53 expression status in breast cancer

M. Kikuyama[1] *, H. Kunimata[2], T. Oka[3], A. Tachibana[1]. [1]*Department of Breast Surgery, Kanto Central Hospital of the Mutual Aid Association of Public School Teachers, Tokyo, Japan,* [2]*Diagnostic Imaging Center, Kanto Central Hospital of the Mutual Aid Association of Public School Teachers, Tokyo, Japan,* [3]*Department of Pathology, Kanto Central Hospital of the Mutual Aid Association of Public School Teachers, Tokyo, Japan*

Goals: The p53 alteration is known to be a prognostic factor in breast cancer. Determining the p53 status by sequencing is more accurate compared with immunohistochemistry (IHC), because not all mutations result in p53 protein accumulation. However, IHC has a widespread clinical use due to a simple and affordable technique.

In this study, we aimed to confirm the association between the p53 status by IHC and clinicpathological characteristics.

Methods: We selected 281 patients with breast cancer who underwent surgery between January 2009 and December 2013. The p53 expression status was measured using IHC and the cutoff value was determined as 45% according to a receiver operator characteristic curve for predicting recurrences.

Results: The patients were divided into two groups: the "p53-high group" (p53 expression ≥45%) and the "p53-low group" (p53 expression <45%). Out of the 281 patients, 48 patients (20.6%) were in the p53-high group. The number of premenopausal patients was 6 (12.5%) in the p53-high group and 56 (23.9%) in the p53-low group (p = 0.002). The nuclear grade in the p53-high group was higher than that of the p53-low group (p = 0.0016). The estrogen receptor was positive in 30 patients (62.5%) of the p53-high group and in 194 patients (82.9%) of the p53-low group (p = 0.0017). The progesteron receptor was positive in 19 patients (39.6%) of the p53-high group and in 162 patients (69.2%) of the p53-low group (p = 0.0002). The human epidermal growth factor receptor type 2 was positive in 11 patients (22.9%) of the p53-high group and in 24 patients (10.3%) of the p53-low group (p = 0.047). The ki 67 was ≥14% in 32 patients (66.6%) of the p53-high group and in 98 patients (42.0%) of the p53-low group (p = 0.0061). The hormone therapy after surgery was given to 28 patients (58.3%) of the p53-high group and to 185 patients (79.4%) of the p53-low group (p = 0.0069). The poor disease-free survival (p = 0.0013) and overall survival (p = 0.0088) for the p53-high group was significant.

Conclusion: In this study, p53 expression ≥45% in breast cancer was associated with poor prognoses. Determination of an optimal cutoff value of the p53 status and further investigations are needed to apply this to clinical practice.

Disclosure of Interest: No significant relationships.

P251

The correlation between ^{18}F-fluorodeoxyglucose uptake and 21-gene recurrence score in breast cancer

M.H. Lee*, Eun Sung Lee, S.K. Kim, J.Y. You, E.J. Song, S. Jung, S.Y. Lee, H.S. Kang, Eun Sook Lee. *Center for Breast Cancer, National Cancer Center, Goyang, Korea*

Goals: The 21-gene recurrence score (RS) assay has been reported to accurately predict the risk of disease recurrence and has been clinically validated in breast cancer. Tumors with increased ^{18}F-fluorodeoxyglucose (FDG) uptake can be considered to show more aggressive behavior than tumors with decreased uptake. We analyzed association of RS with clinicopathologic parameters and ^{18}F-FDG uptake of primary tumor in hormone receptor (HR)-positive breast cancer patients with node-negative or N1 status.

Methods: The 21-gene assay was performed on 230 patients with HR-positive early breast cancer. Maximum standardized uptake values (SUVmax) were calculated by measuring the absorption of ^{18}F-FDG by tumors in the region of interest.

Results: Among the 230 patients, 132 (62.3%) had a low RS of <18, 60 (28.3%) had an intermediate RS of 18–30, and 20 (9.4%) had a high RS of ≥31. Lymph node metastasis were absent in 100 cases and present in 130 cases. Of node-positive cases, 72 (55.4%) had a low RS, 46 (35.4%) had an intermediate RS, and 12 (9.2%) had a high RS. The results of SUVmax were available in 174 patients and median SUVmax was 4.22 (range, 1.00–20.80). Histologic grade (p < 0.001), Ki-67 (p = 0.001), and SUVmax (p < 0.001) were statistically associated with the RS results. Median SUVmax was 2.91 in low RS group, 2.90 in intermediate RS group and 9.00 in high RS group. High RS was associated with high SUVmax, compared with low and intermediate RS (p < 0.001 and <0.001, respectively).

Conclusion: The 21-gene RS is associated with histologic grade, Ki-67 and SUVmax in HR-positive early breast cancer patients. The patients with high histologic grade, high Ki-67 and high SUVmax may have worse outcome, and if 21-gene RS assay is not available, adjuvant chemotherapy must be considered for those.

Disclosure of Interest: No significant relationships.

Table (abstract P251)

	Recurrence Score risk group			P
	Low (n)	Intermediate (n)	High (n)	
Tumor size				
<1 cm	11 (61.1%)	5 (27.8%)	2 (11.1%)	0.342
≥1, <2 cm	66 (57.4%)	44 (38.3%)	5 (4.3%)	
≥2 cm	55 (56.7%)	31 (32%)	11 (11.3%)	
Histologic type				
Ductal	102 (55.1%)	68 (36.8%)	15 (8.1%)	0.470
Lobular	8 (61.5%)	5 (38.5%)	0	
Other	22 (68.8%)	7 (21.9%)	3 (9.4%)	
Histologic grade				
1	40 (81.6%)	8 (16.3%)	1 (2%)	<0.001
2	87 (57.6%)	59 (39.1%)	5 (3.3%)	
3	4 (14.3%)	12 (42.9%)	12 (42.9%)	
Nodal status				
N0	60 (60%)	34 (34%)	6 (6%)	0.166
N1mi	17 (41.5%)	18 (43.9%)	6 (14.6%)	
N1	55 (61.8%)	28 (31.5%)	6 (6.7%)	
Lymphatic invasion				
No	61 (58.7%)	35 (33.7%)	8 (7.7%)	0.978
Yes	71 (56.8%)	44 (35.2%)	10 (8%)	
Ki-67				
<14	62 (72.1%)	22 (25.6%)	2 (2.3%)	0.001
≥14	69 (48.6%)	57 (40.1%)	16 (11.3%)	
SUVmax, median (range)	2.91 (1.10–16.60)	2.90 (1.00–11.70)	9.00 (1.70–20.80)	<0.001

P252

Predicting risk after breast-conserving surgery alone for DCIS patients

E. Rakovitch[1] *, S. Nofech-Mozes[1], W. Hanna[1], F.L. Baehner[2], R. Saskin[3], L. Paszat[1]. *[1]Radiation Oncolcogy, Sunnybrook Health Sciences Centre, Toronto, Canada, [2]Pathology, Genomic Health, Inc., Redwood City, United States of America, [3]Institute for Clinical Evaluative Sciences, Toronto, Canada*

Goals: Most women with DCIS will be treated by breast-conserving surgery (BCS) often followed by radiation. However, BCS alone is an option for individuals with low risk of local recurrence (LR). Validated biomarkers are needed to improve risk assessment and treatment of DCIS. The Oncotype DX® DCIS Score (DS) was shown to predict the risk of LR in selected individuals treated by BCS alone in the ECOG E5194 clinical trial. Our objective was to confirm these results in a larger population-based cohort of individuals with DCIS treated by BCS alone.

Methods: We used an established population-based cohort of individuals diagnosed with DCIS from 1994–2003 treated with BCS alone. Treatment and outcomes were validated. Expert breast pathologists centrally reviewed H&E slides. Cases with invasive cancer or positive margins were excluded. The DCIS Score was obtained by quantitative RT-PCR. The DS was evaluated as a continuous score (0–100) and by pre-specified risk groups (low risk DS <39, intermediate risk DS 39–54; high risk DS >55). Cox model was used to determine the relationship between independent covariates, the DS (hazard ratio (HR)/50 units) and LR. Kaplan–Meier method (log rank test) was used to compare differences in 10 year risk of LR by risk group. The primary objective was to determine the relationship between the risk of LR and the DS in patients treated with BCS alone (with ER+ tumors or regardless of ER status) and negative margins (no ink on tumor).

Results: The population cohort includes 1658 cases of pure DCIS treated by BCS alone. Tumor blocks were collected for 828 patients. Final evaluable population includes 571 cases with negative margins. Median follow-up was 9.6 years. 100 cases developed LR (DCIS, N = 44; invasive, N = 57). The 10 year risk of LR was 19.2%. In the primary pre-specified analysis, the DS was associated with LR (DCIS or invasive) in ER+ patients (HR 2.26; P < 0.001) and in all patients regardless of ER status (HR 2.15; P < 0.001). DCIS Score was associated with LR after adjusting for age, tumor size, multifocality and subtype (adjusted HR 1.68; P = 0.02). The DS was associated with invasive LR (unadjusted HR 1.78; P = 0.04) and DCIS LR (unadjusted HR 2.43; P = 0.005).

DCIS score risk group	N	10 Year KM risk of local recurrence (95% CI)
Low (<39)	355	12.7% (9.5%, 16.9%)
Intermediate (39–54)	95	33.0% (23.6%, 44.8%)
High (≥55)	121	27.8% (20.0%, 37.8%)
Log rank P-value	571	<0.001

Conclusion: The DCIS Score predicts and quantifies individualized recurrence risk in a population of patients with DCIS treated by BCS alone and can help guide treatment recommendations for women diagnosed with DCIS.

Disclosure of Interest: I am the Principal Investigator for this study and my insitution received funding from Genomic Health, Inc.

P253

Economic impact of 21-gene recurrence score testing on early stage breast cancer in Ireland

L. Smyth[1] *, G. Watson[1], C.M. Kelly[2], M. Keane[2], M.J. Kennedy[2], Seamus O'Reilly[2], M. O'Connor[2], K. Verleger[3], Susan O'Reilly[4], J.M. Walshe[1]. *[1]Medical Oncology Dept, St Vincent's University Hospital, Dublin, Ireland, [2]All-Ireland Co-operative Oncology Research Group, Dublin, Ireland, [3]Heor, Pharmerit GmbH, Berlin, Germany, [4]National Cancer Control Programme, Dublin, Ireland*

Goals: International guidelines recommend chemotherapy (CT) for most patients (pts) with hormone receptor positive (HR+) breast cancer (BC). The **21-gene breast cancer test** is a validated multi-gene diagnostic test that predicts the likelihood of adjuvant chemotherapy benefit in a subset of breast cancer patients. Ireland was the first public health care system to reimburse this test in Europe. Objectives of this study were to analyse both the clinical and economic impact of the 21-gene breast cancer testing on adjuvant treatment decisions since reimbursement, using real-world data. Correlative factors for a low, intermediate and high Recurrence Score (RS) with the 21-gene breast cancer test, were also investigated.

Methods: Between October 2011 and February 2013, a national, retrospective, cross-sectional observational study of HR+ BC pts who were tested with the 21-gene breast cancer test, was conducted in Ireland. A survey of lead breast medical oncologists in Ireland, provided the assumption for the decision impact analysis that grade (G) 1 pts would not have received CT before testing (i.e. negative pre-test CT decision) and G2/3 pts would have received CT before testing (i.e. positive pre-test CT decision). Descriptive statistical analyses were performed. No adjustment was made for multiple testing.

Results: 633 pts were identified including 41 with N1 disease tested as part of the ongoing RxPONDER trial. Mean age was 56 years. Mean tumour size was 1.96 cm. 342 pts (54%) had a low RS, 222 (35.1%) an intermediate RS, 61 (9.6%) a high RS and 8 (1.3%) unknown RS's. Mean age was comparable in all groups. 409 (64.6%) pts had G2 tumours, 135 (21.3%) had G3 tumours and 86 (13.6%) had G1 tumours and 3 (0.5%) had unknown G. Post RS, 361 pts (57%) experienced a change in CT decision, 351 were changed to hormone therapy alone and 10 were advised to receive CT. In total, 196 (30.9%) pts received CT and 3 declined it. Of those pts treated with CT, 27 (13.7%) had low RS, 113 (57.7%) had intermediate RS and 57 (29%) had high RS. The most commonly prescribed regimen was docetaxel and cyclophosphamide (TC), administered in 121 pts (61.7%). The 21-gene RS assay achieved a 55% net reduction in the use of CT. IDC morphology and G3 tumours were associated with a higher probability of a high RS. Analysis restricted to node-negative patients resulted in similar results. Deducting the cost of the assay, reimbursement of the 21-gene test led to net chemotherapy cost savings of € 388,000 from the perspective of the national public payer.

Conclusion: Ireland was the first European public healthcare system to approve reimbursement for the 21-gene breast cancer testing. In the first 18 months following its reimbursement, this test led to a 55% net reduction in CT use and net savings of just under € 400,000.

Disclosure of Interest: No significant relationships.

P254

Circulating tumor cells before neoadjuvant chemotherapy in operable breast cancer

J. Horiguchi *, D. Takata, R. Nagaoka, A. Sato, H. Tokiniwa, T. Higuchi, S. Uchida, M. Tsuboi, M. Kikuchi, I. Takeyoshi. *Breast and Endocrine Surgery, Gunma University Hospital, Maebashi, Japan*

Goals: To evaluate the presence of circulating tumor cells (CTCs) before neoadjuvant chemotherapy (NAC) in operable breast cancer

and to study whether CTC detection has a prognostic impact in these patients.
Methods: In 112 consecutive patients with Stage II/III breast cancer who received NAC between April 2008 and November 2012, CTCs were evaluated with CellSearch (Veridex Corp, Warren, NJ) before NAC. NAC consisted of anthracycline and paclitaxel chemotherapy and additional trastuzumab treatment for patients with HER2-positive tumors. Pathological complete response (pCR) was defined as no invasive cancer in the breast.
Results: Median age of the patients was 52 years (range 30–78). 61 patients had Stage II disease and 51 had Stage III disease. One or more CTCs were detected in 20 (18%) of 112 patients. 19 (95%) of 20 CTC-positive patients were negative for CTCs after NAC. A pCR was achieved in 34 (30%) of 112 patients. CTC-positive patients were seen more frequently ($p = 0.02$) in those with Stage III disease than those with Stage II disease. There was no association between CTC detection and pCR. Distant metastasis-free survival was better in patients with small tumor, early stage disease, negative CTC and pCR. In non-pCR patients, CTC-negative patients showed a better DMFS than CTC-positive patients.
Conclusion: CTC before NAC in patients with operable breast cancer is a possible prognostic factor.
Disclosure of Interest: No significant relationships.

P255
Bcl-2 in blood of breast cancer patients: correlation with prognosis and other prognostic factors

A. Kulić[1], N. Dedić Plavetić[2], M. Sirotković-Skerlev[3], D. Vrbanec[2]*. [1]*Clinical Hospital Center, Zagreb, Croatia,* [2]*Department of Medical Oncology, University Hospital Center Zagreb, Zagreb, Croatia,* [3]*University of Zagreb, School of Medicine, Zagreb, Croatia*

Goals: Avoidance of apoptosis is one of the cancer hallmarks. Increased expression of anti-apoptotic proteins, such as Bcl-2, leads to accumulation of tumor cells regardless of their proliferative potential. Increased expression of Bcl-2 protein has been shown in many tumors, including breast cancer. The aim of this study was to investigate the presence of Bcl-2 in blood from breast cancer patients and healthy controls and to correlate the results with various clinicopathologic parameters: patient's age, size and histological grade of the tumor, status of axillary lymph nodes, expression of estrogen and progesterone receptors and Cathepsin D levels in tumor tissue. Prognostic value of blood Bcl-2 was also evaluated.
Methods: Eighty-two patients with invasive breast cancer and twenty individuals without malignancy were included in the study. Blood Bcl-2 levels were measured by enzyme-linked immunoadsorbent assay (ELISA).
Results: Sixty-one (74%) of 82 patients with breast carcinoma had Bcl-2 blood values higher than 124 U/ml. One healthy control had increased value of blood Bcl-2, while all others had values lower than 124 U/ml (cut-off value 124 U/ml was defined according to receiver operator characteristic (ROC) analysis). Circulating levels of Bcl-2 in breast cancer patients were significantly higher that those in healthy controls. We found statistically significant correlation between Bcl-2 levels and the tumor size, status of axillary lymph nodes and the histological grade of tumors. A negative correlation was observed between Bcl-2 blood levels and the patient's age. There was no correlation between Blc-2 values and estrogen and progesterone status, or the value of the cathepsin D in the tumor tissue. Kaplan–Meier analysis showed that breast cancer patients with high Bcl-2 blood levels (>200 U/ml) had poorer prognosis (5-year survival) than those with lower Bcl-2 concentrations.
Conclusion: Our results suggest relationship between higher blood Bcl-2 values of and shorter five-year survival of breast cancer patients as well as correlation with some negative clinicopathologic parameters.
Disclosure of Interest: No significant relationships.

P256
Ki67 level as prognostic parameter in triple-negative breast cancer: single center experience

W. Wang*. *Comprehensive Breast Health Center, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China*

Goals: Recent studies indicate that Ki67 expression level may be a prognostic maker in hormone-receptor positive breast cancer, while the prognostic value of the Ki67 level is yet unclear in triple-negative breast cancer (TNBC). The aim of this study was to investigate the influence of Ki67 expression level and other pathological features on the prognosis of TNBC.
Methods: The demographic, clinical and histopathological features of 336 TNBC patients that were treated between the years 2004–2012 in our center were reviewed retrospectively. Receiver-operating characteristic (ROC) curve analysis evaluating the predictive value of the Ki67 score for relapse was conducted to select the cutoff value of Ki67. The Kaplan–Meier curves and Log-rank test were used to assess influence of different factors on disease-free-survival (DFS), relapse-free-survival (RFS) and overall survival (OS). A multivariate Cox proportional hazards regression model was performed to analyze the independent prognostic factors.
Results: The median Ki67 expression level was 40%, and the Ki67 expression level was significantly associated with tumor grade ($P < 0.001$), while its correlations with tumor size, lymph node status or tumor stage were not ($P > 0.05$). According to ROC curve analysis, 37.5% was selected as the cutoff value of Ki67 index. 147 patients were classified as Ki67 low expression and 187 patients as high expression accordingly, and the clinicopathologic features of patients in two groups were well balanced. Median follow-up time was 34 months (5.2–120.0 months). In univariate analysis, high Ki67 expression as well as larger tumor size and lymph node positivity was associated with shorter DFS, RFS and OS. In multivatiate analysis, Ki67 is an independent prognostic factor for DFS (Risk Ratio, RR: 2.170, 95% confidence interval, 95% CI: 1.220–3.860, $P = 0.008$) RFS (RR: 2.323, 95% CI: 1.227–4.397, $P = 0.010$) and OS (RR: 4.396, 95% CI: 1.742–11.095, $P = 0.002$). Subgroup analysis showed that the prognostic value of Ki-67 is significant in lymph node negative TNBC patients.
Conclusion: The level of Ki67 expression is an independent prognostic factor predicting DFS, RFS and OS in TNBC patients, especially in node-negative TNBC patients. TNBC is probably a heterogeneous disease with different characteristics and prognosis, and may be further subdivided according to the Ki67 expression levels.
Disclosure of Interest: No significant relationships.

P257
Clinical features and survival of women diagnosed with invasive lobular carcinoma in Thailand

S. Samphao[1]*, W. Tangjatuporn[1], S. Mahattanobol[1], P. Tanaanantarak[2]. [1]*Department of Surgery, Faculty of Medicine, Songkhla, Thailand,* [2]*Department of Radiology, Faculty of Medicine, Songkhla, Thailand*

Goals: Recent increases in breast cancer affect women around the world, including Thailand. A little is known about invasive lobular carcinoma (ILC) due to a small incidence of disease. Difficulty in detection, bilateral and multifocal/multicentric disease in nature may affect survival outcomes. We examined clinical, pathological and survival data in this population, compared with women diagnosed with invasive ductal carcinoma (IDC).

Methods: Records review identified 1,240 women diagnosed with breast cancer from 1998–2007. Women diagnosed with ILC (n = 43) and IDC (n = 1,197) were compared in means of tumor detection, operative procedures, tumor characteristics, systemic treatment and survival.
Results: Overall, median age at diagnosis was 48 (23–87). Most of the patients presented with palpable mass. Only half the patients underwent mammography at the time of diagnosis. The ILC group had higher rates of BIRADS 4, compared with the IDC group (34.8% vs. 26.5%). Mastectomy rate was higher in the ILC group (90.7% vs. 81.7%). Median tumor size was 2.8 cm in both groups with almost half of them had axillary lymph node involvement. No differences in pathological staging, tumor grade and lymphovascular invasion between the two groups. Positive estrogen (65.1% vs. 49.1%) and/or progesterone receptors (62.8% vs. 41.2%, p = 0.01) were higher in the ILC group. There were no differences in adjuvant chemotherapy (86.0% vs. 79.3%), hormonal therapy (67.4% vs. 63.5%) and radiotherapy (48.8% vs. 42.1%) between the two groups. At a median follow-up of 85 months, there were no differences in 5-year disease-free survival (60.5% vs. 65.7%), distant disease-free survival (62.8% vs. 69.2%) and overall survival (72.1% vs. 73.5%) between the two groups. Pathological staging (stage 3; HR 1.83, 95% CI 1.11–3.02, p = 0.02) and nodal involvement (HR 1.98, 95% CI 1.45–2.70, p < 0.001) were predictive factors for disease recurrence and death.
Conclusion: Although difficult in tumor detection, women with ILC have comparable clinical and tumor characteristics with IDC, resulting in equivalent survival outcomes. Pathological staging and nodal status are predictive factors for survival.
Disclosure of Interest: No significant relationships.

P258
Prognostic value of tumor biology and adjuvant systemic therapy in breast cancer stage I

I.V. Kolyadina[1]*, I.V. Poddubnaya[2], G.A. Frank[2], A.I. Karseladze[3], D.V. Komov[3]. *[1]Surgical Oncology, Russian Medical Academy of Postgraduate Education, Russian Cancer Research Center, Moscow, Russian Federation, [2]Oncology Chair, Russan Medical Academy of Postgraduate Education, Moscow, Russian Federation, [3]Pathology, Russian Cancer Research Center, Moscow, Russian Federation*

Goals: to study the prognostic value of clinical and morphological factors for the risk of recurrences in breast cancer stage I.
Methods: In study included 1341 women with breast cancer stage I (T1a-b-cN0M0), treated in the RCRC and RMAPE 1985–2012. We analyzed the clinical factors (age, local and adjuvant systemic treatment) and morphological factors (status of estrogen and progesterone receptors, HER2 and KI67, biological subtype, presence of lymph vascular invasion and intraductal component and the tumor size T1a-b-c). We assessed the risk of recurrence (median follow up – 96 months), the rate of relapse and disease-free survival in different subgroups using univariate and multivariate COX-regression analysis.
Results: In univariate COX-regression analysis we found the prognostic value for the risk of recurrences of such morphological factors: grade of tumor (p = 0.034), histological type (p = 0.025), tumor size T1a-b-c (p = 0.004), presence of lymph vascular invasion (p = 0.03) and biological subtype of breast cancer (p = 0.002). The most favorable is the luminal A subtype with minimal rate of distant relapses (1.6%), the maximum time to progression (median 48 months) and the best rate of the 5- and 10-year disease-free survival (97.2% and 93.8%, respectively). The most important clinical factors were age (p = 0.001), the volume of surgery (p = 0.032), and adjuvant systemic therapy (chemotherapy, endocrine therapy or both therapies) in accordance with the biological subtype, p < 0.0001. In multivariate regression analysis, only two factors were significant for predicting the risk of recurrence of breast cancer stage I: biological subtype and adjuvant systemic therapy. Compared with luminal A subtype the risk of relapse is significant higher in luminal B subtypes (HER2-negative: HR 1.393; HER2-positive: HR 1.321), in triple negative subtype – HR 2.297 and, especially, in hormone negative HER2-positive subtype – HR 6.001, p = 0.04. Adjuvant systemic therapy reduce the risk of recurrence until 74% in breast cancer stage I (HR = 0.276, p < 0.0001).
Conclusion: The tumor biology and adjuvant systemic therapy determines prognosis in breast cancer stage I.
Disclosure of Interest: No significant relationships.

P259
Outcome of elderly women with breast cancer

N. Kobayashi*, K. Ushimado, M. Hikichi, T. Utsumi. *Breast Surgery, Fujita Health University, Toyoake Aichi, Japan*

Goals: Women in Japan have the longest life expectancy in the world at 86.6 years old. We retrospectively reviewed the clinical and pathologic data including intrinsic subtypes and outcome of the breast cancer patients diagnosed at age 70 and older.
Methods: From January 2000 to June 2014, 313 patients with breast cancer (≥70 years) who were treated at our hospital were included. The median age of the patients was 76 years, with a range of 70 to 92 years old. Ki-67 labeling index (LI) was categorized as low (<20%) and high (≥20%) in invasive cancer breast (IBC). Tumors were classified as luminal A (ER+ and PR+, and HER2− and Ki67 low), luminal B (ER+ and/or PR+, and HER2+ or Ki67 high), HER2 disease (ER−, PR−, HER2+), or triple negative (TN) (ER−, PR−, HER2−). Disease-free survival (DFS) and overall survival (OS) curves were generated using the method of Kaplan and Meier. Survival comparisons were made with the log-rank test. The level of significance was taken to be 0.05. SPSS 18.0 software package was used for statistical analysis.
Results: The median tumor size was 2.1 cm. The 313 cases of breast cancer had the following distribution by stage: stage 0, 16 (5.1%); stage I, 126 (40.3%); stage IIA, 95 (30.3%); stage IIB, 39 (12.5%); stage IIIA, 6 (1.9%); stage IIIB, 21 (6.7%); stage IIIC, 3 (1.0%); stage IV, 7 (2.2%). The Number of patients with IBC (n = 293) in each subtype was as follows; luminal A 144 patients (49.2%), luminal B 77 patients (26.3%), HER2 disease 19 patients (6.5%), and triple negative 53 patients (18.0%). Of the 293 patients, 280 patients (95.5%) underwent surgery. The 90-days mortality was 0%. Patients with node negative (n = 207; 70.6%) had better prognosis than those with node positive (n = 86; 29.4%) [5-year DFS: 92.4% (node negative) vs. 76.7% (node positive), p = 0.002, 5-year OS: 89.2% vs. 77.4%, p = 0.002]. Eighty-seven percent of the patients with IBC were treated with anti-cancer drug [chemotherapy (n = 45), endocrine therapy (n = 217) and anti-HER2 therapy (n = 15)]. The patients who were treated with anti-cancer drug had better prognosis than those who did not [5-year OS: 87.3% vs. 73.8, p = 0.002]. TN was a significant predictor of worse OS [5-year OS: luminal A: 90.5%, luminal B: 86.9%, HER2 disease: 100%, and TN: 77.8%, p = 0.002]. High Ki-67 LI was also a significant predictor of worse outcome. ER status and PgR status were not associated with clinical outcome.
Conclusion: Nodal status, Ki-67, and TN were prognostic factors in elderly women with breast cancer.
Disclosure of Interest: No significant relationships.

P260

Evaluation of PgR expression as a prognostic factor in luminal HER2-negative breast cancer

R. Tashima[1]*, R. Nishimura[2], N. Arima[3], M. Hujisue[2], M. Nakano[2], Y. Okumura[2], T. Osako[2], Y. Toyozumi[3]. *[1]Surgery, Kumamoto City Hospital, Kumamoto, Japan, [2]Breast and Endocrine Surgery, Kumamoto City Hospital, Kumamoto, Japan, [3]Pathlogy, Kumamoto City Hospital, Kumamoto, Japan*

Goals: According to the St. Gallen breast cancer international conference, the distinction between the luminal A and luminal B (HER2−) tumors is recommended using the Ki-67 index value (2011) and progesterone receptor (PgR) expression (2013). Although a low PgR expression correlates with poorer prognosis, it is still unclear how PgR expression correlates with the prognosis according to menopausal status. The aim of this study was to investigate PgR expression as a prognostic factor in relation to menopausal status and to determine the optimal cut-off point for PgR expression in luminal/HER-negative breast cancer patients.

Methods: In this retrospective study, the characteristics and prognosis of 863 luminal HER2-negative premenopausal and 1,498 postmenopausal breast cancer patients from January 2002 to September 2014 were analyzed (excluding patients with stage IV and neoadjuvant chemotherapy). The factors investigated included tumor size, nuclear grade (NG), and lymph node metastasis, and ER/PgR status, Ki-67 index value, HER2 and p53 overexpression were evaluated using immunohistochemistry (IHC). The relationship between PgR status (using optimal cut-off point) and the clinicopathological characteristics were then investigated. The expression rates for ER/PgR were evaluated as percentages of positively stained cells and a value of ≥1% was considered positive. Cox's proportional hazard model was used to perform univariate and multivariate analyses of the factors related to disease-free (DFS) and overall survival (OS) using several PgR expression cut-off points (every 10% from 0% to 80%). The hazard ratios (HR) and the p values were compared to determine the optimal cut-off point for the PgR expression.

Results: The median PgR expression rate was 85% (mean±SD 70±33%) in premenopausal patients and 50% (48.4±36%) in postmenopausal patients. Patients with PgR ≥1% had significantly better DFS and OS than those with PgR<1% in premenopausal patients, whereas in postmenopausal patients PgR positivity was not a significant factor for OS. Multivariate analysis revealed that the PgR expression was a significant factor in premenopausal patients. Moreover, the cut-off points of 20% had lower p-values and higher HR for DFS and OS. These findings indicate that the optimal PgR cut-off point is 20% in premenopausal patients. In addition, a higher PgR expression (≥20%) significantly correlated with a higher Ki-67 index value, larger tumor size, higher NG and lymph node metastasis.

Conclusion: The PgR expression rate was a useful prognostic factor in premenopausal luminal/HER2-negative breast cancer patients, and the optimal PgR cut-off point was found to be 20%.

Disclosure of Interest: No significant relationships.

P261

Proposed criteria for luminal A breast cancer accurately predict Oncotype dx™ recurrence score

F.S. Heinemann*. *Pathology, Hoag Memorial Hospital, Newport Beach, United States of America*

Goals: Most patients with ER+/Her2− breast cancer do not benefit from currently available chemotherapy regimens and identification of the subset who will benefit is a major challenge. The Oncotype DX™ recurrence score assay is a mainstay of this therapeutic decision, but is costly. Maisonneuve et. al. recently proposed a classification of ER+/HER2− tumors based on quantitative analysis of PR and Ki67 (Breast Cancer Research 2014; 16(3): R65). The aim of this study was to see how accurately the Maisonneuve classification of ER+/HER2− breast cancer predicts the Oncotype DX™ recurrence score.

Methods: We compared the Oncotype DX™ scores of 317 tumors resected during 2011–2013 at a single institution with their Maisonneuve classification. We also analyzed the Oncotype DX™ scores of 6 subgroups of ER+/HER2− patients defined by the PR and Ki67 cut points specified in the 2014 Maisonneuve proposal.

Results: In this study of ER+HER2− patients who had been selected for Oncotype DX™ testing to guide chemotherapeutic decision making, 76% (242/317) were classified as luminal A and 24% (75/317) were classified as luminal B; 8.5% (27/317) of patients had an Oncotype DX™ score ≥31 and 16.4% (52/317) had an Oncotype DX™ score ≥25. No tumor classified as luminal A had a high risk Oncotype DX™ recurrence score (RS). In contrast, 36% (27/75) of patients classified as luminal B had a high risk RS. Thus, 75 of the 317 patients in this study (24%) would have been classified as a candidate for chemotherapy either by the Maisonneuve criteria for luminal B cancer, or by an Oncotype DX™ recurrence score of ≥31. Only 27 patients (8.5%) would have been classified as a candidate for chemotherapy by both methods. This lack of concordance is entirely due to cases classified as luminal B by the proposed Maisonneuve criteria who have an RS <31. In a subset analysis, 66% (19/29) of tumors we defined as type B3 ($PR^{low}Ki67^{high}$) had a high risk RS. Patients we classified as type B1 ($PR^{low}Ki67^{int.}$) and B2 ($PR^{high}Ki67^{high}$) had a high risk RS in 28% (2/7) and 15% (6/39) of cases, respectively. We also analyzed our data in relation to an RS score of ≥25. Using the lower cut point, 42% (3/7) of type B1 tumors, 28% (11/39) of type B2 tumors, and 86% (25/29) of type B3 tumors had Oncotype DX™ recurrence score ≥25. In addition, 5% (13/242) of tumors classified as Luminal A had a RS ≥25.

Conclusion: The criteria proposed by Maisonneuve et al. for luminal A cancer are highly predictive of an Oncotype DX™ recurrence score <31. Since patients with an Oncotype DX™ score <31 do not benefit from Cytoxan/Methotrexate/5-Fluorouracil (CMF) chemotherapy, the same can be said of patients classified as luminal A by the criteria proposed by Maisonneuve et al. It remains to be seen whether any of these patients benefit from 2nd or 3rd generation chemotherapy regimens.

Disclosure of Interest: No significant relationships.

P262

Are biomarkers predictive of anthracyclines-induced cardiac dysfunction?

A. Malik[1]*, P. Jeyaraj[2], R. Calton[3], B. Uppal[4]. *[1]Radiotherapy, All India Institute of Medical Sciences, New Delhi, India, [2]Radiotherapy, Christian Medical College And Hospital Ludhiana, Ludhiana, India, [3]Cardiology, Christian Medical College And Hospital Ludhiana, Ludhiana, India, [4]Biochemistry, Christian Medical College And Hospital Ludhiana, Ludhiana, India*

Goals: To assess the usefulness of cardiac troponin T (cTnT) and NT-ProBNP estimation in early prediction of anthracycline induced cardiotoxicity.

Methods: In a prospective study, patients with pathological diagnosis of carcinoma breast who had been scheduled to receive anthracycline containing combination chemotherapy were enrolled in department of Radiotherapy, Christian medical college and hospital, Ludhiana. Baseline cardiac evaluation was done by echocardiography (ECHO), electrocardiography (ECG) and biomarkers like cardiac troponin T (cTnT) and N Terminal-Pro Brain natriuretic peptide (NT-ProBNP) estimation. All patients underwent ECG, cTnT and NT-ProBNP estimation within 24 hours of each cycle of chemotherapy. All patients followed up after 6 months of initiation of chemotherapy and any changes in follow up ECG and ECHO were

compared to ECG and ECHO at baseline and ECG, cTnT and NT-ProBNP levels after each cycle of anthracycline based chemotherapy.
Results: Out of 33 evaluable patients, mean change in left ventricular diastolic diameter (LVDD) within 6 months was 0.154±0.433 cms (p value = 0.049). Seven out of 33 patients had an increase in biomarker cTnT levels (p value =0.5). A significant change in baseline and followup LVDD was observed in patients with raised cTnT levels (p value = 0.026) wheresa no change was seen in ejection fraction (EF) and left atrial diameters (LAD) within 6 months of chemotherapy. NT-ProBNP levels increased in significant number of patients (p value = <0.0001) but no statistically significant change was observed in the ECHO parameters within 6 months.
Conclusion: Functional monitoring is a poorly effective method in early prediction of anthracycline induced cardiac dysfunction. Estimation of biomarkers after chemotherapy may allow stratification of patients in various risk groups, thereby opening window for interventional strategies in order to prevent permanent damage to the myocardium.
Disclosure of Interest: No significant relationships.

P263
Prognostic factors of locally advanced breast cancer patients in Morocco

L. Amaadour[1]*, N. Benaicha[2], C. Nejjari[2], H. Fatemi[3], S. Arifi[1], N. Mellas[1]. *[1]Medical Oncology, Hassan II University Hospital, Fez, Morocco, [2]Laboratory of Epidemiology, Faculty of Medicine, Fez, Morocco, [3]Pathology, Hassan II University Hospital, Fez, Morocco*

Goals: Neoadjuvant chemotherapy is known to be beneficial for down-staging patients with locally advanced breast cancer. Clinical stage, degree of cell differentiation and expression of estrogen/progesterone receptors and HER2-neu are all prognostic factors that may effect survival of patients with locally advanced breast cancer (LABC). The present study was conducted to determine clinical and histologic factors that influence survival in a series of moroccan patients with LABC.
Methods: We reviewed respectively a total of 102 patients with locally advanced breast cancer in Hassan II University hospital of Fez Morocco, from January 2009 to December 2013. Treatment consisted of neoadjuvant sequential chemotherapy followed by mastectomy, radiotherapy and hormonotherapy for ER/PR positive tumors. Survival analysis with Kaplan Meier was tested for age, body mass index (BMI), clinical stage, degree of histological differentiation, molecular subtypes (Luminal A, luminal B, HER2 amplified and basal-like). To find the most important influencing factors, significant variables were tested with multivariate Cox regression.
Results: Mean age of patients with locally advanced breast cancer was 48.6 years [range30–74 years], most were between 40–60 years old (45.8%), 23.4% (21/102) were stage IIIA and 69.8% (71/102) of tumors were of ductal histologic type. Luminal tumors were the most frequent molecular subtype: 58.4% (67/102). Her2 positivity was found in 19 patients (18.3%) and a moderate histological grade in 61 (50%). 48% (58/102) of patients had a high body mass index (≥30). Median follow up was 31.6 months [10–60]. Tumor characteristics that did influence survival were advanced stage ($p < 0.001$) and histological grade ($p < 0.001$), while molecular subtypes had no effect.
Conclusion: Clinical stage and degree of histological grade are the most significant prognostic factors for Moroccan locally advanced breast cancer cases, while age, BMI and molecular subtype did not appear impact on our patients' survival.
Disclosure of Interest: No significant relationships.

P264
Predicting late distant recurrence risk in ER+ breast cancer after five years of tamoxifen

E. Mamounas[1]*, N. Wolmark[1], F.L. Baehner[2], S.M. Butler[3], G. Tang[1], F. Jamshidian[3], A.P. Sing[3], S. Shak[3], S. Paik[1]. *[1]Breast Cancer Committee, NSABP Operations and Biostatistical Center, Pittsburgh, United States of America, [2]Pathology, Genomic Health, Inc., Redwood City, United States of America, [3]Genomic Health, Inc., Redwood City, United States of America*

Goals: Identification of molecular determinants predicting late recurrence (>5 yrs) in stage I and II breast cancer has become clinically important in light of data demonstrating a benefit for 10 yrs of tamoxifen administration. Since the 21-gene Recurrence Score (RS) is commonly utilized in early stage BC, we wished to determine its utility in predicting distant recurrences beyond 5 yrs as a function of quantitative ER expression.
Methods: The 21-gene RS was assessed in 1065 chemo and tam-treated, ER+, node-positive pts from NSABP B-28 and 668 tam-treated, ER+, node-negative pts from NSABP B-14. Cox PH models, KM estimates and log rank statistics were used to assess the association of the RS with risk of DR by quantitative ER expression, using the 21-gene assay, in pts event-free after 5 yrs. We established an ER cut-point (high vs low) in B-28, and tested the cut-point in B-14, formally evaluating the interaction of RS and ER.
Results: Median follow-up was 11.2 yrs (B-28) and 14.5 yrs (B-14). 832 B-28 pts and 564 B-14 pts were DR-free after 5 yrs. A reference normalized ER cut-point of 9.1 C_T was established in B-28 based on the association of the RS with DR after 5 yrs. Of the event-free pts at 5 yrs, 68% in B-28 and 88% in B-14 had ER >9.1. In B-28 the RS result was strongly associated with DR after 5 yrs in the higher ER expressing pts (log rank P = 0.001), but not in the lower ER expressing pts (log rank P = 0.87). It was confirmed in the B-14 data that RS was associated with DR after 5 yrs in higher ER pts (Table) but not in the lower ER pts (interaction P = 0.03). The association of RS risk groups within clinicopathologic subgroups for the higher ER patients still at risk at 5 years will also be presented.

Table: DR Risk after 5 yrs in B-14 by RS Risk Group for pts with ER >9.1 C_T

RS risk group	N (%) pts	% DR KM estimate (95% CI)	
		5–10 years	5–15 years
Low	289 (58%)	4.7 (2.8–8.0)	6.8 (4.4–10.6)
Intermediate	111 (22%)	4.1 (1.6–10.6)	11.2 (6.2–19.9)
High	97 (20%)	12.6 (7.4–21.2)	16.4 (10.2–25.7)

Log rank P = 0.01.

Conclusion: For late recurrences (beyond 5 yrs), the RS is strongly prognostic in pts with higher quantitative ER expression (>9.1). The findings suggest that extending tamoxifen beyond 5 yrs may be most beneficial in pts with high (and intermediate) RS with higher quantitative ER expression and of limited benefit in pts with a low RS (>50% of population under study).
Disclosure of Interest: No significant relationships.

P265
Presenting findings and recurrence patterns of breast cancer subtypes as defined by St.Gallen 2013

I. Vasconcelos[1]*, A. Hussainzada[1], F. Siedentopf[2], W. Schoenegg[1]. *[1]Breast Surgical Oncology, Breast Center Kurfürstendamm, Berlin, Germany, [2]Martin Luther Hospital, Berlin, Germany*

Goals: Determine whether presenting features and patterns of first recurrence differ according to major breast cancer subtypes, as defined by the St. Gallen International Expert Consensus 2013.
Methods: Subtypes were classified by immunohistochemistry as luminal A (LA – hormone receptor [HR] positive (estrogen and/or

progesterone), HER-2− and ki67% <20%), luminal B (LB – HR+ and either HER-2+ or simultaneously HER-2− and ki67% ≥20%), HER-2 non-luminal type (HR−, HER-2+) or basal-like (HR− and HER-2−). Data were retrospectively obtained from systematically reviewing breast cancer cases treated at our institution. The χ^2 test and analysis of variance were used to determine associations between subtype, clinicopathologic variables and recurrence sites. Disease free interval (DFI) events were invasive recurrence in ipsilateral breast, nodal, bone, or visceral sites. Time to first site-specific recurrence was evaluated by using Kaplan–Meier analysis.

Results: A total of 2,440 tumors were classifiable into molecular subtypes. Median follow-up was 64.6 months. The distribution of subtypes was LA, 48%; LB HER-2− 19%, LB HER2+, 14%; HER2+ non-L 8% and basal-like, 11%. Marked differences in age, bilateral disease, tumor size (T), extent of lymph node involvement (N), nuclear grade (G), multicentric/multifocal disease (MF/MC), lymphovascular invasion (LVI), extensive intraductal component (EIC) and recurrence rates were observed among subtypes ($p < 0.0001$). HER2+ tumors (LB HER2+ and HER2+ non-L) did not differ in any parameter. LB HER2− tumors differed from LA tumors in terms of T, N, G, LVI and recurrence rate ($p < 0.0001$). Recurrence site differed among the subtypes, LA: nodal, LB HER2−: bone and basal-like/HER2+ (independently of HR status): visceral ($p = 0.001$). Disease free interval was longer for patients with LA (154 months) compared with LB HER2− (130 months), basal-like (125 months), LB HER2+ (105 months) and HER2+ non-luminal (100 months; $p < 0.0001$).

Conclusion: Tumor presentation, recurrence patterns and DFI vary among molecular subtypes; the distinction between HER2+ luminal-type vs. non-luminal type appears to be unimportant in both cliniopathological presentation, DFI and recurrence pattern, whereas the distinction between LA and LB Her-2−, based on a ki67% cut-off of 20% appears to be of clinicopathological value, with differing DFI and recurrence sites.

Disclosure of Interest: No significant relationships.

P266

Prognostically distinctive subgroup in stage IIIc breast cancer

T. Kim*, H.K. Park, K.H. Lee, K.I. Kim. *Breast Cancer Center, Gachon University Gil Hospital, Incheon, Korea*

Goals: We often encounter patients who show discordance between TNM stage and prognosis. Especially, in high nodal stage group (N3), we clinically face some patients who are in disease-free status for long periods. We investigated whether there are prognostically different subgroups among patients with stage IIIc (anyTN3M0) breast cancer.

Methods: The records of 180 patients who operated for stage IIIc breast cancer from January 2002 to september 2009 were reviewed. Excluded were patients who received neoadjuvant therapy. All patients received adjuvant therapy planned according to standard protocols. The primary outcome was recurrence-free survival (RFS). We calculated the cumulative incidence of events and performed mutivariate analysis using the Cox proportional hazards model.

Results: Of these, tumor biology and nodal ratio (ratio of positive over excised lymph node) were the only relating factors with prognosis. Age, tumor size, tumor grade and supraclavicular LN status at diagnosis were not statistically significant with prognosis. According to the St. Gallen 2013 updated definition of intrinsic molecular subtypes, patients who were grouped as HER2 negative Luminal B [ER or PR positive, 'high' (≥14%) Ki67 level, HER2 negative] type showed far better outcome (5-year RFS 85.2%) while patients in group with triple negative phenotype (TNP, ER and PR negative, HER2 negative) showed poorer outcome (5-year RFS 39.5%). The 5-year RFS for the patients who were Luminal A, HER2 positive Luminal B and non-luminal HER2 type were 64.6%, 55.8% and 55.5%, respectively (P value 0.008). In all patients, the RFS was significantly better in patients with low nodal ratio (<0.65) ($P = 0.004$). In the patient subgroups with HER2 negative luminal B type, those with nodal ratio lesser than 0.65 had significantly better RFS, whereas in the patient subgroup with TNP had worse RFS regardless of nodal ratio. Other tumor biology groups had no prognostic significance with nodal ratio status.

Conclusion: Patients with N3 but HER2 negative Luminal B tumor biology had similar clinical outcomes as those with stage II breast cancer, and had more favorable prognosis in case with low nodal ratio. High level Ki67 is presumed to be good responder to adjuvant chemotherapy to be 'down staging' effect in high nodal stage breast cancer. The current results show that intrinsic subtype has a greater prognostic impact in predicting clinical outcomes, in addition, different patient subgroups may be offered different treatment strategies.

Disclosure of Interest: No significant relationships.

P267

Blood group: is it associated with tumor biology in breast cancer?

D. Mizrak, P. Kubilay, B. Ozturk, H. Akbulut, H. Onur*. *Medical Oncology, Ankara University, Ankara, Turkey*

Goals: Multiple factors are associated with breast cancer development. And lots of factors affect breast cancer prognosis. We aimed to investigate the relationship of ABO blood groups/Rh factor, with breast cancer prognostic factors.

Methods: All breast cancer patients treated in Ankara University's Department of Medical Oncology in the last five years were retrospectively screened. A total of 277 cases with known ABO blood group/Rh factor included in the study. We studied the frequency of blood groups based on the tumor grade, estrogen receptor (ER), progesterone receptor (PR), and HER2 status.

Results: The median age was 51 years (range: 18–85). Of 277 patients; 39.9% A Rh+, 6.9% A Rh−, 3.4% O Rh+, 27.6% O Rh−, 10.3% B Rh+, 3.0% B Rh−, and 8.9% was AB Rh+. Estrogen receptor and HER2 was positive in 80.8% and 12.8% of patients, respectively. No significant difference was found between blood groups and estrogen receptor status ($p = 0.44$), progesterone receptor status ($p = 0.207$), HER2 status ($p = 0.195$), and tumor grade.

Conclusion: ABO blood group is not associated with breast cancer prognostic factors. Further studies with larger number of patients may provide more information about blood group and breast cancer prognosis.

Disclosure of Interest: No significant relationships.

P268

Recurrence risk in small, node-negative, early breast cancer

R. Nagaoka[1]*, J. Horiguchi[2], D. Takata[2], A. Sato[2], H. Tokiniwa[2], T. Higuchi[2], S. Uchida[2], M. Tsuboi[2], M. Kikuchi[2], I. Takeyoshi[1]. *[1]Thoracic and Visceral Organ Surgery, Gunma University, Graduate School of Medcine, Gunma, Japan, [2]Breast and Endocrine Surgery, Gunma University Hospital, Maebashi, Japan*

Goals: As recurrences and deaths less frequently occur in small, node-negative breast cancer patients, decision on adjuvant treatments remains controversial. In this study, we evaluate recurrence risk in patients with pT1mic/T1a/T1b, node-negative, breast cancer, accordingly with some prognostic factors.

Methods: We retrospectively evaluated 173 pT1mic/T1a/T1b, pN0 patients treated between 2004 and 2010 in our institution. Patients treated by neoadjuvant chemotherapy were excluded. We defined 4 different cohorts: ER positive/HER2 negative (ER+HER−), ER positive/HER2 positive (ER+HER+), ER negative/HER2 positive (ER−HER+), and triple negative (TN).

Results: pT1mic was seen in 11% of patients, 29% pT1a, 60% T1b. Concerning the 4 different cohorts, 82% were ER+HER−, 2.3% were ER+HER+, 4.7% were ER−HER+, 10.9% were TN. Adjuvant therapy was given to 86.7% of patients (83% hormone therapy, 6.4% chemotherapy, 4.6% trastuzumab). At a median follow-up of 69 months, 5-year DFS and OS was 98.3% and 100%, without differences among pT1mic,a,b, or among the 4 cohorts.
All recurrence patients were without adjuvant therapy. For HER+ cohorts, patients treated by trastuzumab had a good prognosis.
Conclusion: Five-year DFS and OS was very favorable in this series of small, node-negative cancers, but patients without adjuvant therapy have a worse outcome. Effective adjuvant treatment should be considered in these favorable subgroups.
Disclosure of Interest: No significant relationships.

P269
Silver in situ hybridization and FISH for determination of HER2 gene status in breast carcinoma

A. Kram[1] *, M. Stepaniuk[1], L. Teresinski[1], E. Bocher[1], W. Ploszynska[1], M. Salamaga[2], L. Wozniak[2], I. Mirwa-Tomczak[2], M. Holicki[2], J. Sola[1]. *[1]Pathology, West Pomeranian Cancer Center, Szczecin, Poland, [2]Radiology, West Pomeranian Cancer Center, Szczecin, Poland*

Goals: The significance of HER2 status in breast cancer treatment has focused attention on clinical assays to appropriately assign HER2 amplification status. Disadvantages of fluorescence in situ hybridization (FISH) testing include long time necessary for preparing slides, requirements for fluorescence microscopy, and loss of the signal of the fluorescent dye in time. Silver-enhanced in situ hybridization (SISH) is a fast and fully automated assay providing everlastingly stained slides that are interpreted by conventional microscopy which enables pathologists to evaluate slides within the background of cancer morphology. This study evaluates the concordance between SISH and FISH assays in determining the status of HER2 gene amplification in a cohort of 66 primary invasive breast carcinomas.
Methods: 900 cases of primary breast cancer were diagnosed in the Department of Pathology, West Pomeranian Cancer Center from February 2013 to June 2014. In 84 cases (9.3%) with equivocal (2+) immunohistochemical HER2 expression, HER2 was quantified by SISH by the ratio of HER2 to CHR17 signals using the College of American Pathologists reporting scheme. In 66 cases comparison with FISH results was also done.
Results: SISH HER2 showed amplification in 19 cases, and no amplification in 65 cases. For the 66 cases with both SISH and FISH methods done, 56 cases (86.1%) showed ino amplification and 9 cases (13.6%) were amplified, Overall concordance between SISH and FISH was identified in 65 of 66 cases (98.4%).
Conclusion: In conclusion, SISH represents a novel and easy to use approach for the determination of HER2 status in breast cancer. The overall concordance between SISH and FISH is very good. Interpretation of SISH results by pathologists is a very good example of simultaneous morphological and molecular assessment of breast cancer tissue.
Disclosure of Interest: Dr Andrzej Kram received travel and conference fee support from Roche Diagnostics Poland.

P270
Outcome of HER2 positive breast cancer by PR expression since the introduction of trastuzumab

K. Van Asten[1] *, L. Jongen[1], B. Beuselinck[2], A. Laenen[3], H. Wildiers[2], A. Poppe[4], G. Floris[5], M. Christiaens[6], P. Neven[4]. *[1]Oncology, KU Leuven, Leuven, Belgium, [2]General Medical Oncology, UZ Leuven, Leuven, Belgium, [3]Interuniversity Center for Biostatistics and Statistical Bioinformatics, KU Leuven, Leuven, Belgium, [4]Gynaecology and Obstetrics, UZ Leuven, Leuven, Belgium, [5]Imaging and Pathology, UZ Leuven, Leuven, Belgium, [6]Surgery, UZ Leuven, Leuven, Belgium*

Goals: Most data on the prognostic value of progesterone receptor (PR) expression in early HER2 positive breast cancer (BC) are from the era before adjuvant trastuzumab (T). Little is known about the prognostic effect of PR expression after treatment with T and chemotherapy (CT), standard of care since 2006. For the estrogen receptor (ER), several studies have demonstrated a crosstalk between ER and HER2 that has an impact on BC outcome. Here, we report the impact of PR expression on outcome of consecutive patients treated in one center with CT and T for early HER2 positive BC.
Methods: Patients with an invasive stage I–III HER2 positive BC diagnosed and treated between January 2000 and December 2012 and that received (neo-) adjuvant CT and T were retrieved from the UZ Leuven database. Differences between three groups of ER and PR status (ER+PR+, ER+PR− and ER−PR−) regarding distant metastasis free interval and BC specific survival (BCSS) were analyzed with log-rank tests. ER+PR− and ER−PR− subgroups were individually and together compared to ER+PR+ BCs. Median follow-up was measured from diagnosis to last visit or death. Censoring occurred at end of follow-up, death without previous metastasis or death from other causes.
Results: In total, 271 patients were treated with CT and T. 46.9% were ER+PR+, 17.0% were ER+PR− and 36.2% were ER−PR−. Median follow-up was 5.1 years. Distant metastatic relapse (DMR) was observed in 16 cases (5.9%) and BC death in 7 (2.6%) while 3 died of unrelated causes. ER+PR+ (1.6%) tumors were less likely to metastasize during the time of follow-up as compared to ER−PR− (11.2%) as well as ER+/−PR− (9.7%) lesions ($p = 0.004$ and $p = 0.0084$, respectively). Regarding BC death, no evidence was found for a difference between the three groups ($p = 0.69$) nor between ER+PR+ and ER+/−PR− ($p = 0.48$).
Conclusion: PR status influences outcome in HER2 positive BC at the era of T. DMR was significantly lower in ER+PR+ patients as compared to ER−PR− and ER+/−PR− patients. No difference was found for BCSS, but longer follow-up is warranted. In addition, we observed that patients with a triple positive BC receiving CT and T are unlikely to develop a distant metastasis, at least within 5 years of diagnosis. Current and future adjuvant clinical trials with new or multiple anti-HER2 agents should probably take into account the ER and PR status.
Disclosure of Interest: No significant relationships.

P271
Circulating miR-133a as diagnostic and prognostic biomarker for Taiwanese breast cancer

F. Chen[1], Y. Ting[2], Z. Chen[3], M. Hou[1], Y. Yeh[2] *. *[1]Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung, Taiwan, [2]Department of Medical Laboratory Sciences and Biotechnology, Fooyin University, Kaohsiung, Taiwan, [3]Kaohsiung Medical University, Kaohsiung, Taiwan*

Goals: Muscle-specific miR-133a is currently demonstrated as a promising biomarker in several human diseases and cancers. This study aimed to explore circulating miR-133a profiles as well as its diagnostic and prognostic value in Taiwanese breast cancer, early onset and lower incidence as compared with Western population.
Methods: MiRNA level was performed by a stem-loop quantitative reverse-transcription PCR (RT-qPCR) assay from serum samples of

66 healthy subjects and 191 patients as well as 120 paired and matched cancer and non-cancer tissues. Data were presented as the mean±SD. The predictive value and correlations of results with clinicopathological characteristics and overall survival were further statically analyzed using receiver operating characteristic (ROC)-curve analysis, chi-squared test, two-tailed Student's t-test, Kaplan–Meier (K-M) survival curve and multivariable COX regression model. A p-value of <0.05 was considered statistically significant.

Results: Circulating miR-133a levels were significantly lower in healthy controls (6.52±15.42, n = 66) than in total (Stage I to III, 73.55±156.10, n = 191) and early stage (stage I, 75.93±166.13, n = 83) breast cancer patients (p = 0.001 and 0.001), and a corresponding area under curve (AUC) was 0.802 (for total cases, p < 0.001) and 0.790 (for early stage cases, p < 0.001) in the ROC-curve analysis. It is noted that the expression levels of miR-133a were positively correlated (p < 0.001) but were not significantly different between paired cancer and non-cancer tissues. And circulating miR-133a levels were positively correlated with expression levels in both non-cancer and cancer tissues of 120 matched cases (p = 0.028 and 0.011). In addition, the levels of circulating miR-133a were increased in ER-positive, PR-positive, and Her2-negative patient groups (p = 0.33, 0.028, and <0.001). Circulating miR-133a levels categorized by median value were inversely correlated with recurrence and Her2 status (p = 0.046 and 0.030). The K-M survival curve showed that increased levels of circulating miR-133a were associated with a poor overall survival rate (p < 0.001). Multivariable COX regression model demonstrated that circulating miR-133a was a significant determinant for patient survival (OR = 2.071, p = 0.001). Furthermore, those patients who received hormo- and chemo-, but not radio-, therapy would have an improved survival rate when they presented with high circulating miR-133a levels (p = 0.005, 0.033 and 0.121).

Conclusion: Our results showed that circulating miR-133a levels might serve as a diagnostic and prognostic biomarker in Taiwanese breast cancer.

Disclosure of Interest: No significant relationships.

P272

Using next-generation sequencing to predict clinical outcome of triple negative breast cancer

B. Thouvenot[1]*, S. Verdun[1], J. Tomasina[1], B. Hilselberger[1], M. Brulliard[1], L. Bonnard[1], M. Trarbach[1], J. Armand[2], V. Ogier[1], B.E. Bihain[1]. *[1]Genclis, Genclis, Vandoeuvre les Nancy, France, [2]Ditep, Institut Gustave Roussy, Villejuif, France*

Goals: Develop novel methods that accurately predict individual triple negative breast cancer severity in order to allow rationale adjuvant chemotherapy decision.

Methods: Sequencing (NGS) of RNA and DNA from 65 patients diagnosed with pathologically confirmed non metastatic triple negative breast cancer before the age of 65 yrs was performed. The cohort was divided in a training set of 20 patients: 9 were alive after 2500 days of follow up and 11 died within 1000 days that followed diagnosis, and a replication set of 45 patients. NGS data were analyzed to measure somatic mutations affecting DNA, RNA expression and a specific algorithm was developed to quantify RNA DNA divergences i.e. sequence variations present on RNA level but not detected on DNA. A discriminant analysis using 5 transcripts was used to separate good outcome from poor outcome patients.

Results: Patients from the training set were effectively (>90% accuracy) separated according to their good or poor clinical outcome based on either somatic mutation rate (SM), expression profiling (EP) and RNA DNA Divergences (RDD) rate. However SM and EP model performances dropped dramatically after cross-validation while RDD model retained >90% accuracy. Accordingly, blinded application of the 3 models to the 45 patients of the replication set yielded non-significant predictive value in Kaplan–Meier analysis for the SM and EP models but the RDD model effectively predicted clinical outcome. The probability of survival at 2500 days is estimated to be 100% for patients predicted with good outcome and only 24% for those predicted with poor outcome (p < 0.0001). Of note, one patient (38 yrs) of the replication set diagnosed with in situ disease and predicted with poor outcome by the RDD model died after 1999 days. We verified that performances of the RDD model were not affected by biases due to recruitment centers, basal or non-basal like status of TNBC, ethnic origin or menopausal status. Finally, we found that RDD model predictive of TNBC clinical outcome has no predictive value for ER positive breast cancers.

Conclusion: RDD are previously unsuspected molecular events are strongly associated with the severity of the diseases. Analysis of the molecular events causing RDD and expending the finding to larger cohort of TNBC patients are the next steps toward clinical development of this novel concept.

Disclosure of Interest: B. Thouvenot, S. Verdun, J. Tomasina, B. Hilselberger, M. Brulliard, L. Bonnard, M. Trarbach, V. Ogier and B. E. Bihain are employed by Genclis SAS.

P273

Autophagy-related proteins ATG5 and FIP200 predict favorable prognosis in breast cancer patients

L. Wang[1]*, L. Yao[1], Y. Zheng[1], Q. Xu[2], X. Liu[3], X. Hu[4], P. Wang[5], Z. Shao[1]. *[1]Department of Breast Surgery, Fudan University Shanghai Cancer Center, Shanghai, China, [2]Department of Finance and Control Science, School of Mathematical Science, Fudan University, Shanghai, China, [3]Department of Pathology, School of Basic Medical Sciences, Fudan University, Shanghai, China, [4]Department of Breast Surgery, Key Laboratory of Breast Cancer in Shanghai, Shanghai, China, [5]Key Laboratory of Systems Biology, Shanghai Advanced Research Institute, Chinese Academy of Sciences, Shanghai, China*

Goals: Autophagy is a self-digesting system primarily responsible for removal and recycling of long-lived proteins and damaged organelles in order to maintain cell homeostasis. Recent studies have implicated dual roles of autophagy in cancer: suppressing tumor progression as well as promoting survival. This study sought to investigate the prognostic value of autophagy-related proteins autophagy-related gene 5 (ATG5) and FAK family kinase-interacting protein of 200 kDa (FIP200) in patients with operable breast cancer.

Methods: The expression of ATG5 and FIP200 was evaluated by immunohistochemistry in surgical specimens from 200 patients diagnosed with histologically proven invasive ductal breast cancer. A stepwise Cox multivariate analysis was performed to construct the risk prediction model.

Results: In this retrospective cohort study, both ATG5 (HR = 0.465, 95% CI 0.247–0.872, P = 0.017) and FIP200 (HR = 0.521, 95% CI 0.278–0.979, P = 0.043) correlated with prolonged disease-free survival (DFS). In the receiver operating characteristic (ROC) analysis, addition of ATG5 and FIP200 led to a significantly improved the area under the time-dependent ROC curve (AUC) at 3 year (0.748 versus 0.680, P < 0.001) and 5 year (0.756 versus 0.699, P < 0.001).

Conclusion: Collectively, our findings established the prognostic significance of ATG5 and FIP200 in patients with breast cancer.

Disclosure of Interest: No significant relationships.

P274

New circulating lipid markers related to breast cancer

I. Dale[1] *, A. Roscher[2], H. Fiegel[3], E. Guimarães Do Turco[4], M. Hubalek[3], I. Himmel[5], S. Prader[6], C. Troi[6], A. Lopes Carvalho[7], R.A. Da Costa Vieira[7]. *[1]Gynecology Department, Federal University of São Paulo, Sao Paolo, Brazil, [2]Children's Research Center, Ludwig-Maximilians Universität München, München, Germany, [3]Frauenheilkunde, TILAK, Innsbruck, Austria, [4]Surgery, Federal University of Sao Paulo, Sao Paulo, Brazil, [5]Department of Gynaecology and Obstetrics, Hospital Meran, Meran, Austria, [6]Department of Gynaecology, Hospital Brixen, Brixen, Italy, [7]Barretos Cancer Hospital, Barretos Cancer Hospital, Barretos, Brazil*

Goals: In the present study we describe the identification of a blood metabolomics signature able to discriminate breast cancer women from controls with higher sensitivity and specificity than imaging approaches.

Methods: The present prospective case–control study included a total of 1014 plasma samples being 213 from breast cancer women (BC) (Stages I to III), 520 normal healthy controls (HC). Initially, a discovery set was assembled and samples (29 breast cancer women × 93 healthy controls) were then examined by a global exploratory untargeted shotgun approach, on an independent service, at the AB-SCiex Laboratory located in São Paulo, SP, Brazil. To corroborate findings, two independent validation sets were performed in a fee-for-service basis, with no phenotypic information, using the targeted quantitative MS/MS metabolomics platform at Biocrates Life Sciences AG, Innsbruck, Austria. The first was composed of 30 breast cancer women and 111 controls and the second, with 0.8 of statistical predictive power, was composed of 520 healthy controls and 154 breast cancer patients including 70 early stage T1 tumors. Targeted quantitative data depicting the absolute micromolar concentrations of metabolites was then imported to ROCCET (ROC Curve Explorer & Tester) available at http://www.roccet.ca/ROCCET/ for the generation of uni- and multivariate Receiver Operating Characteristic (ROC) curves obtained through Support Vector Machine, Partial Least Squares-Discriminant Analysis, Random Forests and Monte-Carlo cross validation.

Results: High discrimination (Table 1) between breast cancer women and controls was obtained using a blood metabolite signature composed by the combination of arachidonic plasmalogen/plasminogen phosphatidylcholines, hydroxylated sphingomyelins and amino acids.

Table 1. Main study results

	Training Set (29 BC × 93 HC)	Validation Set 1 (30 BC × 111 HC)	Validation Set 2 (154 BC × 520 HC)
AUC (95% CI)	0.968 (0.972–1)	0.966 (0.884–1)	0.993 (0.988–0.996)
p-value*	<0.001	<0.001	<0.001
Sensitivity (%)	93.55	100.00	98.09
Specificity (%)	90.35	98.23	97.01
PPV (%)	72.50	93.75	90.59
NPV (%)	98.10	100.00	99.43
Accuracy**	0.889	0.975	0.967

BC, breast cancer; HC, healthy controls; NPV, negative predictive value; PPV, positive predictive value.
*Performance measure (AUC) after 1000 permutations.
**Average accuracy after 100 cross validations.

Conclusion: The high predictive values achieved in the present study suggest that blood metabolomics might add significant sensitivity and specificity to the current breast cancer screening techniques and have a potential to substitute mammography for breast cancer screening.

Disclosure of Interest: No significant relationships.

P275

Implications of discordance between reference genomes applied in breast cancer exome sequencing

N. Van Der Merwe[1] *, A. Peeters[1], S.J. Van Rensburg[1], R. Pienaar[2], J. Bezuidenhout[1], M.J. Kotze[1]. *[1]Pathology, Stellenbosch University, Cape Town, South Africa, [2]GVI Oncology, Panorama, Cape Town, South Africa*

Goals: A combination of genetic and pathology tests was used as a pre-screen step to exclude causative mutations in the BRCA1 and BRCA2 genes prior to whole exome sequencing (WES) in a mother and daughter diagnosed with early-onset breast cancer. Previous identification of the MTHFR 677 C>T mutation and exclusion of CYP2D6*4 in both patients contributed towards the analytical validation of the sequencing platform and variant calling pipelines used in this study. The aim was to identify potential causative mutations and to provide an explanation for medication side effects reported in the family.

Methods: WES was performed using the Proton next generation sequencing (NGS) apparatus, followed by variant calling with the public human genome reference sequence (hg19). The variants identified were evaluated in relation to publicly available mutation and single nucleotide polymorphism (SNP) databases to exclude errors due to incorrect base calling and sequencing artefacts. The finding that hg19 contains minor alleles at >1 million loci led to repeated variant calling using a major allele reference sequence (MARS).

Results: Homozygosity for MTHFR 677C>T and the absence of CYP2D6*4 and deleterious BRCA mutations was confirmed in the breast cancer patients with use of both hg19 and MARS. Initial analysis of other known cancer-related genes using hg19 versus MARS revealed several discrepancies. While MARS identified 65 536 unfiltered variants, hg19 identified merely 52 146. This translated into a very high discordance rate of approximately 20%. A total of 18 661 variants identified using hg19 was not detected with application of MARS.

Conclusion: At loci where the major alleles of variants with potential high impact are absent from hg19, potential causative variants may have been missed. In this study, the need for improvement of hg19 used as an intermediate bioinformatics step for data translation between the laboratory and clinical application was addressed by the use of MARS. WES applied beyond the limited scope of single-gene testing has the potential to detect both known and novel mutations across diagnostic boundaries to facilitate prevention of cumulative risk underlying the development of breast cancer and associated co-morbidities.

Disclosure of Interest: Professor MJ Kotze is a shareholder and director of Gknowmix (PTY) LTD.

P276

Effect of tumor hormonal and HER2 status on localization of metastases in recurrent breast cancer

D. Mizrak, H. Onur*, B. Ozturk, P. Kubilay, H. Akbulut. *Medical Oncology, Ankara University, Ankara, Turkey*

Goals: Following initial treatment for breast cancer, patients require surveillance for tumor recurrence. Several factors predict for recurrence and early diagnosis of recurrence is important because this situation can be treated with curative intent. Periodic history/physical examination and annual mammography are recommended for surveillance of early stage breast cancer. The routine performance of laboratory testing and imaging methods are not included in most guidelines in the absence of symptoms. Despite this, physicians often order additional tests to detect early recurrences. We aimed to investigate early localization of recurrences according to HER2 and hormonal status of tumor.

Methods: Clinical records of early stage breast cancer patients treated in Ankara University Department of Medical Oncology between January 2009 and December 2013 reviewed retrospectively. 291 patients with early stage cancer, whose recurrence determined surveillance, were included in the study.
Results: The median patient age was 47 (18–85) years. 22.7% of tumors were HER2 positive and 82.7% were hormone receptor positive. Localization of recurrence was 38.5% in viszeral organs, bone in 29.2%, local in 25.1%, and brain in 7.2% of patients. We detected a significant difference in localization of recurrence according to HER2 status. Local recurrence was 22.6% for HER2 negative tumors and 33% for HER2 positive cancers. Bone recurrence were found in 33% of patients with HER-negative tumors, and in 15.1% of patients with HER-positive tumors ($p = 0.091$). We found no correlation between hormonal status and localization of recurrence.
Conclusion: Laboratory tests and imaging modalities used for surveillance of breast cancer patients can differ among medical centers. It can be useful to keep in mind bone recurrence for HER2 negative tumors, and local recurrence in HER2 positive tumors.
Disclosure of Interest: No significant relationships.

P277
CD24 and CD44 expression in Indian breast cancer patients and response to chemotherapy

A.A. Sonkar[1] *, J.L. Miller[1], A.A. Agarwal[1], K.R. Singh[1], N. Husain[2], J.K. Kushwaha[1]. [1]*Surgery, King George's Medical University, Lucknow, India,* [2]*Pathology, RML Institute of Medical Sciences, Lucknow, India*

Goals: Cancer Stem cells (CSC) are thought to have the characteristics of unlimited proliferation and differentiation and therefore an aberration in the CSC's could be responsible for tumor formation and progression, and metastasis. The well accepted cancer stem cell surface markers are CD44, CD24, CD133, CD166, EpCAM in different tumors including breast, lung, pancreas, prostate, colon and rectum, renal and ovarian. $CD44^+/CD24^-$ phenotype has been associated with stem cell-like characteristics with enhanced invasive properties, radiation resistance and with distinct genetic profiles suggesting a correlation to adverse prognosis in western literature. With this need in mind, efforts to identify new prognostic markers to accurately establish innovative therapies to eradicate metastatic breast cancer cells at the primary tumor stage is on.
Methods: N = 61 cancer breast patients in the Department of Surgery, KGMU and consenting to participate in the study were included between August 2013 to July 2014. Tru-cut biopsy/Incisional biopsy/ Post mastectomy specimens were sent for histopathological examination and receptor studies (ER, PR, Her2 NeU, CD44 and CD24). Response was determined using WHO clinical criteria.
Results: Mean age at presentation 47.78 ± 10.04 years (Range: 25–75). Majority of patients, 70.6% presented in Stage III and belonged to the Her2 neu enriched subtype. Of the 39 patients with ER-negative status, 33 (84.6%) have been found in the $CD44^+/CD24^-$ phenotype and 82.5% of all the CD $44^+/CD24^-$ patients were ER negative ($p = 0.001$). 34 (75.5%) of the PR-negative patients showed the $CD44^+/CD24^-$ phenotype and of all the $CD44^+/CD24^-$ patients, 85% were PR negative ($p = 0.006$). 36 (75%) of Her-2-Neu positives were $CD44^+/CD24^-$. 92% of the Her-2-Neu patients expressed $CD44^+/CD24^-$ and 76.9% of all the triple negative patients were found to be $CD44^+/CD24^-$ expression ($p = 0.001$). 57 patients completed NACT; none had CR, 42/57 (73.68%) PR, 9 (15.7%) no change and 6 (10.52%) PD. No statistically significant association between $CD44^+/CD24^-$ phenotype and response to chemotherapy.
Conclusion: $CD44^+/CD24^-$ had significant association with adverse prognostic factors like stage of disease and tumors being negative for hormonal receptors, Her-2 enriched sub type and triple negative sub type in developing countries also. However, the sample size of this study was small and the follow up short, to establish routine use of CD44/CD24 expression as a prognostic factor in breast cancer.
Disclosure of Interest: No significant relationships.

P278
Effect of HER2 and hormonal status to FDG uptake on PET/CT imaging in recurrent breast cancer

D. Mizrak[1] *, H. Onur[1], B. Ozturk[2], P. Kubilay[2], G. Utkan[1], H. Akbulut[1]. [1]*Medical Oncology, Ankara University, Ankara, Turkey,* [2]*Internal Medicine, Ankara University, Ankara, Turkey*

Goals: FDG does not enter metabolic processes in contrast to normal glucose and trapped within the cell and its uptake show a correlation with tumor aggressiveness. For breast cancer, guidelines do not recommend the use of PET/CT for the evaluation of recurrent disease. FDG PET/CT is optional if other imaging results are suspicious. There is limited evidence about in which subgroup of breast cancer, FDG PET/CT imaging can be useful to determine the extent of disease and guide the treatment modality. We investigated the relationship between HER2 and hormonal status of tumor and FDG intensity in recurrent breast cancer.
Methods: Medical records of all recurrent breast cancer patients evaluated with PET/CT imaging in Ankara University Department of Medical Oncology between January 2009 and December 2013 were retrospectively reviewed. Lesions with SUV max values over 3 g/dL was regarded as PET positive. A total of 123 recurrent patients with a PET/CT imaging included in the study.
Results: Median age was 57 year (28–90). 75.9% of patients were hormone receptor positive and 28.5% were HER2 positive. Of hormone receptor positive cases 90.6% had a high FDG (≥3 g/dL) intensity whereas it was 85.2% for hormone receptor negatives ($p = 0.429$). High FDG (≥3 g/dL) intensity ratios were detected in 91.4% and 85.2% for HER2 positive and negative patients respectively ($p = 0.356$).
Conclusion: Our results suggest that there is a slight correlation between tumor HER2 positivity and FDG intensity in recurrent breast cancer. With larger studies usefulness of PET/CT imaging in HER2 positive recurrent breast cancer patients can be shown.
Disclosure of Interest: No significant relationships.

P279
More prognostic factors in early stage breast cancer

D. Mizrak[1] *, B. Ozturk[2], P. Kubilay[2], H. Akbulut[1], H. Onur[1]. [1]*Medical Oncology, Ankara University, Ankara, Turkey,* [2]*Internal Medicine, Ankara University, Ankara, Turkey*

Goals: The widespread use of adjuvant therapy has reduced mortality from breast cancer. Although many patients are not treated appropriately, with some overtreated and others undertreated. It would be of great value to have more prognostic factors that could help select patients with recurrence risk and would benefit from therapies. The known prognostic factors are tumor grade, tumor size, lymph node involvement, estrogen receptor (ER) status, and HER-2/neu expression status for early stage breast cancer. We aimed to investigate the relation of platelet count, neutrophil count, hemoglobin, and albumin level measured at diagnosis with these known prognostic factors.
Methods: Medical records of all early stage (I, II) breast cancer patients evaluated in Ankara University Department of Medical Oncology between January 2009 and December 2013 were retrospectively reviewed. A total of 722 patients with invasive ductal carcinoma included in the study.
Results: Median age was 49 year (24–86). We determined a positive correlation between HER-2 positivity and grade. 61.7% of HER-2 positive patients had grade 3 tumors, it was 32.8% for HER-2 negatives ($p < 0.0001$). There was a similar correlation with tumor

size, 73.7% of HER-2 positive patients had T2–3 tumor, it was 64.6% for HER-2 negatives (p = 0.008). We found no correlation between HER-2 status and lymph node involvement. HER-2 positivity was significantly high in hormone receptor negative patients (p < 0.0001). Estrogen receptor positivity was significantly correlated with tumor grade, ki-67, and size of the tumor. In ER-negative patients 66.1% of tumors were grade 3, in ER-positives it was 36.0% (p < 0.0001). T2–3 tumor ratios were 80% and 65.2% in ER negatives and positives respectively (p = 0.025). There was no correlation between hormone status and lymph node involvement. We found a positive correlation between lymph node involvement and platelet count (p = 0.016) and a negative correlation with serum albumin (0.002) and hemoglobin (0.018) levels. We found no correlation of these parameters with tumor size and grade. In hormone receptor negative patients neutrophil count was significantly high (p = 0.017) and in HER-2 positive patients platelet count was significantly high (p = 0.061).

Conclusion: Our results suggest that hormone receptor and HER-2 positivity are primarily related with local tumor growth. Patients with low hemoglobin, albumin levels and high platelet counts should be followed up with more care.

Disclosure of Interest: No significant relationships.

P280

Differentiation between luminal-HER2 and HER2-enriched breast cancer in clinical course

Y. Koi[1]*, S. Akiyoshi[1], M. Oikawa[1], C. Koga[1], S. Nishimura[1], Y. Nakamura[1], M. Ishida[1], S. Ohno[2]. *[1]Breast Oncology, National Kyushu Cancer Center, Fukuoka, Japan, [2]Clinical Research Institute, National Hospital Organization Kyushu Cancer Center, Fukuoka, Japan*

Goals: HER2 positive breast cancer is divided into Luminal-HER2 and HER2-enriched type, according to the hormone receptor status. The biological behavior may be different among these types, whereas little is known about the characteristics and prognosis. The purpose of our study is to evaluate the characteristics, prognosis and the effect of systemic treatment in patients with Luminal-HER2 and HER2-enriched type of early and recurrent breast cancer.

Methods: We retrospectively examined patients with early and recurrent HER2 positive breast cancer who were treated at National Kyushu Cancer Center. We evaluated HER2 status with immunohistochemistry (IHC) or fluorescence in situ hybridization and ER/PgR status with IHC.

(1) Recurrent breast cancer: Five hundred two patients (pts) with recurrent breast were divided into two groups according to the time of recurrence. The recurrence was diagnosed between 1992 and 2000 in 171 pts, between 2001 and 2007 in 237 pts. The overall survival (OS) rates of these two groups were compared according to the intrinsic subtype, especially in Luminal-HER2 and HER2 enriched type.

(2) Early breast cancer: In order to determine five year disease free survival (DFS) rates, we reviewed four hundred and forty-eight patients with operable HER2 positive breast cancer from 2000 to 2013. Among them, 181 underwent surgery between 2000 and 2006, and 277 between 2007 and 2013.

Results: (1) Recurrent breast cancer: The median OS were 4.3 years in pts with diagnosis of recurrence between 2001 and 2007, which was significantly better than 1.9 years of those between 1992 and 2000 (p < 0.001). This prolongation is seen in both Luminal-HER2 and HER2-enriched groups, and there is no obvious differentiation between them.

(2) Early breast cancer: clinical characterisitics as tumor size or nodal status were no difference between two groups. Patients who received neoadjuvant chemotherapy were 31 pts in Luminal-HER2 and 13 pts in HER2-enriched group. HER2-enriched group is more likely to acquire pCR than Luminal-HER2 (pCR rate is 9.7% in Luminal-HER2 and 38.5% in HER2-enriched each). Post operative prognosis of HER2 positive breast cancer have been improved from 76.8% to 94.2% of 5-year DFS, in comparison of those between 2000 and 2007 and 2008 and 2013. As for Luminal-HER2 type, 5-year DFS was 74.4% of 99 pts between 2000 and 2007, and 95.3% of 170 pts between 2008 and 2013. Five-year DFS of HER2 enriched type were 78.8% of 82 pts between 2000 and 2007, and 92.5% of 107 pts between 2008 and 2013. There were no difference in prognosis between Luminal-HER2 and HER2 enriched type.

Conclusion: Luminal-HER2 and HER2-enriched breast cancer have different characteristics. To build the best individual treatment strategies for HER2 positive breast cancer, we have to make continuous evidence from research of biology about Luminal-HER2 and HER2-enriched groups.

Disclosure of Interest: No significant relationships.

P281

Comparison of HER2 dual-color and fluorescence ISH in breast cancer: a study of equivocal cases

T. Shao[1]*, M. Wood[2], A. Wing[2], M. Hnatovska[2], M. Mendes[2], J.B. Mullen[2], M.C. Chang[2]. *[1]Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada, [2]Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Canada*

Goals: HER2 is of prognostic and predictive significance in breast cancer, and is determined using immunohistochemistry (IHC) or in situ hybridization (ISH). Both fluorescence (FISH) and dual color (DISH) methods are now available and are highly concordant in large validation studies. However, a recent study (Mansfield et al., 2013) highlighted difficult cases in which FISH and DISH disagreed. Our goal was to compare FISH and DISH on a cohort enriched for equivocal cases, with respect to both HER2/Chr17 and HER2 copy number.

Methods: Consecutive cases were selected for testing over a 1.5 year period, based on Equivocal (2+) HER2 IHC (Ventana 4B5) and technically satisfactory DISH (Ventana INFORM). The cohort was enriched for equivocal cases by excluding cases that were clearly Negative or clearly Positive by visual inspection of the DISH slide. The remaining eligible cases were tested by FISH (Abbott Vysis). DISH and FISH were evaluated using standard protocols by at least 1 of 2 technologists (MW, MH), and re-reviewed by at least 1 of 2 pathologists (JBM, MC). Results were evaluated using descriptive statistics.

Results: A total of 109 cases (median age 67 years, median tumor size 2.4 cm) were identified. The hormone receptor status was known in 87 cases, among which 70/87 (80%) were ER-positive and 61/87 (70%) were PgR-positive. The mean HER2/Chr17 ratio determined by DISH was 1.63±0.08 compared to 1.59±0.26 by FISH (p = 0.45, paired t-test). The mean HER2 copy number by DISH was 4.56±0.45 compared to 4.75±1.08 by FISH (p = 0.004, paired t-test). A comparison of HER2 status between DISH and FISH is summarized in the table.

Table: HER2 status by DISH vs FISH (2013 ASCO/CAP Criteria)

FISH	DISH			
	HER2 Positive	HER2 Equivocal	HER2 Negative	Total
HER2 Positive	7	16	2	25
HER2 Equivocal	2	65	4	71
HER2 Negative	0	10	3	13
Total	9	91	9	N = 109; κ = 0.27

Among DISH-Equivocal/FISH-Positive cases, 14/16 differed by HER2 copy number and 2/16 differed by HER2/Chr17 ratio. Of the 2 cases that were DISH-Negative/FISH-Positive, both differed by HER2/Chr17

ratio and were monosomic by FISH. Both cases that were FISH-Equivocal/DISH-Positive differed with respect to HER2/Chr17 ratio. Agreement was slightly higher when the 2007 criteria were used ($\kappa = 0.45$, $p = 0.1$ with 95% CI).

Conclusion: Although both DISH and FISH are valid methods of assessing HER2 with the same criteria for interpretation, there may be reduced agreement between DISH and FISH for cases in the equivocal range. In our series highly enriched for equivocal cases, the numerical values of HER2 copy number, but not HER2/Chr17 ratio, were significantly lower using DISH. This difference has increased in clinical significance with the shift to the 2013 ASCO/CAP guidelines emphasizing copy number. To avoid under-treatment, HER2 Equivocal results by DISH with HER2 copy number between 5 and 6 should be interpreted with caution, and additional testing by FISH may be considered.

Disclosure of Interest: No significant relationships.

P282

Significance of tumor-infiltrating lymphocytes in breast cancer with neoadjuvant chemotherapy

Y. Miyoshi[1] *, T. Shien[1], M. Omori[2], Y. Abe[1], A. Watanabe[1], A. Hara[1], T. Mizoo[1], T. Nogami[1], N. Taira[1], H. Doihara[1]. [1]*Breast and Endocrinological Surgery, Okayama University Hospital, Okayama, Japan,* [2]*Department of Pathology, Okayama University Hospital, Okayama, Japan*

Goals: Recently, association stromal lymphocytic infiltration in cancer tissue with response to chemotherapy and prognosis were reported. However the detail is not determinate yet.

Methods: We evaluated the breast cancer patients received surgery after NAC in Okayama University Hospital between January 2003 and December 2013. We retrospectively analyzed the correlation between expression of stromal TIL in pretreated CNB specimen and response of NAC, clinicopathological and radiological factors. TIL was defined as percentage of tumor stroma area that contains a lymphocytic infiltrate. Lymphocyte-predominant breast cancer (LPBC) was defined as cases with more than 50% of TIL. Pathological complete remission (pCR) was defined as the absence of residual invasive or noninvasive tumor cells in primary breast tumor.

Results: 47 cases were analyzed. The median age was 51 years old. The median tumor size was 40 mm. 34 patients (72%) had clinically lymph node metastases before NAC. Anthracycline and Taxane were administered in 46 patients (98%) respectively. Herceptin was administered in 7 patients (15%) with HER2 positive tumor. ER positive/HER2 negative (ER type) was 26 patients (55%). ER positive or negative/HER2 (HER2 type) was 12 patients (25%). ER negative/HER2 negative (TN type) was 9 patients (20%). pCR rate was 23% in ER type, 50% in HER2 type, and 22% in TN type. The rate of LPBC was 4% in ER type, 25% in HER2 type, and 33% in Triple negative type. The rate of pCR in LPBC cases was 0% in ER type, 100% in HER2 type, and 33% in TN type. In HER2 type, LPBC was significantly associated with pCR ($p = 0.04$) and nuclear grade ($p = 0.04$).

Conclusion: In only HER2 type, the presence of TIL in CNB specimen before NAC could predict pCR.

Disclosure of Interest: No significant relationships.

P283

Histomorphological parameters of nipple areolar complex as a predictor in carcinoma breast

S. Mallappa *, U. Sharma, M. Ak. *Pathology, VMMC Safdarjung Hospital, New Delhi, India*

Goals: The study is designed to predict involvement of Nipple Areola Complex in carcinoma breast, so that nipple areola sparing mastectomy may be performed to reduce psychological morbidity. There is increasing interest in preservation of the nipple and/or areola in hopes of achieving improved cosmetic and functional outcomes; however, the oncologic safety of nipple–areolar complex (NAC) preservation is a major concern. Reported rates of neoplastic involvement of NAC by various studies range from 0% to 58%.

Methods:

- A prospective study was done on a total of 30 mastectomy specimens between 2011–2013.
- All mastectomy specimens were inked and sectioned from medial to lateral into no greater than 1 cm thick tissue sections and grossly examined.
- Saggittal and horizontal sections from nipple and areola were taken from 4 quadrants. Each quadrant was divided into 3 equal horizontal sections representing 3 levels:
  - level 1, Nipple papilla,
  - level 2, Areola,
  - level 3, Retroareolar region.

Results:

- The present study showed NAC involvement of 50%.
- Statistically significant association was found between NAC involvement and Tumour–NAC distance ($P = 0.010$, likelihood ratio 0.003).
- There was increased percentage of NAC involvement with
  - large tumour size,
  - centrally located tumours,
  - tumours with >2 positive lymph nodes.
- Retroareolar level was the most commonly involved in our study (93.33% of NAC involved cases) followed by areolar level (66.66% of NAC involved cases).
- More than one level was involved in 9 cases.
- Nipple papilla was involved in 6/15 cases, and was not involved alone.
- Skip lesion with involvement of only middle level (areolar) was seen in only one case.

Conclusions:

- If only gross involvement of nipple is taken into consideration large amount of occult NAC involvement will be missed out, which can be picked up only by extensive sampling of NAC.
- Tumour–NAC distance is an important parameter in determining the NAC involvement.
- Retroareolar tissue examination can give a clue as to whether nipple papilla is involved or not.
- There is an increased percentage of NAC involvement with large tumour size, centrally located tumours and tumours with >2 positive lymph nodes.

Disclosure of Interest: No significant relationships.

P284

Stathmin-based signature is associated with survival outcomes of breast cancer patients

X. Kuang[1] *, Z. Zhang[2], Y. Liu[1], Y. Zheng[1], X. Hu[1], Z. Shao[3]. [1]*Breast Surgery, Key Laboratory of Breast Cancer in Shanghai, Shanghai, China,* [2]*School of Public Health, Fudan University, Department of Epidemiology and Biostatistics, Shanghai, China,* [3]*Breast Surgery, Shanghai Cancer Center, Fudan University, Shanghai, China*

Goals: Stathmin 1 (STMN1) is known to be overexpressed across a broad range of human malignancies. The activity of STMN1 can be modulated by its phosphorylation of multiple Serine residues (Ser16, Ser25, Ser38, and Ser63). In this study, we evaluated the expression of STMN1 and its phosphorylated forms to develop a STMN1-based classifier to predict disease-free survival (DFS).

Methods: In the training set, STMN1 and phospho-STMN1 signature were assessed, respectively, by immunohistochemistry via a tissue microarray consisting of 204 patients who had histologically confirmed as primary breast cancer and underwent mammectomy

in the Department of Breast Surgery in Shanghai Cancer Center during 2001 to 2006. Then we collected another cohort with 106 patients operated between 2007 and 2011 for a validation.
Results: The median follow-up in the training cohort was 102 months (range 0.5–144 months). In Kaplan–Meier analysis, STMN1, Ser25 and Ser38 were strongly associated with poorer DFS (P = 0.044 for STMN1, P = 0.045 for Ser25, P = 0.009 for Ser38), whereas Ser16 and Ser63 were associated with better DFS (P = 0.015 for Ser16, P = 0.010 for Ser63). Then the variables including clinicopathological factors and those five markers with P value less than 0.05 under univariate analysis were used to build the multivariate Cox proportional hazards models. We combined those five markers and some well-known clinical characters to establish a prognostic model and calculate a score for metastatic risk, where risk score = 0.173·STMN1 − 0.608·Ser16 + 0.743·Ser25 + 0.685·Ser38 − 0.342·Ser63 + 0.459·(histological grade) + 0.448·(tumor size) + 0.946·(lymphatic metastasis). This model shows a better prognostic value than the TNM stage (AUC for the model: 0.812; AUC for TNM stage: 0.658, P < 0.001). A cutoff score of 2.2 by ROC analysis for this model was defined. We included the patients with a risk score of 2.2 or higher in the high-risk group and those lower than 2.2 in the low-risk group. Further Kaplan–Meier analysis showed that this novel model was able to identify a significant difference in DFS between two groups (HR = 6.792, 95% CI: 3.159–14.604, P < 0.001). Subtype analysis indicated that the risk score only had a perfect prognostic value in the luminal subtype (P = 0.002). Moreover, the interaction between the risk score and paclitaxel-based chemotherapy strongly impacted DFS. Patients classified as high risk by this model derive less benefit from paclitaxel (HR = 3.532, 95% CI 1.577–7.913, P = 0.002).
Conclusion: Our results revealed expression of STMN1 and phospho-STMN1 puls clinicopathological characteristics in breast cancer had significant prognostic value in DFS. This model could improve the identification and course prediction of patients with luminal subtypes of breast cancer at the time of primary diagnosis and predict their sensitivity to paclitaxel, thereby enabling oncologists to target those likely to relapse or metastasize for appropriate treatment.
Disclosure of Interest: No significant relationships.

Radiotherapy/IORT

P285
Re-irradiation for locally recurrent refractory breast cancer

T.R. Merino Lara[1]*, W.T. Tran[1], G.J. Czarnota[2]. [1]*Department of Radiation Oncology, Sunnybrook Health Sciences Centre, Toronto, Canada,* [2]*Department of Radiation Oncology, Faculty of Medicine, University of Toronto, Toronto, Canada*

Goals: A retrospective analysis of treatment outcomes of a cohort of patients re-irradiated for recurrent refractory breast cancer (RRBC) was carried out.
Methods: Between 2008-and 2013, 55 women (mean age 60 years) were re-irradiated for locally RRBC. Staging and tumor characteristics of original and recurrent tumor were identified. Outcome measures were captured using a Kaplan–Meier log rank to compare curves and Cox regression for multivariate analysis. Outcomes included (1) overall survival, (2) time to re-treatment, (3) survival without systemic progression, and (4) survival without local recurrence.
Results: 46 Patients were re-treated and 2 were re-treated bilaterally. Seven patients received a 3rd course of radiotherapy treatment. 32 patients had macroscopic disease at the time of re-irradiation, 34 had chemotherapy, and 20 had hormonal therapy. 48 patients were treated using radiation to the breast/chest wall, and 8 had partial breast irradiation. The cumulative dose equivalent to the whole breast and tumor cavity ($\alpha/\beta = 3$) was 9980 cGy and 10,906 cGy, respectively. Patients initially had significant symptoms before radiation due to local recurrence including bleeding, pain, ulceration, lymphedema, brachial plexus dysfunction. The median follow-up time was 17 months for overall survival. Overall survival was 0.73 (SE = 0.07) at 1 year and 0.67 (SE = 0.07) at 2 years. Local control was 0.62 (SE = 0.07) and 0.50 (0.081) at 1 and 2 years, respectively. Acute radiation dermatitis was G1–2, G3, G4 in 14, 4, 1 patients, respectively. One patient presented with necrosis. The most common long term toxicity was G3 fibrosis in 4 patients and telangiectatic changes in 3 patients. Median time to re-treatment was 41 months and to systemic failure was 50 months. Multivariable analysis showed that skin involvement [hazard ratio 6.6 (1.4–31), p = 0.016] and time to local recurrence <2 yr [hazard ratio 3.1 (1.04–9.7), p 0.042] predicted for local recurrence.
Conclusion: High dose re-irradiation is feasible for locally recurrent refractory breast cancer. This approach can have a significant benefit to this very high risk group. Predictors of local progression are needed to best sequence treatment.
Disclosure of Interest: No significant relationships.

P286
Single dose with IORT for breast cancer: initial experience with Latin American women

J.E. Bargalló Rocha[1]*, C.H. Flores Balcázar[2], V.M. Pérez Sánchez[3], J. Corona[1], A. Mohar Betancourt[1], C. Villarreal Garza[1], C. Robles Vidal[1], G. Santiago Concha[2]. [1]*Breast Cancer Department, National Cancer Institute Mexico, Mexico City, Mexico,* [2]*Radiotherapy, National Cancer Institute Mexico, Mexico City, Mexico,* [3]*Pathology, National Cancer Institute Mexico, Mexico City, Mexico*

Goals: Report initial experience with Latin American patients in the National Cancer Institute of Mexico.
Methods: Prospectively gathered estrogen receptor-positive, clinically node-negative patients with invasive breast cancer <2.5 cm receiving using the Intrabeam system were reviewed. IORT-related effects and early postoperative outcome were assessed.
Results: Fifty-five patients (median age 67 years) underwent lumpectomy, sentinel lymph node biopsy, and concurrent IORT from March 2013 to August 2014. Ninety-five percent of patients had invasive ductal histology with a median tumor size of 1.5 cm.
Conclusion: Variety of APBI techniques are currently available for clinical use, our early Latin American operative experience with IORT shows it is well tolerated with low morbidity. The addition of WBI may be necessary in situations for positive margns and/or microscopic nodal disease in patients who do no undergo additional surgery. Implementation of IB impacts treatment planning and operating room use a multidisciplinary breast cancer program. The safety profile, ease of administration, and reduced costs of IB favor its more widespread use in high selected patients with early-stage breast cancer.
Disclosure of Interest: No significant relationships.

P287
Indication of PMRT associated with risk of locoregional and distant recurrence in patients with N1–3 axillary nodal metastasis

M. Ishida[1]*, A. Saruwatari[2], Y. Koi[1], S. Akiyoshi[1], M. Oikawa[1], S. Nishimura[1], C. Koga[1], Y. Nakamura[1], S. Ohno[3]. [1]*Breast Oncology, National Hospital Organization Kyushu Cancer Center, Fukuoka, Japan,* [2]*Surgery, St. Mary's Hospital, Fukuoka, Japan,* [3]*Clinical Research Institute, National Hospital Organization Kyushu Cancer Center, Fukuoka, Japan*

Goals: We evaluated the locoregional recurrence and distant metastasis rate and the risk reduction of the post-mastectomy

radiotherapy (PMRT) with N1–3 breast cancer patients in our country, and we compared those with data of EBCTCG.
Methods: We reviewed retrospectively 2422 cases with Stage I–III primary breast cancer receiving surgery at National Hospital Organization Kyushu Cancer Center between 2000 and 2009. 776 of them underwent mastectomy, and 547 of them received no PMRT, and 129 of them were known biology. We analyzed the risk of locoregional and distant recurrences in relation to clinicopathologial factors, the status of hormone receptor and HER2, especially in cases with N1–3.
Results: Median follow up is 7.3 years. 94 of 129 cases (95%) had adjuvant systemic therapy. Chemotherapy is: anthracycline (A) only or taxanes (T) only or A+T, 82 cases (64%); CMF, 10 cases (8%); other, 2 cases (2%). Endocrine therapy is: SERM +/− LHRH agonist, 52 cases (81%); aromatase inhibitor (AI), 31 cases (24%); switch (SERM→AI), 13 cases (10%). 5-year disease free survival (DFS) is 24.8%, 10-year DFS is 37.2%, which is lower than in EBCTCG (35.6% and 45.5%). In the first recurrence cases, locoregional recurrence only, 12 cases (6%); locoregional + distant recurrence, 4 cases (1.2%); distant metastasis only, 24 cases (20.5%). According to recurrence site, 5-year overall survival (OS) after operation for locoregional recurrence only (100%) is significantly better compared with locoregional + distant recurrence (65%) and distant metastasis only (50%) ($p = 0.02$). 5-year DFS according to biology: HR+/HER2− 81.4%, HR+/HER2+ 72.2%, HR−/HER2+ 61.1%, HR−/HER2− 66.7% ($p = 0.43$). 5-year DFS according to first recurrence site and biology: locoregional group, HR+/HER2− 5 cases (42%), HR+/HER2+ 3 cases (25%), HR−/HER2+ 4 cases (33%); locoregional + distant metastasis group, HR+/HER2− 1 case (25%), HR+/HER2+ 1 case (25%), HR−/HER2− 2 cases (50%); distant metastasis only group: HR+/HER2− 17 cases (71%), HR+/HER2+ 1 case (4%), HR−/HER2+ 4 cases (17%), HR−/HER2− 2 cases (8%). Only HR−/HER2− did not have local recurrence.
Conclusion: The presented trial SUPREMO is progressing at present, and the recurrence rate is estimated to decrease in our country. The indication for PMRT has to be carefully considered, depending on tumor biology and systemic therapy for N1–3 breast cancer patients.
Disclosure of Interest: No significant relationships.

P288
Comparison of hypofractionated and conventional whole breast irradiation for early breast cancer

I. Abdel-Halim[1] *, W. El-Sadda[2], M. Magdy[1], M. El-Ebrashy[1]. [1]*Clinical Oncology, Mansoura University, School of Medicine, Mansoura, Egypt*, [2]*Radiological Sciences, Al-Ghad International Health Sciences Colleges, Najran, Saudi Arabia*

Goals: Radiotherapy has been proven to reduce the risk of local-regional recurrence and to reduce the breast cancer mortality. The large numbers of breast cancer patients who received radiotherapy after breast-conserving surgery in addition to financial considerations has caused many to think that a shortened course of radiotherapy would significantly reduce the radiotherapy machine time, working hours and fewer patients' visits. This study was designed to evaluate the acute skin effects and cosmetic results of short course radiotherapy in women with early stage breast cancer compared to conventional treatment methods.
Methods: One hundred patients, aged over 18 years, with early breast cancer T_{1-2}, N_{0-1}, M_0 who underwent breast-conserving surgery with no immediate surgical reconstruction between January 2012 to October 2013 were randomly assigned to receive conventionally fractionated whole breast irradiation (CF-WBI) administered at 50 Gy in 25 fractions (2 Gy/fraction) over 35 days, group A and group B, where patients received hypofractionated whole breast irradiation (HF-WBI) administered at 40 Gy in 15 fractions (2.66 Gy/fraction) over 21 days using 6 MV linear accelerator. All patients in both groups received additional boost dose 10 Gy in 5 fractions over 5 days to the tumor bed and 2 cm around.
Results: There were no skin changes during the 1st or the 2nd week of treatment in the two groups, cutaneous complications began after the third week as grade I skin toxicity, after termination of the HF-WBI but there were no difference in complication rate after 4 weeks of treatment in the two groups. Six months and one year after treatment, no differences in terms of skin complications or cosmetic outcome were noted in both groups.
Conclusion: Although the use of HF-WBI schedule was associated with desirable outcomes, in terms of skin toxicity and cosmesis, future studies with larger number of patients and longer follow up periods are needed to confirm these results.
Disclosure of Interest: No significant relationships.

P289
The evaluation of safety of postmastectomy radiation therapy after immediate breast reconstruction

Y. Abe*, T. Shien, S. Watanabe, T. Nogami, T. Iwamoto, T. Motoki, N. Taira, J. Matsuoka, Y. Kimata, H. Doihara. *Breast Cancer Treatment and Reconstruction, Okayama University Hospital, Okayama, Japan*

Goals: With the recent advances in oncoplastic breast surgery, immediate breast reconstruction has become a standard surgery practice for primary breast cancer (BC) patients. Also, postoperative radiotherapy play an important role as an adjuvant therapy. Safety of postmastectomy radiation therapy (PMRT) after immediate breast reconstruction is under debate. We are actively doing PMRT for locally advanced breast cancer patients after immediate reconstruction surgery. The aim of this study is to investigate the safety of thePMRT after immediate breast reconstruction.
Methods: Between 2009 and 2014, 164 patients received immediate breast reconstruction at Okayama University Hospital and 24 patients (14.6%) underwent PMRT. We retrospectively investigated pathological characteristics of tumor, radiation dose distribution, adverse event, and the timing of PMRT.
Results: The median age was 46 years (range 24–65). Clinical T stage was Tis: 27 (22%), T1: 19 (18%), T2: 38 (35%), T3: 14 (13%), T4: 6 (6%). In total 20 (83%) of 24 patients had axillary lymph node metastasis more than 4 nodes and 4 patients had large tumor with skin invasion. 5 patients (20%) were Luminal A, 9 patients (37%) were luminal B, 2 (8%) were HER2 enriched type and 3 (12%) were triple negative breast cancer. Reconstruction methods were latissimus dorsi flaps (LD): 4 (16%), DIEP flap: 10 (41%), tissue expander/implant (TE): 9 (37%). Neoadjuvant chemotherapy was performed on 12 (50%) of 24 patients. The distribution of irradiation field is almost even (98–104%). Adverse events were experienced by most patients (70%), and the most frequently occurring type of complications was dermatitis, but no accidents such as infection, or fat necrosis occurred. The duration from the operation until starting PMRT widely varied depending on the method of reconstruction; the duration of TE patients was longer than immediately autologous patients. 3 patients had distant metastasis, and there was no local recurrence except for one patient who had triple negative, inflammatory breast cancer.
Conclusion: PMRT was performed equally to the reconstructed breast and regional lymph node. No serious complications were occurred. Start of radiotherapy for TE reconstructed patients is more likely to be delayed compared with patients having undergone breast reconstruction with autologous tissue.
Disclosure of Interest: No significant relationships.

P290

Postmastectomy radiation in patients with negative lymph nodes after neoadjuvant chemotherapy

M. He[1] *, J. Li[2], X. Ni[1], S. Chen[1], Y. Jiang[1], X. Yu[2], Z. Shao[1], G. Di[1]. [1]*Breast Surgery, Fudan University Shanghai Cancer Center, Shanghai, China,* [2]*Radiotherapy, Fudan University Shanghai Cancer Center, Shanghai, China*

Goals: The aim of this study is to evaluate the role of postmastectomy radiotherapy (PMRT) in clinical stage II and III breast cancer patients who achieved negative node status (pN0) after neoadjuvant chemotherapy (NAC).
Methods: We retrospectively analyzed the outcomes of 143 patients with pN0 after NAC and mastectomy at Fudan University Shanghai Cancer Center. In total, 103 (72%) patients received PMRT, and 40 (28%) patients did not. Univariate and multivariate survival analyses were performed to evaluate the effect of PMRT on locoregional recurrence-free survival (LRRFS) and overall survival (OS) of the two groups.
Results: There were no differences between the two groups with respect to age, nuclear grade, estrogen receptor (ER) status, HER2/neu receptor status, lymphovascular space invasion (LVSI) status or pathological tumor size. However, a significantly higher proportion of patients in the irradiated group (64%) had clinical lymph node involvement than in the nonirradiated group (45%). After a median follow-up time of 49 months, 10 locoregional recurrence events occurred. For the entire cohort of patients, use of radiation therapy improved the 5-year LRRFS rate (94.5% vs. 80.2%; P = 0.032) but not the 5-year OS rate (92.2% vs. 88.7%; P = 0.617). In the subset of patients who presented with clinically stage II disease, the 5-year LRRFS and 5-year OS did not differ significantly between the PMRT and no-PMRT group (96.3% vs. 91.3%; P = 0.190 and 96.2% vs. 91.3%; P = 0.199, respectively). For patients with stage III disease at diagnosis, a trend was seen toward better local regional control with PMRT (the 5-year LRRFS rate was 92.7% vs. 64.2%; P = 0.063), although the benefit from radiation with respect to OS was not significant (5-year OS rate was 88.1% vs. 85.2%; P = 0.657). On multivariate Cox regression analyses, the clinical tumor size (hazard ratio [HR], 3.27; 95% confidence interval [CI], 1.05–10.18; P = 0.041), pathologic breast tumor response (HR, 1.82; 95% CI, 1.11–3.77; P = 0.046) and delivery of radiation therapy (HR, 1.27; 95% CI, 1.08–9.25; P = 0.047) were independent predictors of locoregional recurrence.
Conclusion: For patients who achieved pN0 after NAC, PMRT seemed to provide a clinical benefit for breast cancer patients with stage III disease. Omission of PMRT in patients with stage II disease did not increase the risk of locoregional recurrence and death.
Disclosure of Interest: No significant relationships.

P291

Influence of radiation boost on local control in patients with ductal carcinoma in situ

J. Gugic[1] *, A. Gojkovic Horvat[1], C. Grasic Kuhar[2], I. Ratosa[1], T. Marinko[1], E. Majdic[1], S.M. Paulin Kosir[1], P. Korosec[1], V. Jugovec[1], E. Matos[2]. [1]*Department for Radiation Oncology, Institute of Oncology, Ljubljana, Slovenia,* [2]*Department for Medical Oncology, Institute of Oncology, Ljubljana, Slovenia*

Goals: Whole breast radiotherapy (WBRT) after breast conserving surgery (BCS) for ductal carcinoma in situ (DCIS) halves the rate of local recurrence. However, the role of radiation boost to the tumor bed is still unclear.
Methods: We analysed medical charts of all women diagnosed for DCIS and treated with BCS and WBRT +/− radiation boost to the tumor bed in Department of Radiation Oncology (Institute of Oncology Ljubljana) from January 1994 till December 2009.
Results: 217 cases of DCIS, treated with BCS and WBRT were identified, 168 (77%) of them received radiation boost. The dose of the boost varied from 7.5 Gy (in three daily fractions) to 16 Gy (in eight daily fractions), but most women (133/160, 80%) received additional 10 Gy (in four or five daily fractions) with boost. After median follow up of 88 months (6–237 months), cumulative local recurrence rate for boost and non-boost group was 8.9% and 10.2% (p = 0.105), respectively.
Conclusion: According to our results, administration of radiation boost to the tumor bed after BCS and WBRT for DCIS is not associated with lower recurrence rate.
Disclosure of Interest: No significant relationships.

P292

Partial-breast irradiation using multicatheter brachytherapy: a 6-year experience with 252 cases

K. Sato[1] *, Y. Mizuno[1], H. Fuchikami[1], N. Takeda[1], T. Shimo[2], J. Kubota[2], M. Kato[2]. [1]*Department of Breast Oncology, Tokyo-West Tokushukai Hospital, Tokyo, Japan,* [2]*Department of Radiation Oncology, Tokyo-West Tokushukai Hospital, Tokyo, Japan*

Goals: Breast-conserving therapy (BCT) consists of breast-conserving surgery followed by adjuvant breast irradiation, and whole-breast irradiation (WBI) is generally recommended as radiation therapy. The efficacy of partial-breast irradiation (PBI) has been investigated, and we had initiated a prospective observational study on brachytherapy PBI. Here, we report a 6-year experience of PBI to compare the results of WBI with PBI.
Methods: We evaluated consecutive patients with T ≤3.0 cm N0–1 breast cancer who underwent BCT between October 2008 and December 2014. PBI was considered to be an alternative to WBI in patients meeting the eligibility criteria of age ≥40 years, unifocal disease, sentinel nodes negative for metastases, and no prior treatment. WBI patients received 50 Gy in fractions of 2 Gy to the entire breast. Patients with risk factors, such as positive margins and young age (<40 years old), generally received a subsequent 10-Gy boost using electrons to the tumor bed. Regional nodal irradiation was added in patients with ≥4 positive nodes. In PBI, applicators for the introduction of iridium wires were inserted following the simulation in preoperative planning by enhanced CT. The PTV included the surgical cavity delineated by ligating clips plus a 10–20-mm margin. The maximum dose to the skin and chest wall was kept to less than 75% of the prescription dose. Dose-volume histograms were provided by postoperative CT. PBI was performed in an accelerated fashion with a dose of 32 Gy in eight fractions over 5–6 days.
Results: Of 374 patients who underwent BCT, 122 received WBI and 252 received PBI. The mean age of WBI patients (51.5 years) was significantly lower than that of PBI patients (55.8 years, p < 0.005). At a median follow-up of 3.0 years, the actual rate of ipsilateral breast tumor recurrence was 2.1% and 1.0% in WBI and PBI patients, respectively (p = 0.23). There was no significant difference in the 3-year probability of disease-free survival (96.3% and 97.8%; p = 0.50), and overall survival (97.7% and 99.5%; p = 0.29).
Conclusion: Although this study was based on a small number of patients with a relatively short follow-up period, the feasibility of BCT with PBI using multicatheter brachytherapy to achieve acceptable clinical outcomes in Japanese patients was demonstrated.
Disclosure of Interest: No significant relationships.

P293

PFT change during adjuvant hypofractionated radiation with simultaneous integrated boost for EBC

D. Mondal[1] *, P.K. Julka[1], M. Jana[2], M.A. Laviraj[3], R. Guleria[4], S.V.S. Deo[5], S. Roy[1], K.P. Haresh[1], D.N. Sharma[1], G.K. Rath[1].
[1]Department of Radiation Oncology, All India Institute of Medical Sciences, New Delhi, India, [2]Department of Radiology, All India Institute of Medical Sciences, New Delhi, India, [3]Department of Medical Physics, Radiation Oncology, All India Institute of Medical Sciences, New Delhi, India, [4]Department of Pulmonary Medicine, All India Institute of Medical Sciences, New Delhi, India, [5]Department of Surgical Oncology, All India Institute of Medical Sciences, New Delhi, India

Introduction: An early report of PFT changes during the course of radiation in patients with early breast cancer (EBC) receiving hypofractionated whole breast radiotherapy (WBRT) with simultaneous integrated boost (SIB) is being presented.
Aims and objectives: To prospectively assess radiation pneumonitis in patients undergoing hypofractionated WBRT with SIB technique and to correlate with various dosimetric parameters.
Methods: Patients with EBC undergoing breast conserving surgery requiring WBRT were enrolled in a prospective phase I study. Radiotherapy was planned with SIB. Whole breast and tumor cavity was treated to a dose of 40.5 Gy and 48 Gy respectively in 15 fractions over 3 weeks. Planning was done using Monaco® planning software (Elekta, Sweden). Treatment was delivered with 6 MV photon from Elekta Synergy-S machine. PFT was done every week during radiation, at 1 month and 3 months. Toxicity was scored as per RTOG toxicity criteria. Mann–Whitney U test was used for comparative analysis of the means of PFT parameters. Time trend of PFT parameter changes were analysed. P value of 0.05 or less was considered to be statistically significant.
Results: Data of five patients are being presented. None of them showed any clinical feature of radiation pneumonitis till 3 month after radiation. Mean conformity index of whole breast was 0.96 and that of the boost volume was 0.97. Mean D_{mean}, D_{max}, V_{20} and V_5 for ipsilateral lung were 12.4 Gy, 48.9 Gy, 21% and 61.2% respectively. On statistical analysis, a significant correlation was noted between change of FVC from first week to second week of radiation and ipsilateral lung V_5. Patients with V_5 >61.2% showed a mean 15% reduction of FVC whereas those with V_5 <61.2% showed a mean 11% increment of FVC ($p = 0.022$). The mean change of FEV1/FVC from first week to second week of radiation was significantly associated with ipsilateral lung D_{mean}, D_{max} and V_{20}. Patients with D_{mean} >12.6 Gy, D_{max} >48 Gy and V_{20} >21% showed a mean 6% increase in FEV1/FVC and those with D_{mean} <12.6 Gy, D_{max} <48 Gy and V_{20} <21% showed a mean 9% reduction of FEV1/FVC ($p = 0.049$). Ipsilateral lung V_5 showed only a borderline significance with change in FEV1/FVC from first week to second week of radiation. The pattern of change in FEV1/FVC during early period may be attributed to a reduction of FVC, which may be due to a larger volume of lung being irradiated to a low dose, causing more alveolar damage and gradual stabilization over later period of radiation.
Conclusion: Though radiation pneumonitis is a well known complication after breast radiotherapy, clinical data after 3DRT, IMRT or arc therapy is largely unavailable. The present study throws light on the clinical lung function parameters and their association with dosimetric variables, in absence of symptomatic acute pneumonitis. As the study is ongoing, further follow up with more patients will definitely be meaningful to correlate the changes in PFT parameters and long term toxicity if any.
Disclosure of Interest: No significant relationships.

P294

Breast biopsies during follow up after intraoperative radiotherapy in early breast cancer patients

N. Sikorsky[1] *, V. Schneider[2], J. Goldman[2], M. Leviov[2], L. Leitzin[3], S. Keren[4], M. Steiner[3]. *[1]Oncology Department, Linn Medical Center, Haifa, Israel, [2]Radiology, Lin Medical Center, Haifa, Israel, [3]Oncology Department, Lin Medical Center, Haifa, Israel, [4]Linn Medical Center, Haifa, Israel*

Goals: Intraoperative breast irradiation (IORT) is becoming a new treatment alternative to the standard adjuvant whole breast irradiation in low risk early breast cancer patients. From 2006 we offer IORT to a well selected population of breast cancer patients. A single dose of 20 Gy is administered to the tumor bed by low energy X-ray generating system (IntraBeam, Zeiss). This relatively high single radiation dose may cause significant and unusual post surgery changes in breast tissue that could complicate the radiologic follow up and lead to additive diagnostic procedures.
Methods: We analyzed the first consecutive 300 patients treated by IORT. During median follow up period 56 months (1–96) 38 patients (13%) underwent core biopsy due to clinical or imaging findings in the treated breast.
Results: In 12/38 patients (32%) breast tumor recurrence was diagnosed. In 26/38 patients (68%) the pathology showed benign tissue. In this subgroup of 26 patients the reasons for biopsy were ultrasound findings at the lumpectomy scar in 13 (50%) mammography findings (usually calcifications) around the surgical bed in 8 (19%) and clinical palpable masses in 5 patients (19%). The median time between surgery and core biopsy seems to be shorter in patients with mammography findings (25 months, 16–34) than in patients with palpable findings (38 months, 16–51) or ultrasound lesions (69 months, 14–83). This difference is probably due to the fact that post lumpectomy with IORT mammography calcifications represent fat necrosis and appear earlier while ultrasound and palpatory findings represent fibrotic changes which appear later.
Conclusion: Single high dose irradiation dose administered to the breast tissue is causing unusual clinical and imaging findings. These findings, which represent benign lesions in 68% of patients, lead to increased need for invasive diagnostic procedures like breast core biopsy.
Disclosure of Interest: No significant relationships.

P295

Comparison of complication, cosmetic outcome with or without irradiation after breast reconstruction

J. Ishiguro[1] *, M. Sawaki[1], M. Hattori[1], N. Kondou[1], A. Yoshimura[1], H. Kotani[1], Y. Adachi[1], T. Hisada[1], S. Okumura[2], H. Iwata[1].
[1]Department of Breast Oncology, Aichi Cancer Center, Nagoya, Japan, [2]Department of Plastic and Reconstructive Surgery, Aichi Cancer Center, Nagoya, Japan

Goals: To study complications of irradiation following immediate breast reconstruction using autologous tissue in patients compared with those having no irradiation, and to find predictive factors for complications. Irradiation for chest wall is recommended to improve the outcome in high-risk cases with mastectomy by guidelines of all over the world. However, the safety of irradiation after reconstruction with autologous tissue is still unclear.
Methods: 125 patients who received mastectomy for primary breast cancer and breast reconstruction using autologous tissue with or without radiation therapy between January of 2011 and September of 2014 were included in the study. 106 patients were evaluated, excluding 3 patients with prereconstruction irradiation for metachronous breast cancer, and 16 patients without data of cosmetic outcome. We compared the irradiated group (RT) to the non-irradiated group (OP) after breast reconstruction for cosmetic

outcomes and complications attributable to risk factors: diabetes mellitus, obesity, and smoking. Both groups were evaluated at six months after reconstruction. Cosmetic score was defined as using a subscale consisting of volume, contour, placement of infra mammary fold, scar, hardness, and color using a 0–2 point scale. Full marks were 11 points. Complications involved mastectomy skin flap necrosis (SFN), and fat necrosis (FN).

Results: With a median follow-up of 32 months, no patients in either group developed local recurrence. In OP (n = 94), 61 (65%) patients underwent transverse rectus abdominis myocutaneous flap (TRAM), and 33 (35%) had latissimus dorsi flap (LD). In RT (n = 12), 10 (83%) had TRAM, 2 (17%) had LD. Cosmetic score was 8 points in OP, 7.75 points in RT, respectively. SFN/FN occurred in 20 (21%)/4 (4%) patients and 1 (8.3%)/1 (8.3%) with OP and RT, respectively. We investigated association of each risk factor with cosmetic outcome and complications. Smoker's cosmetic score average was 7.2 points (n = 5) in OP, 5 points (N = 1) in RT, without any complications. For patients with diabetes mellitus, score was 8.6 (N = 3) in OP with 2 FN. For obese patients (BMI ≥25), score was 8.2 (n = 22) in OP.

Conclusion: Irradiation after immediate breast reconstruction using autologous tissue was cosmetically feasible.

Disclosure of Interest: No significant relationships.

P297

Radical IORT: pros and cons; comparison of two trials ELIOT and TARGIT-A in breast cancer management

N. Nafissi, M. Khayamzadeh, S. Mahdavi, H. Mirzaei, Z. Zeinali, M. Hadizadeh, M. Samsami, M. Moradi-Joo, M. Malekzadeh, M.E. Akbari*. *Cancer Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

Goals: IORT is an accepted standard treatment for early stages of breast cancer in selected cases. This is proven in two large trials: ELIOT and TARGIT-A based on electron high voltage beam and low kV X-ray energy respectively.

Methods: Published results of the two trials aimed to evaluating local recurrence as the final outcome. In this study these results were compared with each other.

Results: In the ELIOT study the local recurrence rate is 4/4% versus 0.4% in patients who received IORT and EBRT, in comparison to 3.2% and 1.3% in the TARGIT-A trial; these differences needs to be under more consideration regarding the efficacy and beneficence of IORT. Hereby we are going to analyze the data of these two trials to confirm the strategy of IORT in breast cancer as boost or radical modalities. Patient selection according to classification of ASTRO or ESTRO guidelines confirmed the local recurrence rate of IOERT (ELIOT) in low risk patients similar to TARGIT decrease to less than 1.9%.

Conclusion: Statistical analysis revealed that in patients of both trials with matching clinical, pathological and biological profile for both methods, the radical IORT using electron and low kV X-ray are effective and acceptable. It seems in patients with low risk factors, IORT is more effective than EBRT. We compared ELIOT and TARGIT-A trial documents and found all of similarity and difference and referred to these two trials recommending using IORT for selected cases of breast cancer with at least non inferiority in DFS, OS, with superiority in cosmetic, non breast death and more.

Disclosure of Interest: No significant relationships.

P298

Cardiac toxicity after breast cancer treatment

D. Gabryś[1]*, A. Walaszczyk[2], K. Jelonek[2], K. Trela-Janus[1], S. Blamek[1], A. Namysł-Kaletka[1], I. Wziętek[1], R. Kulik[3], A. Piela[4]. *[1]Department of Radiotherapy, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, Gliwice, Poland, [2]Center for Translational Research and Molecular Biology, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, Gliwice, Poland, [3]Radiotherapy and Brachytherapy Planning Department, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, Gliwice, Poland, [4]Oncological and Reconstructive Surgery Department, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, Gliwice, Poland*

Goals: Radiation and anthracyclines are known to induce cardiac damage. Despite the use of 3D planning the heart is still irradiated with variable doses, therefore this problem needs further investigation. We perform an analysis of cardiac function in the left sided breast cancer survivors. Patients were treated with surgery alone (S), additional radiation (RT), additional anthracycline based chemotherapy (A) or both (RA).

Methods: A total of 100 patients were subjected to cardiac consultation more than 8 years after primary treatment. We performed ECG and ECHO (in part of patients we also had an ECG and ECHO performed before surgery), blood tests, chest X-ray. We also collected additional relevant information on patients (history, comorbidities, current treatment, etc.). Distribution of patients was as follows 56% RA arm, 18% S, 13% RT, 13% A. The mean time from the beginning of the treatment to examination was 12.6 years (8–15.9) in S, 13.8 (9.8–16.9) in A, 9.2 (8–15.3) in RT, 9.6 (8.1–14.5) in RA. The majority of patients were treated with amputation (69%), the remaining with BCT. In chemotherapy arms 51% were treated with FAC, 32% with CAF, 14% with AC, and 3% with TE. Hormonal treatment was given to 62% of patients, in the majority it was tamoxifen-based. Radiotherapy dose varied between 50–70 Gy.

Results: There was no difference in ejection fraction (EF) between the groups: median 55 (50–60) in S, 55 (45–60) in A, 55 (50–65) in RT and 55 (45–67) in RA. Other evaluated parameters as size of right and left ventricle, left atrium, diameter of septum and posterior wall also did not differ between groups. In the whole group in 8% of patients we observed clinically symptomatic cardiac motion abnormalities (3 patients in RA and 1 patient in S, R and A), 45% had mild impaired contractility of no clinical significance, in 47% the functioning of the heart was in the normal range. In 56% of patients there were other cardiovascular disorders as hypertension, hypercholesterolemia, arrhythmias, valves disorders. We found only two patients who developed substantial changes in the heart related to the treatment; one was treated with CAF, second with combination CAF/RT.

Conclusion: We did not notice significant increase in cardiac disorders in long-term survivors after breast cancer radiation and anthracyclines treatment.

Disclosure of Interest: The research received funding from National Science Center Poland under grant no. N N 402 685640.

P299

Local recurrence after breast conserving surgery for ductal carcinoma in situ

A. Gojkovic Horvat[1] *, J. Gugic[1], I. Ratosa[1], E. Majdic[1], T. Marinko[1], S.M. Paulin Kosir[1], V. Jugovec[1], P. Korosec[1], A. Demsar[2], C. Grasic Kuhar[2]. *[1]Department for Radiation Oncology, Institute of Oncology, Ljubljana, Slovenia, [2]Department for Medical Oncology, Institute of Oncology, Ljubljana, Slovenia*

Goals: To evaluate the effect of margin status on local recurrence after breast conserving surgery (BCS) with or without whole breast radiotherapy (WBRT) for women affected by ductal carcinoma in situ (DCIS).
Methods: We analysed data of all eligible women with DCIS treated between January 1994 and December 2009 at the Institute of Oncology Ljubljana.
Results: Data of 463 patients were analysed. The first group of 246 patients (53.1%) was treated with BCS only. In this group 8 (3.2%) patients had positive margins (PM), 57 (23.2%) had close (0.1–2 mm) margins (CM), 44 (17.9%) had negative (>2 mm) margins (NM) and for 137 (55.7%) margin status was negative, but not defined in millimeters (NMND). The second group, 217 patients (46.9%), received postoperative WBRT. In this group 15 patients (6.9%) had PM, 68 (31.3%) had CM, 43 (19.8%) had NM, and for 91 (42.5%) margin status was NMND.
After median follow-up of 88 months (6–236 months) the local recurrence rates for the BCS-only group and the BCS+WBRT group were 37/246 (15%) and 20/217 (9.2%), respectively ($p = 0.036$). According to margins, the results for the BCS-only and BSC+WBRT groups were 5/8 (62.5%) and 1/15 (6.7%) for those with PM ($p = 0.014$), 12/57 (21%) and 4/68 (5.9%) for those with CM ($p = 0.009$), 4/44 (9.1%) and 6/43 (13.9%) for those with NM ($p = 0.349$), and 16/137 (11.7%) and 9/91 (9.9%) for patients with NMND ($p = 0.662$), respectively.
Conclusion: WBRT is the most effective treatment to avoid local recurrence in patients with positive and close margins.
Disclosure of Interest: No significant relationships.

P300

Cone beam computed tomography for accelerated partial breast irradiation: our experience

M. Valli *, M.F. Belosi, P. Fanti, P. Pittoni, Y. Kaloyan, F. Martucci, N.A. Che, G. Pesce, A. Richetti. *Radiation Oncology, Oncology Institute of Southern Switzerland, Bellinzona, Switzerland*

Goals: The purpose of the present study was to report how 5 titanium clips in the surgical bed and Cone Beam Computed Tomography (CBCT) before radiotherapy could improve target detection in external beam Accelerated Partial Breast Irradiation (APBI).
Methods: Five radiopaque clips were placed after surgery in 26 patients to correcly delineate the surgical bed and used as reference markers for Image Guided Radiotherapy. CBCT and matching of the surgical clips were performed before each session.
Results: The isocenter shifts along the 3 main axes were registered. The vertical, longitudinal and lateral displacements were on average 3.3 ± 2.4, 2.6 ± 1.3 and 2.3 ± 1.2 mm, with maximum range of 14, 11 and 12 mm, respectively.
Conclusion: In our experience daily CBCT reduces uncertainties due to breathing and patient motion in case of external beam APBI. We are still investigating if this could allow a feasible reduction of the safety margins around Clinical Target Volume.
Disclosure of Interest: No significant relationships.

P301

Hypofractionated WBI plus IOERT-boost in early stage breast cancer (HIOB): updated results

G. Fastner[1] *, R. Reitsamer[2], D. Murawa[3], P. Milecki[4], E. Hager[5], A. Ciabattoni[6], R. Brimmer[7], J. Reiland[8], W. Budach[9], F. Sedlmayer[1]. *[1]Radiotherapy and Radio-oncology, Paracelsus Medical University, Landeskrankenhaus, Salzburg, Salzburg, Austria, [2]Special Gynecology and Gynecology, Paracelsus Medical University, Landeskrankenhaus, Salzburg, Salzburg, Austria, [3]Surgical Oncology and General Surgery, Wielkopolska Cancer Centre, Poznań, Poland, [4]Radiation Oncology and Radiotherapy, Wielkopolska Cancer Centre, Poznań, Poland, [5]Radiotherapy and Radiooncology, Landeskrankenhaus, Klinikum Klagenfurt, Klagenfurt, Austria, [6]Radiotherapy, San Filippo Neri Hospital, Rome, Italy, [7]General Surgery, St. Lukes Hospital, Cedar Rapids, United States of America, [8]Surgery, Avera McKennan Hospital and University Health Center, Sioux Falls, United States of America, [9]Radiotherapy and Radiooncology, University Clinic Düsseldorf, Düsseldorf, Germany*

Goals: To assess the role of an intraoperative electron boost (IOERT) in combination with hypofractionated whole breast irradiation (WBI) in terms of in-breast tumor control and cosmetic outcome.
Methods: Starting in January 2011, a prospective multi-center single arm trial is conducted by the ISIORT. Patients receive an IOERT boost of 10 Gy (Dmax 11.1 Gy) followed by a WBI of 40.5 Gy in 15 fractions (2.7 Gy single dose). 5-year in-breast-recurrence rates will be analyzed in 3 different age groups (35–40 y, 41–50 y, >50 y) and tested against the respective best published results from randomized prospective trials by the use of a sequential probability ratio test (SPRT). Acute reactions are assessed by CTC-scoring, late reactions according to LENT-SOMA criteria. Cosmesis is evaluated by a 5-point-Scoring System (van Limbergen, double evaluation) starting prior to WBI on the basis of repeated photodocumentation in standardized positions.
Results: As of August 2014, within ten active institutions 645 patients have been recruited, 481 of them already in follow-up. For IOERT, the median energy chosen was 7 MeV (range 4–12) with median tube diameters of 6 cm (4–8) and mean prescription depths of 19 mm (6.2 SD), resulting in mean D90 volumes of 19 ml. Perioperatively, no major complications were observed. Four weeks after the end of WBI and 479 evaluated patients, 177 (37%) showed no reactions (CTC 0), 277 (58%) presented with faint (CTC 1) and 24 (5%) with moderate to brisk erythema (CTC 2), respectively. G0-I late reactions (LENT-SOMA) occurred in a mean frequency of 97%, 96%, 98% and 96% after 4–5 months, 1, 2 and 3 years follow-up, respectively. Cosmesis was assessed postoperatively by patients themselves (subjective) and doctors (objective). Baseline appearance was first assessed after wound healing prior to WBI and scored as sufficient (excellent and good) in 69%/74% of 614 subjective/447 objective evaluations. Respective results at 4–5 months, one, two years and three years post RT were 87%/75% of 418/378, 89%/77% of 306/164, 83%/75% of 132/107 and 84%/87.5% of 31/24 ratings. At a median follow-up period of 12.6 months (range 0.5–37), three patients were metastasized, two died, no in-breast recurrence was noted.
Conclusion: Tolerance of a combined IOERT/hypofractionated WBI regimen is excellent, acute reactions moderate and late reactions insignificant in short-term assessment. With regard to postoperative appearance, early cosmetic results are not impaired. Both tumor control and cosmetic outcome have to be evaluated on long-term follow-up.
Disclosure of Interest: No significant relationships.

P302

Postoperative radiotherapy in elderly patients with breast cancer: does it influence survival?

J. Mladenovic[1] *, S. Susnjar[2], S. Pupovac[2], O. Djokic[3], D. Gavrilovic[4]. *[1]Radiotherapy, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia, [2]Daily Chemotherapy Hospital, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia, [3]Medical Center Sabac, Sabac, Serbia, [4]Data Center, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia*

Goals: To evaluate the association of postoperative radiotherapy (PRT) and disease outcome in elderly breast cancer (BC) patients (pts).
Methods: We analyzed a group of BC pts ≥65 years old, diagnosed in stage 1–3, who were treated with surgery [radical mastectomy (RM), breast conserving surgery with axillary dissection (BCSAD) and wide tumor excision (WTE)] at our Institute during 2001/2002. After surgery, the majority of patients received adjuvant (adj) endocrine therapy (tamoxifen, TAM) or adj CMF chemotherapy (CHT) or both, and some of them had PRT, as per protocol. PRT was given to pts after BCSAD and to high risk pts after RM. The irradiation volumes were breast or chest wall and regional lymph nodes in cases of ≥4 positive nodes. Tumor dose was 50 Gy in 25 fractions over 5 weeks to the breast and chest wall, and 48 Gy in 24 fractions over 5 weeks to the regional lymph nodes. The main end points were disease free survival (DFS) and overall survival (OS). Statistics included Pearson c^2 test, Fisher exact test and and Log-rank test.
Results: A group of 98 elderly pts median age of 70 years (range 65–79) were followed for 9 years (median of 109 months (range 7–148). Majority of pts were diagnosed in stage 2 BC (52%), 67/98 (68%) pts undergone RM, 13/98 (13%) pts BCSAD and 18/98 (18%) pts WTE. PRT was given to 32/98 (33%) pts, in 19 pts after RM, in 8 pts after BCSAD and in 5 pts after WTE. PRT was combined with adj CMF CHT in 5 pts, with adj TAM in 16 pts, and with adj CMF+TAM in 11 pts. Significantly higher number of pts with ≥4 involved nodes received PRT (10/15) compared to node-negative pts (7/41), $p = 0.001$. Further on, significantly higher number of pts with HR-negative BCs received PRT (10/16) compared to HR-positive (20/69) BC pts. Disease relapse was confirmed in 31/98 (32%) pts, while 51/98 (52%) died, with 28/51 who died w/o BC progression. Loco-regional relapse developed in 7/98 (7%) pts and 5 of them undergone PRT. There were no difference in DFS and OS between pts with PRT and pts w/o PRT. We also looked at possible influence of PRT on survival of pts who died w/o BC relapse: there were no difference in OS between PRT and non-PRT subgroups.
Conclusion: our results did not show that PRT influences survival in elderly BC pts.
Disclosure of Interest: No significant relationships.

P303

Triple negative breast cancer patients treated by boost-IOERT during breast conserving surgery

G. Fastner[1] *, C. Hauser-Kronberger[2], A. Moder[3], R. Reitsamer[4], F. Zehentmayr[1], P. Kopp[1], C. Fussl[1], T. Fischer[4], O. Dietze[2], F. Sedlmayer[1]. *[1]Radiotherapy and Radio-oncology, Paracelsus Medical University, Landeskrankenhaus, Salzburg, Salzburg, Austria, [2]Pathology, Paracelsus Medical University, Landeskrankenhaus, Salzburg, Salzburg, Austria, [3]Institute of Inborn Errors In Metabolism, Paracelsus Medical University, Salzburg, Salzburg, Austria, [4]Special Gynecology and Gynecology, Paracelsus Medical University, Landeskrankenhaus, Salzburg, Salzburg, Austria*

Goals: To evaluate retrospectively survival and local control rates (LCR) of triple negative breast cancer (TNBC) subtypes classified as 5 marker negative (5NP) and core basal (CB), respectively, after breast conserving surgery (BCS) and intraoperative boost radiotherapy with electrons (IOERT) followed by whole breast irradiation (WBI).
Methods: 71 TNBC patients were enrolled. All patients were treated with BCS including axillary lymph node dissection and received IOERT with 9.6 Gy (median Dmax) followed by normofractionated WBI to median total doses of 54 Gy. Chemotherapy was applied in a neoadjuvant (12%), adjuvant (75%) or combinational setting (7%).
Results: After 97 months (medFU, range 4–170), 5 In-breast tumor recurrences (IBTR) were detected (7.0%). For all patients, 8-year actuarial rates for local control (LCR), metastases free survival (MFS), disease specific survival (DSS), and overall survival (OS) amounted 89%, 75%, 80%, and 69%, respectively. LCR seemed to be negatively influenced by tumor grading: G1/2 (both CB and 5-NP): 100% vs G3: 88% (5NP) and 90% (CB) ($p = 0.65$ and 0.82, n.s.). For DSS, subgroup analyses revealed a trend of inferior outcome for CB compared to 5-NP subtypes: 5-NP: 83% vs CB:54% for G1/G2 tumors, $p = 0.28$; 5-NP: 90% vs CB: 79% for G3 tumors, $p = 0.31$. Only the difference in DSS of the best-prognosis group 5-NP/G3 versus the worst-prognosis cohort CB/G1/2 was statistically significant: 90% vs. 54% ($p = 0.03$).
Conclusion: Boost-IOERT provides acceptable long-term in-breast control also in TNBC. CB-subtype and tumor grading G3 are negative predictors for cancer specific survival and LCR, respectively.
Disclosure of Interest: No significant relationships.

P304

Radiation dose for left anterior descending coronary artery in patients treated with BCT

M. Yoshida *, A. Harada, H. Okubo, T. Asari, T. Toshiyasu, T. Kozuka, M. Sumi, M. Oguchi. *Radiation Oncology, Cancer Institute Hospital of JFCR, Tokyo, Japan*

Goals: Breast conserving therapy (BCT) is standard treatment for early stage breast cancer patients. Because of their good prognosis, later radiation induced toxicity became more concerned. From 2013, we have avoided Left Anterior Descending (LAD) Coronary Artery from the radiation volume to prevent ischemic heart disorders as possible as we could, if tumor bed was not blocked.
Methods: In this study, we compared the radiation dose for LAD in the left side breast cancer patients who were treated with BCT from Jan 2008 to Dec 2010 and Jan 2013 to Oct 2014. Non-contrasted, 5 mm slice-thickness CT was used for 3D-conformal radiation planning, and LAD irradiated dose and volume was estimated by Analytical anisotropic algorithm. Contoured LAD position was checked by beam's eye view, and spared using Multi-leaf collimator (MLC).
Results: From Jan 2008 to Dec 2010 and Jan 2013 to Oct 2014, 32 and 35 patients were treated with BCT consisted with surgery and 50 Gy of radiation therapy for whole breast and 10–16 Gy boost for tumor bed. We exclude 2 patients with 4 axillary lymph node metastases who were irradiated to the internal mammary and supraclavicular lymph nodes area, and 1 patient who undergo 30 Gy for whole breast radiation therapy. Median age of each group was 46 (range: 28–76) and 50 (range: 21–70), respectively. Clinical staging distribution of each group was IA/IIA=2/30 and 0/IA/IIA/IIB=3/12/13/4. Pathological staging distribution was 0/IA/IIA/IIB=4/7/14/7 and 0/IA/IIA/IIB=5/12/11/4. The primary tumor site in the breast was inside/outside=12/20 and 13/19, respectively. The average maximum dose of the LAD of 2 groups were not statically significant different; 42.0 Gy (range 3.85–50.93 Gy, median 47.4 Gy) in former period and 42.4 Gy (range 6.92–50.81 Gy, median 45.9 Gy) in later period, respectively. The average mean dose of the LAD was 13.0 Gy (range 2.098–35.807 Gy, median 11.9 Gy) and 15.8 Gy (range 3.428–35.854 Gy, median 14.6 Gy).
Conclusion: Even avoiding LAD from irradiation field with MLC block, the average mean dose of the LAD was still high to reduce the incidence of ischemic heart disorders.
Disclosure of Interest: No significant relationships.

Surgery

P306

Preoperative diagnosis for metastasis of sentinel lymph node (SLN) using 3D CT lymphography (CTLG)

M. Nakagawa*, M. Morimoto, H. Takechi, Y. Tadokoro, A. Tangoku. *Thoracic, Endocrine Surgery and Oncology, The University of Tokushima, Tokushima, Japan*

Goals: ACOSOG Z0011 showed the possibility of omitting axillary lymph node dissection in T1–2 breast cancer with SLN metastasis. CTLG with a nonionic water-soluble iodinated contrast medium allows quick visualization of direct connection between primary SLN and its afferent lymphatic channels with providing detailed anatomy at the time of preoperative CT scan. We hypothesize that LN metastasis can be diagnosed using CTLG by detecting the obstruction of the lymph vessel and tumor replacement, and established the criteria for diagnosis of metastatic SLN. According to the criteria, 467 patients' CTLG showed accuracy of preoperative diagnosis for metastasis was 87.3%, sensitivity was 58.8% and specificity was 92.4%. To improve the accuracy rate, we examined by diagnose into three categories; metastasis, equivocal and non-metastasis. Our objective is to evaluate the accuracy for diagnosis of SLN metastasis using CTLG by comparing with pathological results.
Methods: From Nov 2013 to Oct 2014, 120 patients with breast cancer underwent surgery in Tokushima University Hospital. CTLG was applied to all patients, and 100 patients who did not receive primary chemotherapy were studied. SLN metastasis was diagnosed according to the following criteria: (A) Defect of the SLN, scissor clubbed defect sign or mottled stain of the LN, (B) Stagnation and (C) Interruption of the lymph vessels, (D) Abnormal rerouting of the lymphatic route. Preoperative diagnosis was compared to pathological report after operation.
Results: Twelve of 100 patients proved metastatic SLN pathologically. We diagnosed 57 cases as non-metastasis, 7 cases as metastasis and 36 cases as equivocal. 64 cases that diagnosed as non-metastasis and metastasis was correctly diagnosed.
Conclusion: CTLG shows number and position of SLN with surrounding detailed anatomy. Moreover non-metastatic SLN can be correctly diagnosed by CTLG. Patients with non-metastatic SLN diagnosed by CTLG might avoid SLN biopsy.
Disclosure of Interest: No significant relationships.

P307

Basic approaches of oncoplastic breast surgery: which operation to which patient?

T. Colakoglu*, H.O. Aytac, T.Z. Nursal, S. Yildirim. *General Surgery, Baskent University, Faculty of Medicine, Adana, Turkey*

Goals: Oncoplastic procedures can be summarized as volume fillings/shiftings, flaps, implants and reduction mammoplasties. Surgical algorithms should be developed regarding patient satisfaction respecting oncological principals and cosmetic expectations for oncoplastic operations.
Methods: In this cohort study, data of 147 patients operated on for breast cancer with oncoplastic methods at our tertiary-referral center between January 2008 and December 2013 were assessed in the context of demographics, surgical techniques, pathologic and cosmetic results.
Results: Oncoplastic procedures offered by our breast surgeons was accepted by 147 (83%) of the 177 patients. Type of the procedure applied was decided in collaboration with the patients. Immediate Latissimus dorsi mini flap reconstruction after lumpectomy was carried out to 46 (31.3%) of the cases. Thirty (20.4%) patients were treated with lumpectomy and volume shifting by areolar transposition, 22 (15%) with skin sparing mastectomy and immediate implant placement, 21 (14.3%) with Modified Radical Mastectomy (MRM) followed by immediate reconstruction with TRAM flap. Immediate reconstruction with Latissimus Dorsi Myocutaneous flap following subcutaneous mastectomy was applied to 11 (7.5%) cases. Seven (4.8%) patients were treated with MRM and immediate expander placement, 5 (3.4%) with bilateral reduction mammoplasty. Late reconstruction was applied to 5 (3.4%) patients who had previous MRM history. Late complementary mastectomy was performed on three (2%) cases due to presence of DCIS at the surgical margin and on two (1.3%) cases due to local recurrence. No distant metastasis or complications related to radiotherapy was observed during follow-up. Ninety percent (127/141) of the patients declared their satisfaction state as "like" or "admire". Aesthetic evaluation by an independent observer surgeon ended as "good" or "very good" in 85% (114/134) of the patients. Bilateral reduction mammoplasty was the favorite both from the patients' and observers' point of view.
Conclusion: Oncoplastic procedures designed suitably for breast cancer cases in terms of patient factors and disease features can result oncology safe, acceptable cosmetic results.
Disclosure of Interest: No significant relationships.

P308

Comparison of implant-based immediate breast reconstruction with and without vicryl mesh

H. Karanlik*, S. Bayrak, M. Fayda, I. Ozgur, S. Kurul. *Department of Surgical Oncology, Istanbul University Institute of Oncology, Istanbul, Turkey*

Goals: Vicryl mesh can be used for implant based breast reconstruction but only limited clinical data are available. The aim of this study whether adding Vicryl mesh in implant based immediate reconstruction improved outcomes when compared with non-Vicryl mesh reconstruction.
Methods: Patients undergoing implant based immediate breast reconstruction at a single university hospital were evaluated. Aesthetic outcomes and postoperative complications were assessed and direct comparisions were made between Vicryl mesh and non-Vicryl mesh cohorts.
Results: A total of 82 surgical procedures were performed in 70 patients during the study period. Of all the procedures, Vicryl mesh technique was used in 35 (43%), non-vicryl mesh techniques were used in 47 (57%) of them. 12 patients (15%) were operated for recurrent breast cancer had previous history of the whole breast radiation therapy. Duration of the hospitalization was not different between two groups ($p > 0.05$). Overall complications encountered in 22% of patients and were not different between two groups ($p > 0.05$). However, capsular contracture ($p = 0.04$), inframammary fold problems ($p = 0.04$) and bottoming-out ($p = 0.04$) were all more frequent in the non-Vicryl mesh group compared with Vicryl mesh reconstruction. The incidence of the seroma/hematoma, infection, wound problems/dehiscence, skin necrosis and implant failure were similar between groups ($p > 0.05$). Overall and inframammarian fold aesthetic outcome of immediate implant based breast reconstruction was higher in the Vicryl mesh than non-Vicryl group ($p < 0.001$).
Conclusion: Optimizing the inframamarian fold with Vicryl mesh creates a superior aesthetic result. Its use appears safe and is associated with less capsular contracture and bottoming-out and improvement in the inframammary fold appearance, without increasing postoperative complications.
Disclosure of Interest: No significant relationships.

P309

The use of Tisseel fibrin sealant in seroma reduction after mastectomy – a pilot study

Q.T. Tan[1] *, C.M. Lee[1], V.K.M. Tan[2], K.W. Ong[2]. *[1]Singhealth-duke Breast, Singapore General Hospital, Singapore, Singapore, [2]Surgical Oncology, National Cancer Centre Singapore, Singapore, Singapore*

Goals: Postmastectomy seroma formation is very common. In some cases, it is associated with increased morbidity, hospital stay and risk of wound infection and breakdown Placement of a surgical drain is also associated with longer hospital stay, drain dislodgement, drain blockage, leaking around drain exit site and wound site infection. Various methods have been described to decrease post-operative seroma formation, including use of pressure garments, immobilization of the ipsilateral upper limb, quilting and use of sclerosing agents. Thus far, no method has been shown to be effective. We explore the use of fibrin sealant to the post-mastectomy wound to reduce seroma formation through improved tissue adherence and hemostasis.
Methods: In this pilot study, we compared the degree of seroma formation patients with 2 ml of Tisseel fibrin sealant applied to the post mastectomy wound cavity before closure with patients who undergo wound closure in the usual fashion (i.e. without the use of Tisseel). 10 patients were grouped into each arm and the amount of seroma formation (assessed by drain volume and volume of seroma fluid aspirated after drain removal) compared between patients with similar bra cup size and mastectomy specimen weight.
Results: The volume of seroma fluid and time to drain removal is significantly reduced in patients who had application of fibrin sealant. Most patients recruited were of similar bra cup size (B) with median breast weight of 462.5 g for the Tisseel group and 600 g for the control group ($p = 0.44$). Median time to drain removal for the Tisseel group is 6.5 days compared to 10.5 days for the control group ($p = 0.06$). Median drain volume for the Tisseel group is 335 ml and 530 ml for the control group ($p = 0.12$). Median aspiration volume after drain removal for the Tisseel group is 52.5 ml and 89.5 ml for the control group ($p = 0.12$). Median total seroma volume for the Tisseel group is 507.5 ml compared to 770 ml for the control group ($p = 0.05$).
Conclusion: The use of fibrin sealants like Tisseel effectively reduces seroma formation. Fibrin sealants have a good safety profile, are easy to use and do not significantly increase operative time. However increased cost may pose to be a problem. A follow-up prospective study of a larger scale is underway to analyze the cost and benefits of this technique.
Disclosure of Interest: No significant relationships.

P310

Local recurrence rates are low in Japanese breast cancer patients after neoadjuvant chemotherapy

T. Shigekawa *, A. Osaki, S. Ueda, H. Takeuchi, E. Hirokawa, I. Sugitani, M. Sugiyama, H. Shimada, T. Takahashi, T. Saeki. *Breast Oncology, Saitama Medical University International Medical Center, Hidaka, Japan*

Goals: In a meta-analysis, it was shown that neoadjuvant chemotherapy (NAC) improved the rates of breast conservative treatment (BCT), and the patients ineligible for BCT have increasingly converted to be candidates for it after NAC, although questions whether BCT provides adequate local control often arise. There is few long-term treatment results about local recurrence (LR) after surgery in the patients treated with NAC in Japan. The goals of this study are to evaluate the rate and clinical characteristics of LR in these patients.
Methods: This study included 101 patients whose symptoms corresponded to the American Joint Committee on Cancer Stage II or III breast cancer and who were treated between April 2007 and March 2010 with NAC that included anthracycline and/or taxane-based regimens and who had undergone definitive surgical therapy. All patients treated with BCT received radiation therapy postoperatively.
Results: 46 patients (45.5%) received BCT and 55 patients (54.5%) received mastectomy. In both of these groups, median tumor size was 36 mm, and in BCT group, 6 patients (13.0%) had positive margins (defined as positive in case of ≤5 mm from the tumor). At a median follow-up of 59 months, 8 patients (7.9%) had LR and 19 (18.8%) had distant recurrence (DR). Of the 8 patients with LR, 7 patients had DR and only one patient had LR alone in the follow-up period. The median periods from surgery to LR were 20 months. In the 8 patients with LR, 6 patients had chest wall skin recurrence after mastectomy, and only 2 patients (4.3%; 2/46) had the ipsilateral breast recurrence after BCT.
Conclusion: The rate of LR after surgery was low in Japanese high-risk breast cancer patients treated with neoadjuvant chemotherapy, and especially the ipsilateral breast recurrence after BCT was rare. LR occurred most frequently in the setting of DR.
Disclosure of Interest: No significant relationships.

P311

How to avoid unnecessary sentinel node biopsy in patients with ductal cancer in situ

A. Karakatsanis[1] *, H. Oloffson[2], L.Å. Bergkvist[3], S. Abdsaleh[4], M. Sund[5], F. Wärnberg[1]. *[1]Department for Surgical Sciences, Uppsala University, Uppsala, Sweden, [2]Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden, [3]Department of Surgical Sciences, Uppsala University, Department of Surgery, Central Hospital, Västerås, Uppsala University, Department of Surgery, Central Hospital, Västerås, Västerås, Sweden, [4]Department of Radiology, Oncology and Radiation Science, Uppsala University, Uppsala, Sweden, [5]Department of Surgical and Perioperative Sciences, Umeå University, Umeå, Sweden*

Goals: To assess preoperative Sienna+ injection (SPIO) for the detection of sentinel lymph node (SN) in patients with ductal cancer in situ (DCIS), and to perform SN biopsy only after a postoperative diagnosis of invasive cancer.
Methods: In a pilot study, SPIO was injected 3 to 15 days before surgery in 12 patients that would undergo SN biopsy. Technetium and blue dye were used routinely at the time of surgery as usual. Pregnant or lactating women, as well as patients with known allergy to iron or dextran compounds, such as hemochromatosis or other iron overload were excluded. Additionally, a healthy volunteer was injected with SPIO in order to follow the decline of the magnetic signal in the SN over time.
Results: In all patients, there was a good signal detected by the magnetometer (SentiMag®) at surgery, and the SNs were detected in all patients. The relation of a good preoperative and intraoperative signal was a constant finding, regardless of the time elapsed between the preoperative injection and the date of surgery. In nine patients, the SNs were identified with all three methods. In two patients, the SNs were detected with the magnetometer only and, in one, with the magnetometer and Technetium, but not with the blue dye. No adverse effects were noted from SPIO injection. The specimens sent for pre- or post-operative mammographic localization were free from any disturbance of the visualization of the lesions. The histopathological examination was not disturbed, neither in the tumour nor in the SN. On the contrary, it seemed like the examination of frozen sections of SNs was easier as the SPIO was not accumulated in metastatic cells. In the volunteer, the counts in the axilla stayed persistently high for more than four weeks.
Conclusion: The use of preoperative SPIO injection is a promising technique in order to avoid unnecessary preoperative SN biopsy in

patients with a preoperative diagnosis of DCIS. Morbidity related to SN biopsy will be reduced and potentially limit the cost of the procedure. A larger study will be consequently performed to evaluate the number of SN biopsies avoided in relation to the number of SN biopsies that have to be performed in a second operation.
Disclosure of Interest: No significant relationships.

P312
Influence of immediate breast reconstruction (IBR) on adjuvant therapy for breast cancer patients

T. Nogami[1]*, N. Taira[1], S. Watanabe[2], Y. Abe[1], T. Mizoo[1], T. Iwamoto[1], T. Motoki[1], T. Shien[1], Y. Kimata[2], H. Doihara[1]. *[1]Breast and Endocrine Surgery, Okayama University Hospital, Okayama, Japan, [2]Plastic and Reconstructive Surgery, Okayama University Hospital, Okayama, Japan*

Goals: Although breast reconstruction has become a standard option for breast cancer patients because of cosmetic reasons, breast reconstruction has specific complications. These complications may obstruct adjuvant therapies to breast cancer, such as a delay of appropriate introduction of adjuvant chemotherapy. We investigated whether particularly immediate breast reconstruction (IBR) for breast cancer patients did harm.
Methods: From 2004 to 2013, 494 breast cancer patients who had operative treatment for breast cancer at Okayama University Hospital (exclude the patients who received preoperative chemotherapy or had Stage IV breast cancer). First, we chose the patients treated with mastectomy who had adaptation of post-mastectomy radiotherapy (PMRT), and divided into two groups; IRB and non-IRB. We investigate whether appropriate adaptation of Radiotherapy was done in the groups. Second, we chose the patients who treated with adjuvant chemotherapy, and divided into also two groups. We investigated the period between surgery and introduction of adjuvant chemotherapy, and compared the two groups.
Results: First, 31 patients had adaptation of PMRT. 11 (33%) patients were IBR group, and 20 (67%) patients were non-IRB group. In IBR group, 8 (73%) patients received PMRT. In non-IRB group, 15 (75%) patients received PMRT. There is no significant difference between IBR group and non-IBR groups ($p = 0.89$). Second, 121 patients received adjuvant chemotherapy. 29 (24%) patients were treated with IBR. The average period between surgery and adjuvant chemotherapy was 35 days in IBR groups, and 36 days in non-IBR groups, respectively. There is no significant difference between IBR group and non-IBR groups ($p = 0.5$). Completion rate of adjuvant chemotherapy was 97% in IBR group and 96% in non-IBR group, respectively. There is also no significant difference between IBR group and non-IBR groups ($p = 0.91$).
Conclusion: In this study, IBR for breast cancer patients did not harm. We must do best for the patients continuously.
Disclosure of Interest: The authors have no conflict of interest to declare.

P313
A new predictive score for axillary lymph node metastases in breast cancer patients

T. Ogura*, T. Kinoshita, K. Jimbo, S. Asaga, T. Hojo. *Breast Surgery Division, National Cancer Center Hospital, Tokyo, Japan*

Goals: The American College of Surgeons Oncology Group (ACOSOG) Z0011 trial demonstrated no difference in overall survival or local-regional recurrence rates between patients planned for breast conservation therapy including whole breast irradiation with one or two positive sentinel lymph nodes (SLNs) randomly selected to undergo axillary lymph node dissection (ALND) versus no further surgery. But, non-SLN status is important for the omitting ALND and the decision of the intensity of adjuvant therapy. Detection of SLN metastases in breast cancer patients has been determined by conventional histological examination or by molecular biological examination such as one step nucleic acid amplification (OSNA). We examine the assessment using a combination of histological examination and OSNA and the possibility of omitting ALND.
Methods: We included 1158 consecutive patients with clinical node-negative cTis-cT3 primary breast cancer who underwent SLN biopsy with intraoperative multi-section histological examination and OSNA between February 2010 and June 2013 at our institution. 311 patients (27%) with positive SLN metastases by either histology or OSNA underwent further ALND. We allotted 3 points to macro metastasis by histology, 2 to micro metastasis, and 1 to isolated tumor cells (ITC). We allotted 3 points to 2+ by OSNA, 2 to 1+, 1 to +I. We defined "NCC-SLN metastatic score (NCS score)" as the sum total points and predicted the existence of non-SLN metastases.
Results: There was a strong correlation between NCS score and non-SLN metastases detection rate, and the correlation coefficient was 0.72. In the invasive lobular carcinoma the correlation coefficient was low (0.45), whereas in the invasive ductal carcinoma the correlation coefficient was high (0.72). The non-SLN metastases detection rate was low (12%) in patients whose NCS score is 3 and below. In patients whose NCS score is from 4 to 12 and 13 and above, the non-SLN metastases detection rate was 37% and 75%. Average number of metastatic non-SLNs is 0.4 and 3.4 in patients whose score is 9 and below and 10 and above respectively.
Conclusion: NCS score had a strong correlation with the non-SLN metastases detection rate in the invasive ductal carcinoma. By using this score we could decide the cases that we omit the further ALND.
Disclosure of Interest: No significant relationships.

P314
Preoperative identification of early breast cancer patients for safely avoiding axillary surgery

C. Listorti[1]*, A. Rulli[1], E. Prosperi[2], P. Covarelli[3], F. Barberini[1]. *[1]Breast Unit, General and Oncological Surgical Unit, Department of Surgery, University of Perugia, Perugia, Italy, [2]Institute of Pathological Anatomy and Histology, University of Perugia, Perugia, Italy, [3]General and Oncological Surgical Unit, Department of Surgery, University of Perugia, Perugia, Italy*

Goals: Almost 30% of patients with breast cancer die despite earlier diagnosis with screening programs and therapeutical improvements. Locoregional metastases occur even in less indolent types of early stage breast cancer, impacting disease free, overall survival and quality of life. For this reason, even if a more conservative surgical approach has been indicated, axillary lymph nodes clearance is still performed in case of sentinel lymph node micrometastasis and Luminal tumor. We conducted a retrospective study in order to find objective parameters to preoperatively identify low risk early breast cancer patients with sentinel node micrometastasis for which is safe to avoid axillary clearance.
Methods: We analyzed data collected between December 2012 and December 2014. Early stage breast cancer patients with clinically negative axilla underwent breast surgery and sentinel node biopsy. Metastases at sentinel lymph node were intraoperatively detected with one-step nucleic acid amplification (OSNA) assay, which analyzes cytokeratin 19 mRNA copy number in the whole lymph node.
Results: A total of 392 patients underwent breast surgery and sentinel node biopsy. Analysis was conducted on 348 patients, among which 99 had sentinel node metastasis. Forty-seven patients had macrometastasis while 52 patients had sentinel node micrometastasis. Among these cases, 40 patients underwent axillary clearance. We found 8 patients (20%) with non-sentinel axillary lymph nodes metastases. We then selected patients with

<2000 cytokeratin 19 mRNA copy number in the sentinel node, Luminal tumor phenotype, non-lobular tumor, unifocal tumor, tumor diameter ≤2 cm. Over a total of 17 patients, we observed only one case with axillary lymph node metastasis (5.9%).
Conclusion: Axillary clearance can be safely avoided in selected early stage breast cancer patients with the following characteristics: <2000 cytokeratin 19 mRNA copy number in the sentinel node, Luminal tumor phenotype, non-lobular tumor, unifocal tumor, tumor diameter ≤2 cm. In order to safely extend this indication to other early stage breast cancer patients with micrometastasis at sentinel node, especially in case of lobular carcinoma, preoperative multi-gene tests have to identify genetic signatures of low risk of recurrence.
Disclosure of Interest: No significant relationships.

P315
Direct to implant breast reconstruction without the use of an acellular–dermal matrix

L.C. Serrurier[1]*, C. Benn[2], S. Rayne[2]. [1]*Plastic Surgery, Milpark Hospital, Johannesburg, South Africa,* [2]*Surgery, Milpark Hospital, Johannesburg, South Africa*

Goals: Direct to implant breast reconstruction is emerging internationally as a predictable and reliable reconstructive method. There are obvious advantages to this technique, however most international authors recommend the use of an ADM or a mesh to reinforce the lower pole of the breast reconstruction. This might potentially simplify the procedure, but is not necessarily associated with decreased complications and a better cosmetic outcome. It however significantly increases the costs of the procedure.
Methods: 273 consecutive patients with 490 immediate direct to implant breast reconstructions from 2 institutions over a 34 month period are included in this study. Mean follow up of this group is 35 months with a maximum and minimum follow 58 and 24 months respectively.
Results: Short term, long term complications and cosmetic outcome will be presented. These results will be compared to the published literature on direct to implant reconstruction using an ADM.
Conclusion: This method of breast reconstruction compares very favorably with published data from other units as far as early and late complications are concerned as well as cosmetic outcome. It avoids the potential higher seroma rate associated with ADMs and is significantly more cost effective.
Disclosure of Interest: No significant relationships.

P316
Axillary node status in breast cancer. How much is it affected by neoadjuvant chemotherapy?

Y.S. Ahmed*. *Surgery Department, Medical Research Institute, Alexandria, Egypt*

Goals: We aimed to evaluate the effect of neoadjuvant chemotherapy on the axillary nodal status in breast cancer regarding the number of AxLNs retrieved at ALND and the degree of response to NAC relative to the primary tumor.
Methods: A retrospective review of all patients with breast cancers who were admitted to the department of Surgery, Alexandria Medical Research Institute hospital in the period between August 2013 and July 2014 and scheduled for ALND. Patients who underwent sentinel lymph node (SLN) biopsy, who were operated by surgeons less than senior residents and cases with level III ALND were excluded. Cases were categorized into two groups; Group I included patients who received NAC then submitted to surgery while Group II included patients who were submitted to surgery without NAC. Data collected from both groups included patient demographics, TNM classification, tumor stage, total number of AxLNs identified in pathologic specimens and number of positive AxLNs.
Results: The study included 237 female patients who were allocated to one of the two groups; Group I included 93 patients (39.2%) while Group II included 144 patients (60.8%). There was no statistically significant difference between the two groups regarding age, tumor grade and tumor type. But significant differences were seen in a variety of baseline criteria between the two groups; the patients who received neoadjuvant chemotherapy had larger tumors (T) ($P = 0.001$), higher lymph node (N) classification ($P = 0.002$) and higher overall disease stage ($P = 0.0001$) than the patients who underwent surgical resection first. After neoadjuvant chemotherapy in group I; AxLNs were significantly more responder to NAC relative to the primary tumor ($P = 0.003$). The number of AxLNs harvested during ALND revealed a significantly lower LNY in patients underwent NAC in comparison to patients who did not with a median total number of 9 nodes in group I compared to 14 axillary nodes in group II ($P = 0.0001$). The number of positive AxLNs was higher in patients who underwent surgical resection first with statistically significant difference ($P = 0.006$).
Conclusion: Neoadjuvant Chemotherapy (NAC) is a significant independent parameter for a reduced LNY number retrieved by ALND. We can also conclude that axillary AxLNs (nodal stage) are significantly more responding to NAC relative to the primary tumor (tumor stage) both clinically (TNM staging) or pathologically (number of positive LNY).
Disclosure of Interest: No significant relationships.

P317
From radical to minimal-invasive – first clinical results of a non-surgical SLNB

S. Paepke[1]*, C. Pfob[2], R. Ohlinger[3], M. Thill[4], T. Kühn[5], J. Blohmer[6], M. Hahn[7], I. Gruber[7], K. Scheidhauer[2], M. Kiechle[1]. [1]*Frauenklinik und Poliklinik, Klinikum rechts der Isar, Technische Universität München, München, Germany,* [2]*Nuklearmedizin, Klinikum rechts der Isar, Technische Universität München, München, Germany,* [3]*Klinik und Poliklinik für Frauenheilkunde und Geburtshilfe, Ernst Moritz Arndt Universität Greifswald, Greifswald, Germany,* [4]*Klinik für Gynäkologie und Geburtshilfe, Agaplesion Markus Krankenhaus, Frankfurt, Germany,* [5]*Klinik für Frauenheilkunde und Geburtshilfe, Klinikum Esslingen, Esslingen, Germany,* [6]*Klinik für Gynäkologie, Charité – Universitätsmedizin Charité, Berlin, Germany,* [7]*Universitäts-frauenklinik Tübingen, Universitätsklinikum Tübingen, Tübingen, Germany*

Goals: Sentinel lymph node biopsy (SLNB) is a surgical procedure despite its pure diagnostic value. We developed the first procedure to perform a non-surgical SLNB. Initial clinical data show the same detection rate and less complications than in the current surgical approach.
Methods: A hand-held gamma camera generates SPECT images and fuses them with live ultrasound images to identify the sentinel lymph node (SLN) (SentiGuide, SurgicEye). The ultrasound overlay allows vacuum-assisted biopsies of SLN-tissue that is evaluated by the pathology. The feasibility of a non-surgical SLNB was validated in 3 steps: Firstly, the imaging of the non-surgical SLNB was evaluated in 59 cases to confirm the detection rate of SLNs compared to planar scintigraphy without performing biopsies. Secondly, the non-surgical method was evaluated in the OR on a patient using a core needle biopsy to gather tissue from the SLN and compare the dignity to the surgically removed SLN. Finally, the method was evaluated in 6 patients in the OR using a vacuum assisted biopsy device to gather more tissue for the pathology. The dignity of those biopsies was compared to the full SLNs.
Results: In total 77 SLNs were identified in 59 cases by planar scintigraphy, all of them could be confirmed by the SentiGuide

system resulting in a sensitivity of 100%. The tissue from the core needle biopsy showed lymph tissue with a micro metastases. The frozen section of the full SLN was negative. The re-evaluation of the SLN after the finding in the core needle biopsy also revealed isolated tumor cells. The SLN-staging would have been false negative. Finally, the new method was evaluated on 6 patients. 5–14 biopsie samples were taken from each SLN. All contained tumor-free lymph tissue. This was in all cases confirmed by the evaluation of the surgically extracted SLNs. The vacuum-assisted biopsy introduced no complications that needed surgical revision or led to post-surgical trauma.
Conclusion: The SentiGuide method introduces a reliable technique to perform non-surgical SLNB. It effectively identifies and stages the SLNs. First results show did not show any complications. The results led to the design of a randomized study with 288 patients to compare the performance between the surgical and non-surgical approaches in sentinel lymph node staging and complication reduction. Results of the first study phase will be presented in March 2015.
Disclosure of Interest: I am a consultant for SurgicEye GmbH Friedenstr. 18A D-81671 München.

P318
Accuracy of frozen section or cytology of sub-nipple tissue to predict nipple involvement for cancer

G.M. Duarte*, A. Oliveira, M.V. Thomazin, F. Tocchet, L. Moreira, A. Worchech, R.Z. Torresan. *Breast Surgery, UNICAMP – State University of Campinas, Campinas, Brazil*

Goals: Occult nipple involvement for cancer occurs about 10–14%. Sub-nipple tissue (SNT) exam has been used by some surgeons to preserve or not the nipple in nipple sparing mastectomy. Then, intraoperative exam of SNT becomes an important tool. However, it is uncertain if the SNT evaluation can safely predict the nipple involvement. The aim of this study was to evaluate the accuracy, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of intraoperative frozen section and imprint cytology, and postoperative paraffin histopathology of SNT to predict involvement of the nipple in breast carcinoma women.
Methods: It was realized a prospective study with 68 consecutive breast carcinoma women (stage 0, I, II and III) undergone mastectomy. It was excluded inflammatory carcinoma and clinical evident nipple involvement. After mastectomy, the nipple areolar complex was dissected simulating nipple-sparing flap. Then, the SNT was removed and submitted to frozen section and imprint cytology in intraoperative time. Subsequently, it was submitted to routine paraffin histopathology. The nipple was examined separately by paraffin histopathology (gold standard). We considered any atypical cells like positive findings in all exams (cytology, frozen and paraffin).
Results: Occult nipple involvement rate was 11.7%; the mean age was 60.8 years; the mean tumor size was 29.7 mm in clinical exam and 27.7 mm in pathological exam. The mean distances from tumor to nipple were 24.3 mm and 33.5 mm in clinical and mammographic exams, respectively. The frozen section, imprint cytology, and paraffin of SNT showed: accuracy 86.8%, 76.5% and 86.8%; sensitivity 50%, 37.5% and 62.5%; specificity 91.7%, 81.7% and 90%; PPV 44.4%, 21.4% and 45.5%; NPV 93.2%, 90.7% and 94.7% respectively. Accuracy of frozen section was similar to paraffin ($p = 0.77$) and both were better than imprint cytology ($p = 0.01$). False negative rate were 6.8% of frozen section and 9.3% of cytology.
Conclusion: Our data suggests that SNT evaluation is a good method to predict nipple occult involvement; on the other hand it is not totally safe. The outcomes showed a good accuracy and low false negative rate of intraoperative exam of SNT (frozen section and cytology). When we compared both exams, frozen section had better accuracy than imprint cytology.
Disclosure of Interest: No significant relationships.

P319
Role of breast MRI in prediction of malignant invasion of nipple areolar complex

H. Lai[1]*, H. Wu[2], D. Chen[1], C. Chen[3], S. Kuo[1], S. Chen[1]. *[1]Department of Surgery, Changhua Christian Hospital, Changhua, Taiwan, [2]Department of Radiology, Changhua Christian Hospital, Changhua, Taiwan, [3]Department of Surgerical Pathology, Changhua Christian Hospital, Changhua, Taiwan*

Goals: Nipple sparing mastectomy is increasingly used as a surgical treatment for breast cancer. To correctly predict the possibility of nipple invasion pre-operatively is critical important to prevent occult nipple invasion or early nipple recurrence. The objective of our study is to assess the diagnostic accuracy of breast MRI for the evaluation of malignant invasion of the nipple-areolar complex (NAC).
Methods: From January 2011 to December 2013, patients with primary operable breast cancer diagnosed and treated at Changhua Christian Hospital (CCH), Taiwan were searched. The inclusion criteria were primary operable breast cancer patients, who received pre-operative breast MRI, and received breast cancer operation at CCH. The exclusion criteria were patients whose primary tumor was removed before definite cancer operation, those who received neoadjuvant chemotherapy, or patient's detailed data not available. Breast MRI examinations were retrospectively reviewed for nipple invasion or retraction, periareolar skin thickening, nipple areolar complex enhancement, relationship to the subareolar mass, malignant mass pattern, thickness of nipple-areolar complex enhancement, tumor-nipple distance, and tumor size and were correlated with pathologic findings. The accuracy of breast MRI to predict nipple invasion was compared with pre-operative image and post-operative pathologic reports.
Results: A total 704 primary operable breast cancers with pre-operative MRI and post operative pathologic reports were enrolled in our current study. Among them 371 (52.7%) patients received total mastectomy, and 333 (47.3%) received partial mastectomy. In the total 704 patients, MRI showed signs of suspect NAC invasion in 160 (22.7%) patients. Total 41 (25.6%) patients were pathologic proven malignant invasion of NAC. In the final pathologic analysis, 57 pathologic confirmed NAC invasions were found in the 704 patients. The overall nipple invasion rate was 8.1% (57/704) in this current study. The sensitivity of Breast MRI to predict NAC involvement was 71.9% (41/57). The Specificity of breast MRI to NAC invasion is 81.6% (528/647). The positive predictive value of breast MRI is 25.6% (41/160). The negative predictive value of breast MRI is 97.1% (528/544). The accuracy of breast MRI to predict NAC involvement is 80.8% ([41+528]/704).
Conclusion: MRI is an useful diagnostic image method for the evaluation of malignant invasion of the nipple-areolar complex. Through preoperative breast MRI evaluation of NAC status, more personalized oncoplastic breast surgery could be performed.
Disclosure of Interest: No significant relationships.

P320
Evaluation of postoperative lymphedema in breast cancer patients undergoing sentinel node biopsies

Y. Ogasawara*, M. Hatono, K. Kawasaki. *Breast and Endocrine Surgery, Kagawa Prefectural Central Hospital, Takamatsu City, Japan*

Goals: Recently, CT lymphography (CTLG) employing a nonionic contrast medium has achieved sentinel lymph node (SLN) identification. This CTLG can visualize the drainage lymphatic pathway clearly and demonstrate the accurate location of SLN. In this study, risk factors for developing lymphedema in breast cancer patients undergoing sentinel lymph node biopsies (SLNBs) were evaluated using CTLG.

Methods: Between May 2008 and October 2012, 127 consecutive breast cancer patients undergoing SLNBs using CTLG were analyzed. Patients with bilateral breast cancer were excluded from this study. CTLG was performed on the day before surgery. In CTLG, the SLN was defined as the first lymph node into which the enhanced lymph vessels drained. With CT image guidance, SLNB was performed using a radioisotope. Lymphedema was evidenced by segmental arm circumference. Every one year after the surgery, measurements were obtained 5 and 10 cm above and below the elbow and at the wrist on the ipsilateral and contralateral limbs. Presence of lymphedema was considered when there was a difference exceeding 2 cm compared to the contralateral limb.
Results: Identification of the SLN(s) was achieved in 122 (96.8%) of the total 126 performances of CTLG. During surgery, SLN(s) were identified in 126/126 (100%) of cases. Post-surgical observations were carried out for between 12 and 62 months (median 25 months), with lymphedema occurring in 12 (9.4%) of the 127 cases. There was no significant difference between the 12 cases in which lymphedema occurred and the 115 in which it did not, in terms of age (61.9 vs. 61.5 years), tumor diameter (1.8 cm vs. 2.0 cm), surgical method (total mastectomy/breast-conserving surgery, 1/11 vs. 25/90), the administration of adjuvant endocrine therapy (administered/not administered 12/0 vs. 106/9), the administration of adjuvant chemotherapy (administered/not administered 1/11 vs. 21/94), or the administration of postoperative radiotherapy (administered/not administered 8/4 vs. 65/50); however, there was a significant difference in BMI (28.6 vs. 23.2 kg/m^2, $p < 0.0001$). Upon studying the location of the SLN based on CTLG images, there was no significant difference between cases experiencing lymphedema and those not experiencing it, in terms of SLN location (central lymph nodes/other lymph nodes 7/5 vs. 67/48) or distance from the SLN to the axillary vein (36.7 mm vs. 30.4 mm); however, cases with lymphedema had a greater distance from the SLN to the skin (27.5 mm vs 21.4 mm, $p = 0.0346$).
Conclusion: Lymphedema occurred in 12/127 (9.4%) cases following SLNB. Post-surgical lymphedema is more likely to occur in obese patients, who have a greater distance between the skin and the SLNs, indicating a need to ascertain the location of SLN using CTLG prior to surgery, then perform SLNB cautiously with a minimum dissection in such a case.
Disclosure of Interest: No significant relationships.

P321
Analgesia with thoracic wall nerve block for breast reconstruction with expander or implant

T. Hisada*, J. Nakada, S. Okumura, N. Kondou, M. Sawaki, A. Yoshimura, Y. Adachi, J. Ishiguro, H. Kotani, H. Iwata. *Breast Oncology, Aichi Cancer Center Hospital, Nagoya, Japan*

Goals: Breast reconstruction with expander or implant is a common surgery for the breast cancer patients. As it is painful due to stretching the pectoralis muscle only by general anesthesia, analgesic drug like morphine are often used. However, nausea caused by those drug often afflict patients. We consider the more effective procedure is necessary to prevent the pain for breast cancer patients with reconstruction using expander or implant. The purpose of this study is to evaluate the efficacy and safety of thoracic wall nerve block as a novel technique to prevent pain for breast cancer patients with reconstruction using expander or implant.
Methods: This study included 38 patients who underwent immediate breast reconstruction with expander or implant in Aichi Cancer Center Hospital. We retrospectively analyzed the pain condition by using the information of clinical reports. We have used continuous subcutaneous (s.c.) injection of morphine (1.0 mg/h) with general anesthesia to prevent the pain from April 2013 to May 2014 (Group A), thoracic wall nerve block and continuous s.c. injection of morphine (0.5 mg/h) with general anesthesia have been used from April 2014 (Group B). We compared these two methods as evaluating efficacy of postoperative analgesia and adverse events such as nausea and emesis. We injected 0.2% ropivacaine between the pectoralis major and minor, and under the serratus anterior muscle due to thoracic wall nerve block.
Results: Among 38 patients, median age is 49.2±18.8 years. There were no significant differences in the ratio of the patients who used no or one rescue during 48 hours after operations (63% in group A and 68% in group B, $p = 0.73$). Whereas the incidence rate of nausea dramatically reduced in group B (89% and 32%, $p = 0.001$). The average time of anesthesia induction was 10 minutes longer in group B (range 7–19 minutes). One patient had a subcutaneous hematoma in thoracic wall nerve block group, but the causation with the nerve block was unclear.
Conclusion: Thoracic wall nerve block might be a safe and efficacious procedure to prevent postoperative pain in patients with immediate breast reconstruction using expander or implant. We are planning the prospective study with appropriate criteria to confirm the usefulness of this procedure.
Disclosure of Interest: No significant relationships.

P322
Preserving areolar skin after mastectomy provides increased sensation in the reconstructed nipple

L.C. Serrurier[1]*, I. Do Vale[2], C. Benn[1], S. Rayne[3], J. Slabbert[1]. *[1]Plastic Surgery, Milpark Hospital, Johannesburg, South Africa, [2]University of the Witwatersrand, Johannesburg, South Africa, [3]Surgery, Milpark Hospital, Johannesburg, South Africa*

Goals: To determine the effect of areolar skin preservation on nipple sensation after NACR compared to traditional methods of NACR.
Methods: This was a prospective study of patients who underwent NACR between 2009 and 2013 in one unit. The study groups comprised patients who had undergone bilateral NACR using preserved areolar skin and full-thickness skin graft (FTSG), following SSM with areolar-skin preservation (A-PNACR). The control group comprised patients with NACR from chest wall skin and FTSG after mastectomy and expander-prostheses reconstruction. Skin sensation was determined by light touch using a cotton swab and sensation using a Semmes-Weinstein monofilament kit exerting between 0.07 g and 300 g pressure. Sensation was tested in four quadrants of each nipple and each areolar (8 patient test-areas (PTA) per patient) using the suprasternal notch as control. Minimum grams of pressure resulting in sensation were recorded for each area.
Results: 29 patients were recruited, 18 in study group (A-PNACR) and 11 as control. The groups were well-matched for age and time since final surgery. Nipple reconstruction used either a Maltese cross (8 study, 11 control) or double opposing tab (10 study, 0 control; $p = 0.002$). Pressure sensation was highly significantly increased in patients with A-P NACR with sensitivity to 0.07 g found in 12 PTA and to 0.4 g in 17 PTA. No sensitivity to 0.07 g or 0.4 g was found in the control group ($p < 0.00001$). Far fewer A-PNACR patients had very poor (300 g) or absent sensation (50 PTA vs 74 PTA; $p < 0.0001$). Light touch was poor in both groups although better in A-P NACR (11.1% vs 4.8%; NS).
Conclusion: This study confirms that an areolar-skin preserved NACR confers significantly better nipple sensation for patients post-operatively than conventional techniques of NACR.
Disclosure of Interest: No significant relationships.

P323

Nomogram predicting axillary PCR after neoadjuvant chemotherapy in node-positive breast cancer

J.Y. Kim*, S. Kim, J. Ryu, H.S. Park, S. Park, S.I. Kim. *Department of Surgery, Yonsei University College of Medicine, Seoul, Korea*

Goals: The purpose of this study was to investigate the factors that predict the axillary pathologic complete response (pCR) and develop a nomogram predicting the probability of axillary pCR in cytologically-proven axillary node-positive breast cancer patients who received neoadjuvant chemotherapy.
Methods: We reviewed the records of 415 patients with cytologically-proven node-positive breast cancer who were treated with neoadjuvant chemotherapy and followed by surgery between 2008 and 2012. Baseline patient and tumor characteristics, chemotherapy regimen, tumor and nodal response were analyzed. Nomogram was developed using a multivariable logistic regression model in a training cohort and validated in an external cohort of 110 patients between 2013 and 2014.
Results: Axillary pCR was achieved in 38.8% of the patients who underwent ALND after NCT. Axillary pCR was associated with early clinical nodal status, negative estrogen receptor status, positive HER2 status treated with trastuzumab, clinical nodal response and clinical tumor response on the multivariate analysis. Nomogram was developed on the basis of significant and predefined predictors. It had good performance with discrimination (AUC 0.822, 95% CI 0.781–0.862) and calibration (P = 0.8806). The nomogram was validated (AUC 0.828, 95% CI 0.754–0.903), indicating good predictive power of the model when applied to the external validation data set.
Conclusion: Our nomogram may be useful to predict the axillary pCR after neoadjuvant chemotherapy in patients with node-positive breast cancer. Patients with a high probability of achieving axillary pCR could be spared axillary lymph node dissection, avoiding postoperative morbidity.
Disclosure of Interest: No significant relationships.

P324

Endoscopic breast surgery can be navigated by virtual mode of 3D-CT

K. Yamashita*. *Breast Surgery, Nippon Medical School, Bunkyo-ku, Tokyo, Japan*

Goals: The conventional breast surgery, including breast conserving surgery (BCS), makes many large wound scars on the breast with granulated ugly scars. We devised endoscopic video-assisted breast surgery (VABS) to perform partial and total mastectomy without any wound on the breast. We have performed on more than 400 patients since 2001. To obtain the minimum clear surgical margins and to improve the aesthetics of the breast after surgery, we tried to navigate VABS by the virtual mode of 3D-CT with endoscopic ultrasonographic probe. We evaluated the long term results of the aesthetics and curability over 10 years after surgery and the efficacy of the new navigation techniques.
Methods: VABS consists of BCS, mastectomy, sentinel node (SN) biopsy, axillary node dissection, and breast reconstructions. It uses periareolar approach and/or axillary approach. Trans-axillary retromammary approach (TARM) is a single port surgery with an axillary skin incision. The each wound length is usually 2.5 cm, but 1 cm for SN biopsy. We cut the mammary gland with clear surgical margin from behind the mammary gland. The virtual endoscopic mode of 3D-CT images are overlaid on the endoscopic view to navigate precise SN biopsy and clear cutting at surgical margin of mammary gland. The endoscopic ultrasonographc probe can show precise position of the tumor and surgical margin from the backside of the mammary gland. The postoperative aesthetic results were evaluated by ABNSW. The sensory tests were performed on the skin of breast and axilla after surgery chronically.
Results: The endoscopic SN biopsy was performed on 400 patients, and 3D-CT lymphography on 300 patients. The virtual navigation helped to detect precise SN successfully. BCS was performed on 300 patients and skin-sparing mastectomy on 50 patients. The operative cost is very low as the conventional one. There was no significant difference in operational infestation. There was no serious complication after surgery. Surgical margin was minimally positive in 2 patients. The original shapes of the breast were preserved well. The follow-up is 160 months at maximum. There is 3 locoregional recurrences and 14 distant metastases. 5-year survival rate is 97.5%. The postoperative esthetic results were excellent and better. The sensory disturbance was minimal. All patients expressed great satisfaction.
Conclusion: VABS can be considered as a good surgical procedure concerning locoregional control and esthetics. The endoscopic navigation system is useful for SN biopsy and partial mastectomy.
Disclosure of Interest: No significant relationships.

P325

Lymphedema incidence over time with sentinel lymph node dissection alone of Japanese women

A. Ogiya[1]*, D. Kitagawa[1], T. Sakai[1], Y. Miyagi[1], K. Iijima[1], H. Morizono[1], M. Makita[1], R. Horii[2], F. Akiyama[3], T. Iwase[1]. *[1]Surgical Oncology, Breast Oncology Center, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan, [2]Pathology, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan, [3]Pathology, Cancer Institute of the Japanese Foundation for Cancer Research, Tokyo, Japan*

Goals: To elucidate the frequency of lymphedema occurrence over time with sentinel lymph node dissection alone of Japanese women.
Methods: This study focused on 355 patients with primary breast cancer who allowed measurements to be taken of their arms before surgery between November 2009 and June 2010. The following circumferences were measured on both arms at the time of surgery and 1 and 3 years postoperatively at (1) 5 cm proximal to the olecranon, (2) 5 cm distal to the olecranon, (3) the wrist, and (4) the dorsum of the hand.
We defined the "L" measurement as: (difference in circumference) = (postoperative circumference of the affected limb − preoperative circumference of the affected limb) − (postoperative circumference of the healthy limb − preoperative circumference of the healthy limb). Edema was considered present when (1) L ≥ 2 cm in at least one instance or (2) it was clearly recognizable to the naked eye ("observable edema"). In the absence of observable edema, a patient was considered to have "latent edema" if L was ≥2 in at least one instance.
Results: There were 239 subjects in the dissection omitted group (SN group) and 116 subjects in the dissection group (Ax group). At 1 year postoperative, the frequencies of lymphedema in the SN and Ax groups were 4% and 13% latent edema and 0% and 9% observable edema, respectively. Three years postoperative, the frequency of lymphedema was 6.5% and 12% in patients with latent edema in the SN and Ax groups, respectively, and 0% and 15% in patients with observable edema in the SN and Ax groups, respectively. Among the nine subjects in the SN group who displayed lymphedema at 1 year postoperative, lymphedema disappeared in three by the third postoperative year. Most cases of lymphedema in the SN group that appeared 1–3 years postoperative were located 5 cm proximal to the elbow.
Conclusion: The frequency of lymphedema occurrence over time increased in the SN group, and all were cases of latent edema.
Disclosure of Interest: No significant relationships.

P326

ARM in breast cancer with enlarged lymph node: a Chinese single center experience

X. Ding*. *Department of Breast Surgery, Zhejiang Cancer Hospital, Hangzhou, China*

Goals: To study the success rate and safety of axillary reverse lymphatic mapping (ARM) and the their effects on the function and lymph edema of ipsilateral upper limb, and the quality of life of patients with early breast cancer after operation, further explore the related factors affecting the success rate of ARM.
Methods: Among of 60 cases of female patients with enlarged axillary lymph nodes in early breast cancer confirmed by the clinical examination, preoperative lymphoscintigraphy by nano carbon was injected into the ipsilateral areola region by clockwise markering (named sentinel lymph node biopsy, SLNB), and intraoperative lymphoscintigraphy by methylene blue were injected into the subcutaneous and intramuscular of the ipsilateral medial arm by reverse markering (named axillary reverse mapping, ARM). In operation, we tried to protect the imaging lymph glands by reverse markering of upper limb (ARM), and only cleanned the axillary lymph nodes by clockwise markering (SLNB). Both the ARM nodes and the cross staining lymph nodes by methylene blue and nano carbon were carried out the intraoperative frozen section examination. We compared to the ipsilateral limb circumference and function and the quality of life of patient between the ARM success and ARM failure group, and actualized the normality test, t test and multivariate Logistic regression analysis for the potential factors of influencing ARM, such as age and body mass index (BMI).
Results: Among of 60 cases patients, 38 cases (63.3%) with successful ARM, 17 cases (28.3%) were not successful, 5 cases (8.3%) with cross staining or cannot distinguish lymph node stained color. Only 1 node was found existing isolated cancer nests in 31 ARM lymph nodes, and 2 nodes were found metastatic carcinoma in 5 cross staining lymph nodes. Whether the ARM success has no statistical difference in the quality of life, but the ARM success group has slightly superiority. In the function of the ipsilateral upper limb, except in the abduction ($P = 0.062$) and external rotation ($P = 0.083$) in ARM success group closing to statistical significance, all the rest patients had no significantly difference ($P > 0.05$). The body mass index (BMI) and degree of upper limb lymphedema in ARM success group were significantly lower than in the ARM failure group ($P < 0.05$), but had nothing to do with age ($P > 0.05$). Multivariate analysis showed whether success of ARM was the independent risk factor of ipsilateral upper limb lymphedema ($P < 0.05$).
Conclusion: To seek ARM in early breast cancer are safe and feasible, it can reduce the occurrence of ipsilateral upper limb edema, and is expected to improve upper limb function, as well as improve the quality of life. Whether ARM success is an independent risk factor for upper limb lymphedema after ALND.
Disclosure of Interest: No significant relationships.

P327

Comparative study of preoperative core needle biopsy and surgical specimens in breast cancer

P. Grigoropoulos[1]*, A. Drakou[2], N. Papakonstantinou[2], D. Karoutsos[2], M. Tsompalioti[2], O. Dagadaki[2], A. Tsipoura[2], D. Issaiadis[2], S. Ammari[2]. *[1]Surgical Clinic, General Oncological Hospital Ag. Anargyroi, Nea Makri, Greece, [2]General Oncological Hospital of Kifissia Ag. Anargyroi, Athens, Greece*

Goals: Core needle biopsy (CNB) is often used as a diagnostic tool in patients who suffer from breast cancer. The purpose of our study is to compare the concordance between the results of the CNB and those of the surgical excision specimens.
Methods: This retrospective comparative study include 45 patients who underwent core needle biopsy (CNB) preoperatively to confirm breast cancer, from 10/2012 to 12/2014 in our clinic. All biopsies were performed under ultrasound-guided with at least five 14-gauge core biopsies being obtained for pathological examination. We examined the histologic type of the cancer, the grade, ER, PR, Her2, Ki67 and p53. In the patients found with Her2 2+ the specimen was examined with FISH or CISH methods. The cut-off of Ki67 was 14%. Specimens are considered positive for ER, PR in cases that staining of the nucleus of the cells is over 1%. Her2 tumors were categorized as positive if >10% of the nuclei was stained. P53 positivity was defined as greater than 5% positivity staining of any intensity in the tissue. All were diagnosed with invasive ductal breast carcinoma.
Results: The average age of patients was 59.5 years (range 30–90). The histologic type in core needle biopsy comparing with that of the surgical excision specimen was the same in all cases. The overall concordance rate of modified by Elston and Ellis scale of Bloom–Richardson score between CNB and histology reports was 100%. Immunohistochemical stainings for ER positive were reported in 37 patients' excisional biopsies (82.2%) and for ER negative in 8 (17.8%). The false positive ER of CNB were 2 (4.44%) and the false negative ER were 1 (2.22%). Immunohistochemical stainings for PR positive were reported in 34 cases (75.6%) and PR negative in 11 (24.4%). 3 (6.66%) false negative PR results of CNB were observed. 8 (17.8%) of our patients were Her2 positive, while 35 (77.8%) diagnosed as Her2 negative. False negative cerb2 observed in 1 case (2.22%) and false positive in 2 (4.44%). As far as p53 concerns, it was positive in 29 patients (64.5%) and negative in 16 (35.5%). False negative and false positive percentage was respectively 4.4% (2 cases) and 6.6% (3 cases). Ki67 is reported <14% in 14 patients (31.1%) and >14% in 31 (68.9%). 3 of these cases (6.6%) had false Ki67 <14% and also 3 cases (6.6%) had false Ki67 >14%.
Conclusion: The discordance percentages that are noted between CNB and surgical excision specimens may be due to many factors, such as sampling of the tumor, preparation techniques of immunohistochemical staining, the time of samples fixation etc. Nevertheless, in the majority of cases CNB findings are in concordance with the findings of histologic features. In conclusion, our study supports the recommendation that core needle biopsy considered the first procedure to assess molecular subtypes and receptor status in invasive breast cancer. The detection of those markers is suggested to be verified with the findings of histologic features.
Disclosure of Interest: No significant relationships.

P328

Does lobular histology matter in the post-Z0011 era?

F. Muscara*, P.A. Barry, C. Richardson, J.E. Rusby. *Breast Unit, Royal Marsden Hospital, London, United Kingdom*

Goals: Invasive Lobular Cancer (ILC) presents challenges in the diagnosis of early primary disease and the determination of tumour size and extent. Assessment of axillary lymph node involvement clinically and by ultrasound (US) before surgery is no trivial matter. In the ACOSOG Z0011 trial only 63 eligible patients (across both arms) had ILC. We aimed to analyse the clinical utility of One-Step Nucleic acid Amplification (OSNA) in intra-operative detection of axillary sentinel lymph node (SLN) involvement after negative axillary US and/or FNA for ILC and mixed ILC and IDC. We also examine standard clinico-pathological (C-P) factors which may predict a positive OSNA SLN result and document the rate of non-SLN involvement with ALND.
Methods: Retrospective analysis of prospectively stored data on consecutive patients with early BC who underwent surgery with SLN biopsy and OSNA analysis between October 2011 and November 2014 at the Royal Marsden Hospital (UK). ALND was performed only

in patients with a "macroscopic" OSNA result. OSNA results from the Sysmex RD-100i was collected in a blinded fashion separately from C-P data combined only after all data collection was complete, pre-analysis.
Results: We identified 199 patients with either ILC or mixed ILC and IDC who underwent SLN biopsy and OSNA analysis. The median patient age was 61 years, 40% of whom were screen detected with 47% having pT1 or pT2 pathology. OSNA sensitivity and specificity to predict axillary non-SLN involvement was 78.4% and 85% respectively. SLNs of 54 patients (27%) were "macroscopic" (CK 19 mRNA ≥5000/ul) by OSNA. In patients undergoing ALND, 45% had ≥3 positive non-SLNs. Analysis of C-P factors showed presentation (screening vs symptomatic), pathological Tsize and lymphovascular invasion to be predictive of macroscopic SLN ($p < 0.05$ for each). Despite pT1, pT2 and pT3 rates of macroscopic SLN involvement of 8.3%, 27% and 50% respectively and of those, non-SLN positivity rates in ALND of 60%, 29% and 80%, the poor correlation of pre-operative ultrasound and MRI with pT size ($R = 0.44$ and 0.55 respectively) makes pre-operative prediction challenging.
Conclusion: The significant non-SLN tumour burden in ALND after positive OSNA-based SLN in patients with ILC coupled with difficulties in determining disease extent (a major predictor of lymph node positivity) a priori, we recommend continued ALND following "macroscopic" SLN detection by OSNA in this histologic subtype.
Disclosure of Interest: No significant relationships.

P329
Sentinel lymph node biopsy after primary systemic therapy for locally advanced breast cancer

S. Takayama*, J. Matsui. *Surgery, Tokyo Dental College Ichikawa General Hospital, Chiba, Japan*

Goals: Sentinel lymph node biopsy (SLNB) after primary systemic therapy (PST) is still controversial because of possibly reduced accuracy. But some recent studies revealed that SLNB correctly identified nodal status after PST in patients with node-negative (N0) and node-positive (N+) breast cancer, and could therefore provide a less invasive option than axillary lymph node dissection (ALND) for nodal staging in this population. The aim of this study was to examine the outcome of SLNB after PST among single institute patients.
Methods: A total of 78 breast cancer patients were treated with preoperative chemotherapy in our hospital from June 2008 to December 2012. The combination of blue dye and radioactive tracer was used for identification of sentinel lymph nodes (SLNs).
Results: SLNB after PST had been performed in 42 patients; all of 34 patients who initially presented with N0, and 8 of 43 patients with N+ before PST. SLN identification rate was 100%, the number of SLNs were 1 to 5 (median 2). Of the 34 patients with N0, 31 patients (91.2%) were pathologically N0 (pN0). Of the 43 patients with N+, 8 patients (18.6%) converted to a N0 status after PST underwent SLNB. 7 of 8 patients (87.5%) were pN0 and omitted ALND. 6 of 8 patients (75.0%) were also pathological complete response cases of primary breast cancer. Of the other 35 patients with N+ underwent ALND without SLNB, 17 patients (48.6%) were pN0.
Conclusion: In this study, we performed SLNB only marked response cases of PST. SLNB after PST could be very useful procedure to spare ALND in selected patients not only with N0 but also N+.
Disclosure of Interest: No significant relationships.

P330
Sentinel lymph node: a secure technique in breast surgery

M. Zoulamoglou[1]*, T. Piperos[2], E. Konstantinou[3], K. Theodoulou[4], S. Tanteles[5], K. Kyriakou[2], T. Mariolis-Sapsakos[1]. *[1]School of Nursing, Laboratory of Anatomy-histology and Embryology, National Kapodistrian University of Athens, Athens, Greece, [2]Department of Surgery, University of Athens, Eugenidion Hospital, Athens, Greece, [3]School of Nursing, Department of Anesthesiology, National Kapodistrian University of Athens, Athens, Greece, [4]Department of Breast Surgery, Mitera Hospital, Athens, Greece, [5]Department of Radiology, University of Athens, Eugenidion Hospital, Athens, Greece*

Goals: To demonstrate the use of sentinel lymph node as a golden standard in contemporary breast surgery and the presentation of the results of this technique in the past five years.
Methods: This is a retrospective analysis of 450 women during a 10 year period from 2006 to 2014, diagnosed with breast cancer with no palpable axillary lymph nodes. The age of patients ranged from 28 to 89 years with median age of 61.4 years.
Results: All patients both in clinical examination and at the mammographic control did not present palpable axillary lymph nodes. Two hundred and eighty-three (62.8%) patients presented with a palpable breast mass with suspicious mammographic findings. 167 (37.1%) patients had a non-palpable lesion but there were mammographic findings, as architectural disorders of the breast. In 294 (65.3%) of the patients the mapping of the sentinel lymph node was achieved with methylene blue infusion, while both methylene blue and a radioactive substance infusion was used for the rest 156 (34.6%) patients. Two hundred and seventy-six (61.3%) patients underwent a lumpectomy and in 174 (38.7%) patients a modified radical mastectomy was performed. In 440 (97.7%) patients the sentinel lymph nodes were discovered while in 10 (2.3%) patients that was not feasible therefore an axillary lymphadenectomy was performed. All sentinel lymph nodes were examined with frozen section. In 329 (74.7%) patients the sentinel lymph node had negative findings while in 111 (25.3%) the sentinel lymph node report was positive and an axillary lymphadenectomy followed. The final pathology report confirmed the findings of the frozen sections.
Conclusion: Sentinel lymph node is a safe and appropriate practice in contemporary breast surgery. The simultaneous infusion of a radioactive substance with methylene blue assists both with the reliable staging for the breast cancer and the avoidance of non-necessary axillary lymphadenectomies with any attendant complications may occur.
Disclosure of Interest: No significant relationships.

P331
Estimation of sentinel lymph node metastasis with CT lymphography after primary chemotherapy

A. Tangoku*. *Department of Thoracic Endocrine Surgery and Oncology, Tokushima University Graduate School, Tokushima, Japan*

Goals: ACOSOG Z0011 showed the possibility of omitting axillary lymph node dissection in T1–2 breast cancer with SLN metastasis. But adaptation of SLNB after primary chemotherapy (PCT) is controversial. CTLG with a nonionic water soluble iodinated contrast medium allows quick visualization of direct connection between primary SLN and its afferent lymphatic channels with providing detailed anatomy at the time of preoperative CT scan. LN metastasis can be diagnosed using CTLG by detecting the obstruction of the lymph vessel and tumor replacement.
Methods: From Jan 2005 to Dec 2013, 169 patients with breast cancer underwent PCT in Tokushima University Hospital. CTLG was applied to all patients. SLN metastasis was diagnosed according to the following criteria: (A) Defect of the SLN, scissor clubbed defect

sign or mottled stain of the LN, (B) Stagnation and (C) Interruption of the lymph vessels, (D) Abnormal rerouting of the lymphatic route. Preoperative diagnosis was compared to pathological report after operation.

Results: 138 of 169 patients diagnosed have metastasis. Accuracy of preoperative diagnosis for metastasis was 73.0%. Positive predictive value was 81.0% and negative predictive value was 69.0% after the surgical pathological diagnosis.

Conclusion: CTLG can detect correct SLN number and position with surrounding detailed anatomy, moreover metastatic SLN can be diagnosed. Patients with non-metastatic SLN diagnosed by CTLG before PCT could avoid SLN biopsy.

Disclosure of Interest: No significant relationships.

P332

Oncological outcomes of breast-conserving surgery using reduction mammoplasty in breast cancer

M.A. Gulcelik*, L. Dogan, N. Karaman, Y.S. Kahraman, C. Ozaslan.
Surgical Oncology, Ankara Oncology Hospital, Ankara, Turkey

Goals: Reduction mammoplasty (RM), which has long been used for the treatment of macromastia, has recently become a preferred technique in the surgical treatment of breast cancer patients with macromastia. There is limited evidence in the literature on the oncologic safety of the oncoplastic procedures. We have reported the results of the 223 breast cancer patients with macromastia treated with this technique in a single centre.

Methods: Two hundred twenty-three breast cancer patients with macromastia who underwent BCT via RM between 2003 and 2014 at Ankara Oncology Hospital were enrolled in the study. The patients who underwent with lower or upper pediculated flaps as a reduction technique are included. Lower pediculated flap technique was preferred for upper quadrant lesions and upper pediculated flap for lower quadrant lesions. The same technique was used for both breasts of the patients. All of the patients were stage I or II. Age, histopathological type, tumor size, local recurrence, distant metastasis, weight of the reduction mammoplasty specimens were analyzed. Following surgical treatment and chemotherapy if required, all patients underwent radiation; 50 Gy were delivered to the whole breast plus a boost of 10 Gy to the tumour bed. Oncological follow-up was performed with six mounth period clinical examination, chest X-rays, and blood tests, annual bilateral mammography. When a clinical suspicion occurred bone scan, liver US scan, and CT scan, were employed to detect distant disease.

Results: Median age was 50.6 years. Eighty-six percent patients were operated with lower pediculated flaps and 14% with upper pediculated flap. Axillary dissection was used for patients with metastatic sentinel lymph nodes proven at frozen section, and for patients with unidentified sentinel lymph nodes and clinically axillary positive. The median follow-up time was 38 months. Median weight of the reduction mammoplasty specimen for the cancerous side was 940±28 g, for the other side was 950±34 g. During follow-up one loco-regional recurrence was noted. The 5-year disease free survival (DFS) rate was 89% and the overall survival (OAS) rate was 95%. In stage I 5-year disease free survival rate was 95% and the overall survival rate was 100%. In stage II 5-year disease free survival rate was 86% and the overall survival rate was 93%.

Conclusion: Reduction mammoplasty provides techniques to achieve good esthetic results while also providing possibility for wide excision margins. Few studies report on long-term oncological results of oncoplastic surgery, our findings indicate that BCS via RM are as effective and safe as standard surgical procedures in breast cancer patients with macromastia. However, further studies in large series and longer follow-up may still be warranted.

Disclosure of Interest: No significant relationships.

P333

BMI and association with histopathological characteristics of the tumor in postmenopausal women

P. Grigoropoulos[1]*, N. Papakonstantinou[2], A. Drakou[2], D. Karoutsos[2], M. Tsompalioti[2], O. Dagadaki[2], D. Issaiadis[2], A. Tsipoura[2], S. Ammari[2]. *[1]Surgical Clinic, General Oncological Hospital Ag. Anargyroi, Nea Makri, Greece, [2]General Oncological Hospital of Kifisia, Ag. Anargyroi, Athens, Greece*

Goals: The purpose of our study is to analyze the association between the increased bodyweight, by using the body mass index (BMI), and the histopathology of breast cancer (size of tumor, grade, hormone receptors, Her2, Ki67, p53, lymph nodes) in postmenopausal women.

Methods: In this retrospective study, 105 patients were examined, who were operated in our clinic who suffer from breast cancer from 10/2012 to 12/2014. ER and PR tumors were categorized as positive if ≥1% of the nuclei was stained. HER2 tumors were categorized as positive if >10% of the nuclei was stained. The patients were categorized as being normal weight with BMI ≤24.9 kg/m^2, overweight with BMI 25–29.9 kg/m^2 or obese with BMI >30 kg/m^2.

Results: The average of BMI was 27.27 kg/m^2 (range 17.63–43.75 kg/m^2).

In the category of normal weight patients (BMI ≤24.9 kg/m^2), we diagnosed 14 patients of stage I (31.8%), 17 patients of stage II (38.6%) and 13 of stage III (29.5%). As far as tumor size concerns, 19 patients were in T1 (43.1%), 21 were in T2 (47.7%), and 4 in T3 (9.1%) stage. Regarding the lymph nodes, 21 patients were diagnosed in N0 (47.7%), 15 in N1 (34.1%), 6 in N2 (13.6%) and 2 in N3 (4.5%). Referring to the hormone receptors and the expression of Her2, the most common combination was ER+ PR+ Her2− in 27 patients (61.36%) followed by ER− PR− Her2+ in 5 (11.36%), ER− PR− Her2− in 4 (9.1%) and ER+ PR+ Her2+ in 3 (6.8%).

In the category of overweight patients (BMI 25–29.9 kg/m^2) we diagnosed 6 of stage I (20%), 11 (36.7%) of stage II, and 13 (43.3%) of stage III. Concerning the tumor size, we had 13 patients in T1 stage (43.3%), 10 in T2 (33.3%) and 6 in T3 (20%). As far as lymph nodes concerns, 14 patients were diagnosed in N0 (46.66%), 6 in N1 (20%), 4 in N2 (13.33%) and 6 in N3 (20%). Referring to the hormone receptors and the expression of Her2, the most common combination was ER+ PR+ Her2− in 16 patients (53.33%), ER− PR− Her2− in 5 (16.66%), ER− PR− Her2+ in 4 (13.33%) and ER− PR+ Her2+ in 4 (13.33%) and ER− PR+ Her2+ in 1 (3.33%).

In the category of obese patients (BMI >30 kg/m^2) the grade was: 10 patients in stage I (33.3%), 10 in stage II (33.3%) and 10 in stage III (33.3%). Referring to the tumor size, we had 10 patients in T1 (33.3%), 16 in T2 (53.3%) and 4 in T3 (13.3%). Respecting the lymph nodes 15 patients were in N0 (50%), 13 patients in N1 (43.3%) and 2 in N2 (6.6%). Concerning the hormone receptors and the expression of Her2 we had ER+ PR+ Her2− in 25 patients (83.3%), ER+ PR− Her2− in 1 (3.33%), ER− PR− Her2+ in 1 (3.33%) and ER+ PR+ Her2+ in 3 (10%).

We could not find correlation between Ki67 and P53 and BMI.

Conclusion: In our study, we demonstrate that in postmenopausal women with BMI >25 we diagnosed larger tumors, more positive lymph nodes and higher grade of breast cancer, which indicates more aggressive growth and characteristics of the cancer cells. These tumors have high expression of ER+ PR+ and low expression of Her2−.

Disclosure of Interest: No significant relationships.

P334

The breast reconstruction in breast cancer patients with a history of Hodgkin lymphoma

Z. Kozomara*, N. Jokic, M. Jevric, I. Spurnic, O. Kosovac, Z. Inic, M. Kocic, M. Buta, M. Oruci, R. Dzodic. *Surgery, Oncology and Radiology, Beograd, Serbia*

Case presentation: A 33-year-old female was referred to our institution in April 2011. Previous medical history was mantle radiation for the treatment of Hodgkin lymphoma.
Physical examination revealed a 10 mm tumor located on the right breast. The armpits did not present lymphadenopathy. Mammographic findings consisted of a noncalcified high density mass and breast ultrasonography revealed a hypoechogenic nodule of irregular shape with partially defined limits measuring $11 \times 11 \times 10$ mm in the right breast. Final Breast Imaging Reporting and Data System (BI-RADS) category was 5: highly suggestive of malignancy. Fine-needle aspiration biopsy of the lesion were performed, and the diagnosis was suspicion of ductal carcinoma. Previous medical and family history were diagnosed with stage IIA nodular sclerosing Hodgkin lymphoma and she underwent a CT followed by mantle radiation for the treatment of Hodgkin lymphoma. The age at the time of mantle radiation was 25 years. The time interval between mantle radiation and the diagnosis of breast cancer was 8 years.
The patient underwent initial unilateral mastectomy and unilateral tissue implants placement. There were no postoperative complications after breast reconstruction. The anatomopathological analysis confirmed the diagnosis of invasive ductal carcinoma with a 10 mm lesion, which was histologic grade 3 and nuclear grade 3. Axillary lymph node dissection did not show any signs of cancer (0/17). In addition, immunohistochemical staining of the tumor was negative for estrogen and progesterone receptors, and HER-2 negative (Score 0). The patient received adjuvant therapy $6 \times$ CMF chemotherapy. Post-therapy follow-up was performed by members of the treatment team and included regular physical examinations and history. Liver function and alkaline phosphatase tests were not indicated during the time the patient was taking therapy. For the last three years of follow-up there was no recurrence of the disease.
Conclusion: The risk of breast cancer is increased after Hodgkin's disease. Screening has been successful in detecting early-stage cancers. Repeat irradiation of the breast can lead to tissue necrosis, and thus, mastectomy remains the standard of care in most cases.
Disclosure of Interest: No significant relationships.

P335

Our preference and clinical experience in oncoplastic breast cancer surgery

M.A. Gulcelik*, L. Dogan, N. Karaman, Y.S. Kahraman, C. Ozaslan. *Surgical Oncology, Ankara Oncology Hospital, Ankara, Turkey*

Goals: Breast cancer is one of the most common cancers worldwide and surgery is still the fundamental part of its treatment. Currently, the main goal of treatment is to perform breast conserving surgery with acceptable cosmetic results. When compared with traditional techniques of breast conserving surgery, oncoplastic surgery provides better cosmetic results with similar oncologic outcomes.
Methods: One thousand nine hundred and fifty breast cancer patients, operated in Ankara Oncology Training and Research Hospital between March 2008 and December 2014, were evaluated retrospectively. The surgical treatments applied were grouped as mastectomy (modified radical or simple), conventional breast conserving surgery and oncoplastic surgery.
Results: The rates of mastectomy, conventional breast conserving surgery and oncoplastic breast surgery were 780 patients (40%), 487 patients (24.9%) and 683 patients (35%), respectively. Applied surgical techniques in patients who underwent oncoplastic breast surgery in order of frequency were; intraglandular flaps (like racquet incision, round block technique, batwing mastopexy etc.) in 553 patients (80.9%), reduction mammoplasty in 78 patients (11.4%), mastectomy with latissumus dorsi flap reconstruction in 26 patients (3.8%), mastectomy with external expandable silicon prosthesis in 20 patients (2.9%) and mastectomy with transverse rectus abdominis musculocutaneous flap reconstruction in 6 patients (1%).
Conclusion: The surgical treatment of breast cancer is changing rapidly and less invasive surgical techniques are performed commonly. Breast conserving surgery may sometimes lead to deformities in the remaining breast. Oncoplastic surgery brings together the oncological and reconstructive principles to the surgical management of breast disease. Oncoplastic surgery is an essential surgical tool in breast cancer treatment.
Disclosure of Interest: No significant relationships.

P336

Outcome of sentinel node biopsy after neoadjuvant chemotherapy in CN0 breast cancer

K. Tsugawa*, R. Hayami, T. Uejima, Y. Kojima, T. Nishikawa, H. Kawamoto. *Breast and Endocrine Surgery, St. Marianna University School of Medicine, Kawasaki, Japan*

Goals: Sentinel node biopsy (SNB) and elimination of axillary clearance (Ax) after neoadjuvant chemotherapy (NAC) are still controversial. However, clinically node-negative patients in both pre- and post-chemotherapies are considered to be safe indicated to SNB from the reports of low false negative rate. Therefore, we evaluated the oncologic outcome of 248 patients underwent SNB after NAC.
Methods: Seven hundred and fourteen patients received NAC during January 2005 to December 2011 in our institute. We indicate SNB after NAC for clinically node-negative patients in both pre- and post-chemotherapies by ultrasonogram and CT scan. The RI and blue dye methods and intraoperative histological diagnoses using H&E frozen sections were performed.
Results: Two hundred and forty-eight patients underwent SNBs after NAC. Identification rate was 99.6% (247/248). Forty-two patients underwent immediate Ax because of positive metastatic nodes proven by intraoperative frozen sections. Two hundred and six cases were eliminated of Ax. False negative rate of frozen section diagnoses was 1.6% (4 cases). Sixty-four percent of patients had positive metastatic nodes in SNs alone. Ipsilateral axillary recurrences occurred in four cases (1.9%) of elimination of Ax cases. One also had ipsilateral breast recurrence and the other also had lung metastases. On the other hand, ipsilateral axillary recurrences occurred in 18 cases (3.9%) of 466 Ax cases.
Conclusion: The eliminations of Ax from results of SNB were safe in the patients with clinically negative nodes in the both pre- and post-chemotherapies.
Disclosure of Interest: No significant relationships.

P337

The evaluation of safety of SSM and NSM with reconstruction after NAC for locally advanced BC

T. Shien[1]*, Y. Abe[1], A. Watanabe[1], Y. Miyoshi[1], T. Nogami[1], T. Mizoo[1], S. Watanabe[2], N. Taira[1], H. Doihara[1]. [1]*Breast and Endocrine Surgery, Okayama University Hospital, Okayama, Japan,* [2]*Breast Cancer Treatment and Reconstruction, Okayama University Hospital, Okayama, Japan*

Goals: Breast reconstruction surgery has become a standard treatment to maintain cosmetic outcome for breast cancer patients. Skin sparing mastectomy (SSM) and nipple sparing mastectomy (NSM), which conserve the skin and nipple–areolar complex (NAC) covering primary tumor have better cosmetic outcome than conventional skin incision. However the evaluation of safety and prognostic impact of these procedure are under debate. Moreover SSM and NSM after neoadjuvant chemotherapy for locally advanced breast cancer patients is not evaluated prospectively yet.
Methods: We enrolled locally advanced breast cancer patients who underwent SSM and NSM with reconstruction surgery retrospectively, and evaluated clinicopathological features and prognosis of these patients.
Results: From October 2007 to May 2013, 144 patients underwent reconstruction surgery in Okayama University Hospital. SSM, NSM and conventional incision for reconstruction surgery were 32 (22%), 82 (57%) and 30 (21%), respectively. 13 patients received NAC before surgery. Median age was 46 years (range 24–64) and median age of patients who underwent SSM, NSM or Bt was 45, 45 and 46 years. Reconstruction procedures were LD 58, DIEP 51, TE 33 and TRAM 2. Median tumor size of patients who underwent SSM, NSM and Bt was 2.3 cm, 2.2 cm and 2.0 cm (N.S.). There was one patient with nipple necrosis. 10/144 had recurrence, including one lymph node, one skin metastases and 8 distant metastases. There was no regional recurrence and two patients with NAC before surgery had distant metastases.
Conclusion: Reconstruction after NAC for locally advanced breast cancer had no significant safety and prognostic risk.
Disclosure of Interest: No significant relationships.

P338

Surgical site infection after breast surgery

Y.S. Ahmed*. *Surgery Department, Medical Research Institute, Alexandria, Egypt*

Goals: The rate of breast SSIs (surgical site infection) range from 1% to 30%, depending on definition of SSIs, type of operation, comorbidities of the patients, time of follow up, perioperative therapy and reporting institution. Surgical site infections (SSIs) are major sources of adverse operation-related events in patients undergoing surgery. This study aimed to identify the rate, the degree, the treatment and the causative organisms of SSI after breast surgery in the hospital of Medical Research Institute, University of Alexandria, which receives the highest rate of breast surgery all over Alexandria.
Methods: The study prospectively included all patients admitted to the department of Surgery, the hospital of Medical Research Institute, University of Alexandria during the period from February 2013 to June 2013 who were planned for breast surgery either minor or major procedures. Patients were followed up to 30 days after surgery if no implant and up to one year if with implant placed during the operation. The grade of SSIs were identified using Southampton wound scoring system.
Results: The study included 124 patients who were admitted to the department of Surgery, the hospital of Medical Research Institute, University of Alexandria during the period from February 2013 to June 2013 who were planned for breast surgery either minor or major procedures. Surgical site infections were diagnosed after 14 operations (11.3%) including both minor and major procedures; twelve cases (85.7%) have been diagnosed after the major procedures while only 2 cases (14.3%) have been diagnosed after the minor procedures. All patients who had SSI after breast surgery have been detected during the outpatient follow up. four cases (28.6%) out of the 14 who had ssi after breast surgery need to be readmitted for management of SSIs. Staphylococcus aureus (S.aureus) was the most common pathogen (isolated from 42.8% of all cases).
Conclusion: SSIs are important and common complications following breast surgery. They can occur after any type of breast surgery either minor or major. Microbiological diagnosis is an essential tool for proper management.
Disclosure of Interest: No significant relationships.

P339

Predictive values for non sentinel lymph nodes in breast cancer with metastatic sentinel lymph node

A. Guzijan[1]*, Z. Gojković[2], B. Babić[3], I. Rakita[2], B. Jakovljević[4], B. Jovanić[5]. [1]*Oncology Clinic – Breast Center, University Hospital, Banja Luka, Bosnia and Herzegovina,* [2]*Oncology Clinic, University Hospital, Banja Luka, Bosnia and Herzegovina,* [3]*Institute of Pathology, University Hospital, Banja Luka, Bosnia and Herzegovina,* [4]*Medical Faculty, University of Banja Luka, Banja Luka, Bosnia and Herzegovina,* [5]*Institute of Clinical Radiology, University Hospital, Banja Luka, Bosnia and Herzegovina*

Goals: Sentinel lymph node biopsy is a standard procedure in early stage breast cancer patients. Following to ACOSOG Z0011 trial, avoiding of axillary clearance in positive sentinel lymph node with macrometastasis is one of the solutions. We analyzed histological and biological parameters of breast cancer as predictive values in sentinel lymph node positive breast cancer patients according to non sentinel lymph nodes in axilla.
Methods: We analyzed breast cancer patients who are undergoing sentinel lymph node biopsy procedure. Patients were age between 30 and 80. Neoadjuvant chemotherapy, previous axillary surgery or radiotherapy and micrometastasis were excluded parameters. From March 2011 to November 2014 we randomized 108 female patients. Sentinel lymph node lymphatic mapping was performed with radioisotope (^{99}Tc), blue dye or both methods.
Results: From 108 analyzed patients, in 24 (22.2%) sentinel lymph node was positive with macrometastasis. From 24 patients in 14 (58.3%) we verified metastatic deposits in non sentinel lymph nodes (Group A), in other 10 (41.7%) patients non sentinel lymph nodes were without metastasis (Group B). Significantly differences were found in histological tumor grade, tumor size and peritumoral lymphovascular invasion ($p < 0.05$). The histological tumor grade 3, tumor size in diameter more than 2 cm and peritumoral lymphovascular invasion was predominant in group A. We did not find significant differences in tumor multifocality and biological markers E-cadherin, ER, PR and HER-2 expression.
Conclusion: Comparing histological and biological characteristics of breast cancer in patients with positive and patients with negative non sentinel lymph nodes, we can conclude that histological grade, tumor size and peritumoral lymphovascular invasion can be predictive factors for avoiding or not axillary clearance in positive macrometastatic sentinel lymph node.
Disclosure of Interest: No significant relationships.

P340

Sentinel lymph node biopsy can be safely performed in patients with suspicious lymph node

R. Nakamura[1]*, N. Yamamoto[2], Y. Oukubo[2], T. Miyaki[2], M. Itami[2]. *[1]Breast Surgery, Chiba Cancer Center, Chiba, Japan, [2]Chiba Cancer Center, Chiba, Japan*

Goals: The ACOSOG Z0011 trial showed that an axillary lymph node dissection (ALND) may be safely omitted in selected patients with a positive sentinel lymph node biopsy (SNB). One of these eligible criteria has non palpable lymphadenopathy. However, the eligibility for patients with a suspicious Ultrasonography (US) is controversial. The purpose of this study was to evaluate the validity of the SNB for patients with suspicious lymph node (sN+) compared to clinical node negative patients (cN0).

Methods: Patients with suspicious axillary lymph node positive breast cancer by preoperative assessed US or CT were performed fine needle aspiration (FNA) cytology between 2004 and 2014. Patients with a negative **axillary** US (cN0 group) or negative **FNAC** (sN+ group) result underwent SNB. All SNB positive patients underwent completion ALND. The number of positive nodes after ALND was compared cN0 group with sLN group.

Results: 530/2683 patients (19.7%) had positive SNB. Ultrasound-axilla was 49% sensitive and 84% specific in predicting SNB metastases. The positive (PPV) and negative predictive value (NPV) was 53% and 81% respectively. For suspicious group, this was 68.4% sensitive and 99.7% specific in detecting SNB metastases. PPV and NPV were 99.6% and 74.2% respectively. The number of metastasis lymph nodes is 1 (48%), 2 (19%), 3 (9%), more than 4 (54%) and N1mic (17%) in the cN0 group, and 1 (37%), 2 (14%), 3 (7%), more than 4 (10%) and N1mic (28%) in the cN1 suspicious group.

Conclusion: These results suggest that patients with suspicious axillary metastases on ultrasound-guided biopsy have less involved nodes than SNB-positive patients with clinical negative node. Therefore, we conclude that SNB can be safely performed in patients with clinically suspicious lymph node on ultrasonography.

Disclosure of Interest: No significant relationships.

P341

Use of fibrin glue in the prevention of seroma formation after axillary lymphadenectomy

J.I. Sánchez-Méndez[1]*, A. Román Guindo[2], C. Martí Álvarez[2], A. Rychlik[2], S. Serrano Velayos[2], G. Steinberg Contreras[2], P. Alonso Fernández[2], M. Lombarte García[2], J. Santisteban Padró[2], J. De Santiago García[1]. *[1]Breast Unit – Gynaecologist, Hospital Universitario La Paz – IdiPaz, Madrid, Spain, [2]Breast Unit – Gynaecologist, Hospital Universitario La Paz, Madrid, Spain*

Goals: The primary objective of this study was to determine the effectiveness of a fibrin sealant in the prevention of seroma formation after axillary lymphadenectomy, in a group of breast cancer patients. Secondary objectives included a comparison with another group of patients, in which an usual surgical drainage was used, regarding hospital stay, operating time, and main postoperative complications.

Methods: We completed an analytical retrospective observational study of patients with breast cancer for whom a fibrin sealant was applied to the surgical site after an axillary lymphadenectomy (fibrin sealant group) and those for whom it was not applied (drain group), based on a review of breast cancer patient records from June 2006 to February 2014.

Results: We studied a total of 317 patients of whom in 192 no sealant was applied to the surgical site after axillary lymphadenectomy, and were managed conventionally with the placement of an axillary drain (drain group). These were compared with 125 patients to whom a fibrin sealant was applied to the surgical site after axillary lymphadenectomy, without drain (fibrin sealant group), over the same time period. In 88.9% of cases of the sealant group the procedure was a complete success and no seroma formation was observed. Only 14 patients from a total of 125 in the fibrin sealant group required percutaneous drainage due to the delayed appearance of seroma. Overall, early discharge – 24 to 48 hours after surgery – was possible in 91.2% of patients. The volume of fluid obtained in the group with drains was significantly larger (361 ml) compared with the volume collected in the fibrin sealant group (170 ml) ($p < 0.05$). Also significant differences in the number of punctures needed to evacuate the seroma between the two study groups were found (3.1 vs 2.3; $p < 0.05$).

A logistic regression analysis was performed, using the hospital discharged (greater than or less than 48 hours) as dependent variable, and age, surgical technique (classic or Ivanovic), histological type (ductal, lobular, others), histological grade (1, 2–3) as independent ones. Only the use or not of fibrin sealant presents statistical significance ($p < 0.005$). .

Conclusion: The use of fibrin sealants with low thrombin concentration is an effective means of preventing the formation of axillary seroma after lymphadenectomy, removing the need for a drain and reducing hospitalization time, with **early autonomous discharge**.

Disclosure of Interest: No significant relationships.

Table (abstract P341)

Group	Drain (N = 192)	Fibrin sealant (N = 125)	p value
Hospital stay, days, mean (SD)	5.15 (0.79)	1.98 (0.68)	0.000 [a]
Patients with prompt discharge (24–48 hours after surgery), n (%)	0 (0%)	113 (90.4%)	0.000 [b]
Early seroma, n (%)	192 (100.0%)	4 (3.2%)	0.000 [b]
Late seroma–percutaneous drainage, n (%)	18 (9.4%)	14 (11.2%)	0.598 [b]
Number of punctures for fluid removal, mean (SD)	3.1 (1.2)	2.3 (0.8)	0.044 [a]
Volume of fluid extracted, ml, mean (SD)	360.6 (175.6)	170.0 (146.8)	0.003 [a]

n, number of patients.
[a] Student's T test, [b] chi-squared test.

P342

A ten year review on macro-, micro-metastasis and isolated tumor cells in sentinel lymph nodes

M. Co*, A. Kwong. *Department of Surgery, Queen Mary Hospital/ The University of Hong Kong, Hong Kong, Hong Kong*

Goals: In patients with negative Sentinel lymph node biopsy (SLNB), axillary dissection (AD) can be avoided to reduce morbidities. However, there is only limited data on the rate of positive non-SLN (NSLN) in those who have micrometastasis and isolated tumor cells (ITC) in the literature.

Methods: We did a retrospective review of all clinically node-negative breast cancer patients with SLNB done at our unit from January 2001 to June 2011. Multivariate analysis was adopted to evaluate the risk factors for NSLN metastasis. Difference in 5-year disease-free survival (DFS) was evaluated with log-rank test.

Results: 537 patients underwent SLNB, 161 (30%) had positive SLN on frozen section (FS), 50 of these patients (31%) had NSLN metastasis, 25 patients had negative SLN on FS but were found to have micrometastasis on histopathology, only 1 (4%) of them

had NSLN metastasis, while 14 patients were found to have ITC in SLN; none of them had NSLN metastasis. Multivariate analysis found that the number of SLN harboring micrometastasis is the only independent risk factor for NSLN metastasis in patients with micrometastasis (p-value = 0.008). On the contrary; Tumor size, grade and biology were not associated with NSLN metastasis. 5-year DFS in patients with macrometastasis in SLN was 94.2%, while that in patients with micrometastasis and ITC was 100% (P-value <0.001).
Conclusion: NSLN metastasis in those who only have micrometastasis and ITC is rare, 5-year DFS is significantly better in this group of patients as well. It is therefore a routine practice in our unit to omit AD in patients with micrometastasis and ITC on SLN.
Disclosure of Interest: No significant relationships.

P343
Oncoplastic surgery for inner quadrant breast cancer: a modified dermoglandular rotation flap

S. Lee[1]*, J. Lee[2], Y. Jung[1], Y. Bae[1]. *[1]Surgery, Biomedical Research Institute, Pusan National University Hospital, Busan, Korea, [2]Surgery, Kyungpook National University Medical Center, Daegu, Korea*

Goals: Glandular rotation flap technique has been widely used for small defect after partial mastectomy in breast cancer patients. However, this technique is hardly performed for relatively large defect because of difficulty in obtaining a sufficient amount of tissue to fill the defect. In addition, conventional rotation flap technique for inner quadrant cancers is associated with a poor cosmetic result in spite of a small defect. To overcome these limitation in applying conventional glandular rotation flap technique for relatively large and inner quadrant defect of the breast, we introduce a modified superior-based dermoglandular rotation flap (so called fish-hook incision rotation flap).
Methods: Between January 2007 and December 2012, a total of 34 female patients with breast cancer underwent breast conserving surgery with the 'fish-hook rotational flap'. Data was collected retrospectively based on medical records, imaging findings and histopathologic results of the patients. The cosmetic results were self-estimated according to a four-point scoring system 4 weeks after radiotherapy.
Results: Mean volume loss of the breast was 20.2±9.8%. Location of the tumors were as follows; upper inner quadrant (n = 13, 38.2%), lower inner quadrant (n = 21, 61.8%). The overall cosmetic satisfaction was self-estimated as follows: excellent (n = 19); good (n = 10); fair (n = 4); poor (n = 1).
Conclusion: A modified superior-based dermoglandular rotation flap technique, the 'fish-hook incision rotation flap', is a feasible, effective oncoplastic technique that is applicable to a relatively large defect located in the inner quadrant of the breast. Also this surgical technique allows good cosmetic outcomes.
Disclosure of Interest: No significant relationships.

P344
An international multi-centre review of the malignancy rate of excised papillomatous breast lesions

N.M. Foley[1]*, Cork Papilloma Group[1], Beaumont Dublin Papilloma Group[2], Toronto Papilloma Group[3], Glasgow Papilloma Group[4], Budapest Papilloma Group[5]. *[1]Breast Research Centre, Cork University Hospital, Cork, Ireland, [2]Department of Surgery, Beaumont Hospital and the Royal College of Surgeons in Ireland, Dublin, Ireland, [3]Department of Surgical Oncology and Department of Laboratory Medicine and Pathobiology, University of Toronto, Ontario, Canada, [4]Department of Breast Surgery & Pathology, Victoria Infirmary, Glasgow, United Kingdom, [5]Department of Breast and Sarcoma Surgery, National Institute of Oncology, Budapest, Hungary*

Goals: Papillary lesions of the breast are a relatively rare, but heterogeneous group ranging from benign, to atypical and malignant. Debate exists regarding the optimal management of these lesions. In the absence of more accurate risk stratification models, traditional management guidelines recommend surgical excision, despite the majority of lesions proving to be benign. This study sought to determine the rate of malignancy in excised breast papillomas and to elucidate whether there exists a population, in which surgical excision may be unnecessary.
Methods: A multicentre international retrospective review of core biopsy diagnosed breast papillomas and papillary lesions from 2009 to 2013 was performed. Institutional ethical approval was obtained. Patient demographics, histopathological and radiological findings were recorded. All data were tabulated and statistical analysis performed using Stata (version 9.2, StataCorp, LP, College Station, TX, USA).
Results: 238 patients were included in the final analysis. The age profile of those with benign pathology was significantly younger than those with malignant pathology (<0.001). Atypia on core needle biopsy was significantly associated with a final pathological diagnosis of malignancy (OR = 2.73). The upgrade rate from atypia to malignancy was 40%. The upgrade rate from benign core needle biopsy to malignancy on the final pathological sample was 14.4%, however only 3.7% had invasive cancer.
Conclusion: This international dataset is one of the largest in the published literature relating to breast papillomas. The overall risk of malignancy is significantly associated with increased age and the presence of atypia on core needle biopsy. It may be possible to stratify higher risk patients according to age and core needle biopsy findings and avoid surgery on low risk patients.
Disclosure of Interest: No significant relationships.

P345
Perioperative outcomes of therapeutic breast surgery in the elderly

C.M. Lee*, V.K.M. Tan, B.K.T. Tan, W.S. Yong, P. Madhukumar, C.Y. Wong, K.W. Ong. *Surgical Oncology, National Cancer Centre Singapore, Singapore, Singapore*

Goals: This study aims to determine the perioperative mortality and morbidity of elderly patients who had therapeutic breast cancer surgery under general anesthesia. Parameters associated with increased surgical risk would also be identified.
Methods: Patients older than 80 years of age who underwent therapeutic breast cancer surgery at the National Cancer Centre Singapore and Singapore General Hospital from 1997 to 2010 were identified. Clinicopathological data, operative details and early post operation outcomes were reviewed and analysed.
Results: A total of 109 patients aged over 80 years had surgery during the study period. Ninety (82.6%) patients had at least one comorbidity, with hypertension (70.6%) being the most common preexisting condition, then dyslipidemia (29.4%) and diabetes mellitus (24.8%). Five (4.6%) had an American Society of Anesthesiology (ASA) physical classification score of I, 77 (70.6%) ASA II, 26 (23.9%) ASA III and one (0.9%) ASA IV. Ninety-seven (89%) patients had a mastectomy while 12 (11.0%) had breast conserving surgery. Eighty-eight (80.7%) patients had axillary staging. The median duration of surgery was 90 minutes. Perioperative mortality was zero. Sixty-six (60.6%) patients recovered without any complications. The most common complication was that of seroma requiring aspiration (n = 35, 32.2%). Bleeding occurred in six (5.5%) patients but none required a return to the operating theatre. One patient developed an acute myocardial infarction (0.9%) while another developed deep vein thrombosis. Median length of hospital stay was three days.
Conclusion: Despite the presence of co-morbidities, both curative and palliative breast surgery can be performed safely in those aged above 80 years, with low morbidity.
Disclosure of Interest: No significant relationships.

P346

Volume change of LD muscle after adjuvant therapy on immediate breast reconstruction using LDMCF

H.Y. Kim *, S. Nam, S.H. Lee. *Breast Surgery, Pusan National University Yangsan Hospital, Yangsan, Korea*

Goals: Immediate breast reconstruction using using Latissimus Dorsi musculocutaneous Flap (LDMCF) on breast cancer patient, the volume of flap decreased after chemotherapy and radiotherapy. Hence, in the process of reconstruction, size must be bigger than the original breast size. In particular, neuretomy of the nerve connected to latissimus dorsi muscle could worsen atrophy of muscle and which could cause secondary deformity of breast shape. Since few researches have been done in the matter of the decrease of this muscle volume, the author has conducted progressive study to understand the decrease of muscle volume after chemotherapy and radiotherapy in the process of breast reconstruction using latissimus dorsi muscle flap.
Methods: Research has been conducted from March 2011 to July 2014. Subjects included 10 patients who went through mastectomy due to breast cancer and received immediate reconstruction using latissimus dorsi musculocutaneous flap and those who have conducted CT scan from day 7 to 10 after surgery, received chemotherapy and radiotherapy and conducted CT scan 1 year later. Flap operation has been done by one surgeon, and all operations included neuretomy of the nerve which was connected to latissimus dorsi muscle. Recorded CT scans were then examined With PACS system, each CT scan were measured the area of rotated latissimus dorsi muscle, which can be recognized from up to down range with 5 mm intervals.
Results: Among 10 patients, measured values of flap volume and the decrease rate of volume of post-surgery era and 12 months after chemotherapy and radiotherapy showed that the average value of remaining volume rate was 44.0%, while the decrease rate was 50.0%.
Conclusion: We studied volume changes between before and after of chemotherapy and radiotherapy. From this research, it has been known that immediate reconstruction of breast through latissimus dorsi muscle flap led to 50% decrease of flap volume.
Disclosure of Interest: No significant relationships.

P347

Mammographic findings and early breast cancer: myth or reality?

T. Piperos[1], M. Zoulamoglou[2] *, K. Theodoulou[3], K. Kyriakou[1], T. Mariolis-Sapsakos[2]. *[1]Department of Surgery, University of Athens, Eugenidion Hospital, Athens, Greece, [2]School of Nursing, Laboratory of Anatomy-histology and Embryology, National Kapodistrian University of Athens, Athens, Greece, [3]Department of Breast Surgery, Mitera Hospital, Athens, Greece*

Goals: To present and comparative analyze the mammographic findings of suspicious lesions to the results of the pathology findings in palpable breast tumors.
Methods: This is a retrospective analysis of 250 women during the 5 year period from 2010 to 2014. The age of patients ranged from 23 to 89 years with median age of 57.8 years, who were presented with a palpable breast tumor and BIRADS IV and V mammographic findings.
Results: All patients underwent a mammography due to palpable breast mass during the clinical examination. One hundred and eighty-three (73.2%) patients had a BIRADS IV response – imaging and 67 (26.8%) patients had BIRADS V response – imaging. The clinical examination demonstrated a strong suspicion for malignancy, such as solid tumor and fixation to the thoracic wall, in 161 (64.4%) patients while in 89 (35.6%) the clinical examination did not confirm the mammographic findings. All patients were diagnosed with tumors sized less than 2 cm. All patients underwent a tumor biopsy and frozen section. In 206 (82.4%) out of 250 patients, the biopsy reported positive findings for malignancy, in which 178 (86.4%) of them followed a lumpectomy and in 28 (13.6%) a mastectomy. To the patients with positive frozen biopsy followed sentinel lymph node biopsy. All patients with negative frozen biopsy results had a negative clinical examination as well. The final pathology report confirmed the findings of the frozen sections.
Conclusion: The mammography findings in palpable breast lesions are always evaluated in comparison with the clinical examination. The clinical examination has a great significance even in BIRADS V lesions as shown from the results of our investigation. The frozen section of the lesions constitutes the golden standard for the further therapeutical options.
Disclosure of Interest: No significant relationships.

P348

Did breast MRI decrease the surgical margin involved rate? A case controlled comparison analysis

H. Lai[1] *, D. Chen[1], S. Chen[1], H. Wu[2], S. Kuo[1], C. Chen[3]. *[1]Department of Surgery, Changhua Christian Hospital, Changhua, Taiwan, [2]Department of Radiology, Changhua Christian Hospital, Changhua, Taiwan, [3]Department of Surgerical Pathology, Changhua Christian Hospital, Changhua, Taiwan*

Goals: Resection of primary tumor with clear margin is the goal of surgical management for primary operable breast cancer. Surgical margin involvement was associated with increased local recurrence, and usually mandated further surgery. The objective of current study is to assess whether combining breast MRI would decrease the rate of margin involvement compared with conventional breast image.
Methods: A retrospective, case controlled comparison study was conducted. Patients with primary operable breast cancer who received surgical management were searched from Changhua Christian Hospital (CCH) breast cancer database. The rate of surgical margin involvement was compared between two groups of patients with conventional breast image (Group A: mammogram and sonogram) or combined with breast MRI (Group B: mammogram, sonogram and MRI). Surgical margin involvement was defined as cancer cells present at surgical margin, or <1 mm. To further evaluate the effect of breast MRI on surgeon's margin involved rates, the index surgeons, defined as with more than 100 breast cancer operations in both Group A and Group B, were selected and analyzed.
Results: Group A, the conventional breast image group, consisted of 741 breast cancer patients. Among them, 381 (51.4%) received partial mastectomy, and 360 (48.6%) received total mastectomy. Overall, 66 (8.9%) margin involved events were found in Group A. The margin involved rates in Group A patients who received partial mastectomy or total mastectomy were 14.4% (55/381) and 3.1% (11/360), respectively.
Group B (conventional imaging combined with MRI) consisted of 736 breast cancer patients. Among them, 347 (47.1%) received partial mastectomy, and 389 (52.9%) received total mastectomy. The margin involved rate in Group B was 4.8% (35/736) overall. The margin involved rates in Group B patients who received partial mastectomy or total mastectomy were 6.1% (21/347) and 3.6% (14/389), respectively. The surgical margin involved rate was decreased after combination of breast MRI with conventional breast image: overall 8.9% → 4.8% (P = 0.0022), partial mastectomy 14.4% → 6.1% (P = 0.0004), and total mastectomy 3.1% → 3.6% (P = 0.8336).
Two index surgeons were selected for comparison of surgical margin involved rate before and after breast MRI. Surgeon A's margin involved rates in conventional breast image → combined MRI

were: overall 7.6% → 4.9%, partial mastectomy 14.0% → 8.1%, and total mastectomy 1.3% → 2.2%. Surgeon B's margin involved rate (from no MRI → MRI) was: overall 9.0% → 5.0%, partial mastectomy 12.1% → 3.9%, and total mastectomy 6.2% → 6.59%.
Conclusion: Adding breast MRI to conventional breast image decreased the surgical margin involved rate, with the cost of mild increase the mastectomy rate. This decreasing surgical margin involved rate was not mainly due to increase mastectomy rate, but selection of patients who were not suitable for partial mastectomy to receive total mastectomy.
Disclosure of Interest: No significant relationships.

P349
Comparison of HR and HER2 results between CNB and mastectomy specimen from the same patients

H.Y. Kim *, S. Nam. *Breast Surgery, Pusan National University Yangsan Hospital, Yangsan, Korea*

Goals: In the treatment of breast cancer, hormone receptor (HR) expression and human epidermal growth factor receptor 2 (HER2) gene expression are the most important biomarkers. Therefore, the accuracy of their results is critical.
Methods: We studied the results of HR expression and HER2 gene expression of 153 consecutive patients between March 2009 and February 2014. Estrogen receptor (ER), progesterone receptor (PR) and HER2 gene immunohistochemical (IHC) assay of tissues from mastectomy specimens were compared with their previous core needle biopsy (CNB) ER, PR and HER2 gene IHC assay results.
Results: The tumor of 112 (73.2%) out of the 153 patients are positive HR (ER and/or PR) in CNB specimens and 107 (69.9%) are positive HR in mastectomy specimens. 33 (21.6%) patients are positive HER2 in CNB specimens and 34 (22.2%) are positive HER2 in mastectomy specimens. ER positivity decreased from 71.9% in the CNB to 68.0% in mastectomy specimens, while PR positivity increased from 60.8% in the CNB to 64.7% in mastectomy specimens. The overall agreement between CNB and mastectomy specimens was 92.1% for ER, 86.9% for PR and 98% for HER2.
Conclusion: CNB specimens are associated with the identification of more frequent and higher levels of hormonal receptor proteins than mastectomy specimens. However, there are CNB negative and mastectomy positive disagreements in HR and HER2 cases. Proper hormonal therapy depends on accurate hormone receptor assay results, as well as target therapy depends on HER2 assay results. Both assays of CNB and mastectomy specimens are very helpful in accurate ER, PR and HER2 assay result.
Disclosure of Interest: No significant relationships.

P350
Safety of oncoplastic surgery in early breast cancer: a case–control study

D. Atallah *, M. Moubarak, J. Safi, N. El Kassis. *Obstetrics and Gynecology, Hotel-Dieu de France University Hospital, Saint Joseph University, Beirut, Lebanon*

Goals: Over the last two decades, new breast conserving surgical techniques emerged in early breast cancer (stage I or II). Oncoplastic surgery is a breast conserving surgery aiming for a wide tumor resection associated with good cosmetic results. The aim of this study is to compare oncological safety outcomes of oncoplastic breast conserving surgery to the standard technique in early breast cancer.
Methods: A retrospective case–control study was conducted at Hôtel-Dieu de France, Beirut. We reviewed the clinicopathological data of 280 patients with early breast cancer who underwent breast conserving surgery between 2005 and 2013.
Results: 193 patients had oncoplastic surgery (cases) while 87 patients received the standard technique (controls). Both groups had comparable age, BMI, menopausal status, tumor size and location, histological type, histoprognostic grade and immunohistochemical receptors. The mean resected breast volume was two times larger in the oncoplastic group (438.05 cm^3 vs. 223.34 cm^3, $P < 0.001$). Margins wider than 1 cm were more frequently encountered in the oncoplastic group (59.8% vs. 32.8%, $P < 0.001$). The nearest margin was more found to be lateral in the conventional technique group (38.2% vs. 17.1%, $P = 0.002$). The re-excision rate was higher in the standard group (7.1% vs. 4.7%, $P = 0.4$). No local recurrence was encountered in the oncoplastic group, while it was estimated to be 2.4% in the standard one ($P = 0.045$).
Conclusion: Our findings suggest that the oncoplastic technique is safe. It allows surgeons to remove greater volumes of breast tissue, thus reducing re-excision rates and local recurrences when compared to standard technique. The better oncological outcomes achieved with oncoplastic surgery along with improved esthetic results should encourage surgeons to adopt it. In close, further prospective studies should be conducted in order to consider it as a gold standard technique.
Disclosure of Interest: No significant relationships.

P351
Mammary fibromatosis in a young woman with ipsilateral hypoplastic breast

A. Pazaiti[1] *, E. Lykaki[2], I.K. Papapanagiotou[3], V. Kalles[4], P. Liakou[1], C. Kittas[1], K.D. Grigoriadis[5], M. Kotrotsou[1]. *[1]Breast Department, Athens Bioclinic, Athens, Greece, [2]Radiology Department, General Hospital "Asklepieio Voulas", Athens, Greece, [3]Gynecology Department, Oncological Hospital "Saint Savvas", Athens, Greece, [4]Surgery Department, Naval Hospital of Athens, Athens, Greece, [5]GK Pathology Diagnostic Centre, Athens, Greece*

Goals: Fibromatosis of the mammary gland is an uncommon tumor, very often seen with infiltrating disorders, consisting only 0.2% of the primary tumors of the breast. Due to its rare appearance and its preoperative clinical, radiological and cytological portraiture, it generates great diagnostic dilemmas. Our aim is to describe an extremely rare case of fibromatosis in an ipsilateral hypoplastic mammary gland of a 37-year-old woman.
Methods: The patient attended our Clinic due to a palpable mass of considerable size in her left hypoplastic breast. Mammography, u/s examination and MRM recognized a significantly left asymmetric mammary gland as well as a distortion in the ipsilateral upper outer quadrant, 10 mm anteroposteriorly and 7.5 mm laterolaterally. Fine needle aspiration and Core Biopsy followed for diagnostic and treatment purposes.
Results: Fine-needle aspiration was negative whereas core biopsy advocated fibromatosis with fibrous mastopathy and myoid hyperplasia. Consequently, subcutaneously, surgical resection (quarterectomy) of the tumor was performed, using the skin sparing technique. Due to the hypoplasia of the pectoralis major muscle, segmentation of the insertion of the pectoralis major muscle was decided. Silicone implant was then inserted and the muscle was sutured to mammary's gland lower pole, as a base and cover of the implant. The great deficit created by the tumor excision, in the upper outer quadrant, was treated with auto-lipofilling, thus covering the space between the muscle and the skin flap. Histopathologic examination of the tumor confirmed fibromatosis.
Conclusion: Fibromatosis is a rare uncommon tumor, and to our knowledge up to date, never been described in an ipsilateral hypoplastic breast. Surgical excision remains the main therapeutic strategy, as in our case, where the patient not only purged from the tumor, but also has a great aesthetic result and remains disease free almost 2 years.
Disclosure of Interest: No significant relationships.

P352

A puzzle for breast surgeons: type and timing of the surgery for metastatic breast cancer

H.O. Aytac[1]*, T. Colakoglu[1], G.N. Nursal[2], O. Ozyilkan[3]. [1]*General Surgery, Baskent University, Faculty of Medicine, Adana, Turkey,* [2]*Nuclear Medicine, Baskent University, Faculty of Medicine, Adana, Turkey,* [3]*Medical Oncology, Baskent University, Faculty of Medicine, Adana, Turkey*

Goals: Loco-regional surgical control is believed to be unnecessary in many women with stage IV breast cancer for improved survival. Though, it is usually considered to be incomplete not to operate on for cancer from the point of view of surgeons. As far as current guidelines recommend surgery only for palliation, some recent studies underline the favorable role of surgery for metastatic breast disease. We aimed to assess types of the operations and outcomes in our patients with Stage IV breast cancer who underwent surgery.
Methods: In this retrospective study, patients with Stage IV breast cancers operated on at our tertiary-referral center between October 2011 and September 2014 were assessed in the context of demographics, histopathology, metastatic burden, and type and time of surgery performed.
Results: Four hundred and forty-one patients were operated on for breast cancer; 32 of which have metastasis at the time of diagnosis. Bone was shown to be the most prominent site for metastasis and simple mastectomy for the choice of surgery. Eight of these patients were found not to receive chemotherapy prior to surgery. Although 7 had been demonstrated to have oligometastatic disease limited to bone, surprisingly one had had both liver and bone metastasis at the time of diagnosis.
Conclusion: It would not be wrong to mention that, our surgeons are still a bit confused about the role of surgery in metastatic breast cancer.
Disclosure of Interest: No significant relationships.

P353

Diagnosis and clinical course of benign and malign/borderline phyllodes tumours of the breast

H. Yabanoglu[1], T. Colakoglu[1]*, H.O. Aytac[1], A. Parlakgumus[1], F. Aka Bolat[2], A. Pourbagher[3], S. Yildirim[1]. [1]*General Surgery, Baskent University, Faculty of Medicine, Adana, Turkey,* [2]*Pathology, Baskent University, Faculty of Medicine, Adana, Turkey,* [3]*Radiology, Baskent University, Faculty of Medicine, Adana, Turkey*

Goals: To compare predicting factors for the diagnosis and clinical course of benign and malign/borderline phyllodes tumours (PT) of the breast, and to discuss treatment modalities.
Methods: Clinical and demographic characteristics of the patients with histopathological diagnosis of phyllodes tumour were examined. Patients were divided into group 1 (benign PT) and group 2 (borderline/malignant PT). Groups were compared in terms of demographic and clinical characteristics.
Results: Of the patients studied, 37 (68.5%) had benign, 7 (12.9%) had borderline and 10 (18.5) had malignant histopathology. A statistically significant relationship was detected between the incidence of malignancy and mass diameter ($p = 0.001$) and age ($p = 0.030$) when the two groups were compared. Wide surgical excision was performed on 46 (82.5%) patients, simple mastectomy on 7 (13%) patients and modified radical mastectomy on one (1.9%) patient. Ten (18.5%) patients were re-operated for surgical margin positivity. Local recurrence was determined only in one (1.9%) patient. Distant metastasis due to malignant PT developed in two (3.7%) patients.
Conclusion: Among the patients who were considered to have PT, malignancy was likely to be present, especially if the patient's age was over 40 and the diameter of the mass was above 33.5 mm. Therefore, in patients with similar characteristics, surgical margins should be kept slightly wider or wider excisions should be preferred with or without simultaneous reconstructive surgery in appropriate cases.
Disclosure of Interest: No significant relationships.

P354

Is the surgeon the determining factor for choices of breast cancer surgery?

A. Sattaratnamai[1]*, N. Samankatiwat[1], V. Lohsiriwat[2]. [1]*Department of Surgery, Ratchaburi Hospital, Ratchaburi, Thailand,* [2]*Division of Head–Neck and Breast Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Goals: The majority of breast cancer patients who are being treated in rural hospital still warrant for mastectomy. Thus, some patients have the misconception that to have breast cancer mean they have to undergo mastectomy. Surgeon advice regard surgical procedure is one of the most important factors in decision making. Our study aims to compare the rate of breast conserving surgery (BCS), mastectomy (MT) and mastectomy with immediate breast reconstruction (MTIBR) between the surgeons which offer only MT (group A) and the surgeons who offer BCS MT and MTIBR (group B).
Methods: A retrospective cohort study was conducted at Ratchaburi hospital, Thailand from January 2010 to April 2014. We categorized the patients into 2 groups (group A and B). Patient demographics data, tumor biology and surgical treatment (BCS, MT and MTIBR) were registered. Univariated analysis was selected to determine the factors that associated with the choices of breast surgery.
Results: From January 2010 to April 2014, we recruited 310 breast cancer patients, 221 patients (71.29%) were treated by the surgeons in group A, 89 patients (28.71%) were treated by the surgeons in group B. The mean age of patients is 54.4 years old. Age, marital status, tumor size, staging, location of tumor and type of carcinoma are comparable in both group. Most patients were in stage2 (52.9%) and 60.97% of patient has T2 lesion. Invasive Ductal Carcinoma is the most common cell type (91.2%).

Choice of breast surgery in each group of surgeons

Type of surgery	Number of patients			P-value
	All (n = 310)	Group A (n = 221)	Group B (n = 89)	
MT	271	213	58	<0.001
BCS	14	3	11	
MTIBR	25	5	20	

The choice of breast surgery is significantly different between 2 groups ($P < 0.001$). In group A, 213 (96.38%) patients had MT, only 3 (1.36%) patients had BCS, and 5 (2.26%) patients had MTIBR. Whilst in group B, 58 (65.17%) patients had MT, 11 (12.36%) patients had BCS, and 20 (22.47%) patients had MTIBR. Choice of breast surgery in patients with stage 1, 2, 3 are significantly different between 2 groups ($P = 0.004$, <0.001, 0.025 respectively). Age is the only factor that significantly affects the choice of surgery in the group B but not in group A. Size, location and type of tumor and marital status of patients are not affected the surgical choices in both group.
Conclusion: Surgeon is the influential factor for determining the choice of breast surgery in the rural hospital of Thailand. Surgeon's competency and comprehensive preoperative consultation by offering BCS, MT and MTIBR can affect the choice of surgical procedure for breast cancer patients.
Disclosure of Interest: No significant relationships.

P355

Breast conserving surgery in multifocal breast cancer

S.M. Ninkovic[1]*, V.M. Ninkovic[2], J. Nedovic[3], J. Miljkovic[3], A. Milovanovic[3], M. Jevtic[3], A. Cvetkovic[3], B. Milosevic[3]. *[1]Surgery, Clinical Center "Kragujevac", Kragujevac, Serbia, [2]Special Hospital "Merkur", Vrnjacka Banja, Serbia, [3]Clinical Centre "Kragujevac", Kragujevac, Serbia*

Goals: Few studies dealt with clinical characteristcs and the best surgical treatment of multifocal (MF) and multicentric (MC) breast carcinomas. No one of these studies differentiates between MC and MF breast carcinoma. In our investigation we came at different conclusions.
Methods: We designed and conducted the study in order to define prevalence, clinical features, that is aggressiveness, prevalent histoligical type, and optimal surgical aproach to MC and MF carcinoma. During a five year period (2005–2009), 470 women were operated on with breast carcinoma. Out of that number, in 274 women, neoadjuvantly, the Madden mastectomy was performed, and only these patients were subjected to the histological studies, because in these cases the entire breast can be examined with possibility to compare the postoperative results with preoperative staging.
Results: On the other hand, looking at the clinical characteristics of MC, MF, and unifocal (UF) breast carcinoma, we can suggest the following: 1) MC leasions are more aggressive than those of MF and UF; 2) MC leason are always associated with metastasis in regional lymphatic nodes.
Conclusion: Regarding all these data, if during clinical examination and/or with other diagnostic procedures, the enlarged lymphatic nodes in axillas are diagnosed (N1a–b), and palpable mass in the breast which is by obligatory CORE byopsy hystologically confirmed as lobular hystological type of breast carcinoma, one can suppose that there is MC breast carcinoma. However, growing body of evidence indicates possibility to perform the sparing operations of the breast in MC breast carcinoma. In our investigation it was demonstrated that these procedures are justified only for UF and MF carcinoma. In cases of MF tumors, it is possible to perform quadrantectomy, that is sparing surgical procedure, considering that the aggressiveness of MF tumors is not different than that of UF. Unlike MC carcinoma, with MF breast carcinoma it is also possible to perform SLN biopsy (at the level of mammilla and subcutaneous), so it can be concluded that the surgical treatment of MF carcinoma is not different than that of UF carcinoma.
Disclosure of Interest: No significant relationships.

P356

Occult axillary metastases in breast cancer. Outcomes for post neoadjuvant chemotherapy

V. Pronisceva, S. Wong, A. Poddar*, E. Sharp. *General Surgery, EKUHFT, QEQM Hospital, AN, United Kingdom*

Goals: Assessment of the sentinel nodes in breast cancer identifies patients who may benefit from further axillary surgery and adjuvant or neoadjuvant chemotherapy. Aims:

- To assess breast unit compliance with national standards in pathological and radiological assessment.
- To assess factors contributing to occult axillary lymph node metastases.
- To assess histopathological outcome following neoadjuvant chemotherapy.

Methods: We preformed retrospective analysis of patient data between 4/2009 and 3/2013. As a standard we used Clinical Guidelines for the management of breast cancer: BASO, 2009. Currently there are no standards defining sonographically suspicious lymph nodes.
Results: Median patient age was 58 years, with range 34–90 yr. 100% of the patients had pre-operative US assessment of the axilla. 100% of the patients underwent US guided FNA if there was a presence of suspicious/abnormal lymph node.
Sensitivity of axillary US is 83% (range 75–88%), specificity 80% (range 80–76%), PPV 50%, NPV 95%.
Of the 121 patients with lymph node involvement confirmed on imaging and pathology, 36 (30%) patients had neo-adjuvant chemotherapy, 17 (47%) had complete pathological response in the axilla. 139 (19%) patients had positive sentinel nodes during sentinel lymph node biopsy (national range: 20–40%, screening audit: 16%). From the patients who had further axillary clearance after sentinel lymph node biopsy, 41% had axillary node involvement. 101 (72%) patients had macrometastases and 38 (28%) had micrometastases. In 57 (56%) patients out of 101 who had positive sentinel lymph nodes there was presence of metastases of 5 mm and above. Further review of the patient group who had neo-adjuvant chemotherapy showed median survival rate of 13.5 months and 90% of the relapse cases had evidence of residual disease in axilla.
Conclusion: Unit radiological and pathological assessment of the axilla are consistent with the national requirement. We believe that macrometastases of size 5 mm and above should be reported on US scan. Literature review revealed that most breast units have a similar experience. They report that US of the axilla in preoperative staging of early stage breast cancer is limited by small size of metastases in a substantial number of patients. Although US occult metastases identified during SLNB in this study is lower than the national average of 20–40%, it is higher compared to 16% seen in an audit of "screen detected cancers". This can be explained by early cancer presentation and small tumour sizes in screening patients. Unit sensitivity and specificity of US of the axilla are consistent with national standards. A combination of factors has a strong association with poor overall survival: lymphovascular invasion, ER negative status (triple negative status), high grade disease (G3), multifocal disease. Heavy residual nodal burden following neo-adjuvant chemotherapy is a predictor of poor outcome.
Disclosure of Interest: No significant relationships.

P357

Latissimus dorsi mini-flap: a choice of breast conserving surgery

H.O. Aytac*, T. Colakoglu, S. Yildirim. *General Surgery, Baskent University, Faculty of Medicine, Adana, Turkey*

Goals: Breast refilling procedures can make hard breast conserving operations practicable by maintaining good cosmesis. Latissimus dorsi myocutaneous flap is a well known method which is advantageous when the overlying skin itself is needed to be used as a part of the flap. The less common procedure Latissimus dorsi muscle flap (LD mini-flap) without transferring any skin island is especially suitable for reconstruction after breast conserving procedures. We aimed to assess the oncological outcomes and patient satisfaction status after breast conserving procedures for breast cancer followed by immediate reconstruction with LD mini-flap.
Methods: In this retrospective study, 46 patients operated on for breast cancer at our tertiary-referral center with quadrantectomy or wide excision and immediately reconstructed with LD mini-flap during the last four years interval were assessed in the context of demographics, histopathology, pathologic and cosmetic results.
Results: Most of the breast tumors excised were located in the upper outer quadrant (83%). Mean diameter of mass excised was 25 mm with a volume differing between 71 and 696 cm^3 (median=197 cm^3). Most of the patients had had synchronous axillary dissection (93%). Median distance to surgical margin was calculated as 4 mm. A secondary tumor focus had been demonstrated in the specimen of two patients (4%). Local recurrence was observed in one patient

(2.1%) and complementary mastectomy was performed. Forty-two of 46 patients (91%) declared postoperative satisfaction about the cosmetic results of their operation.

Conclusion: As it allows removal of sufficient volume of breast tissue, provides acceptable oncological safety and creates visual satisfaction, LD mini-flap is a method to keep in mind in the surgical treatment of breast cancer in suitable patients.

Disclosure of Interest: No significant relationships.

The Breast 24S1 (2015) S151–S160

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Author index

*Page numbers for abstracts are followed by the abstract number(s) in parentheses.

*Page numbers for abstracts are followed by the abstract number(s) in parentheses.

*Page numbers for abstracts are followed by the abstract number(s) in parentheses.

*Page numbers for abstracts are followed by the abstract number(s) in parentheses.

*Page numbers for abstracts are followed by the abstract number(s) in parentheses.

*Page numbers for abstracts are followed by the abstract number(s) in parentheses.

*Page numbers for abstracts are followed by the abstract number(s) in parentheses.

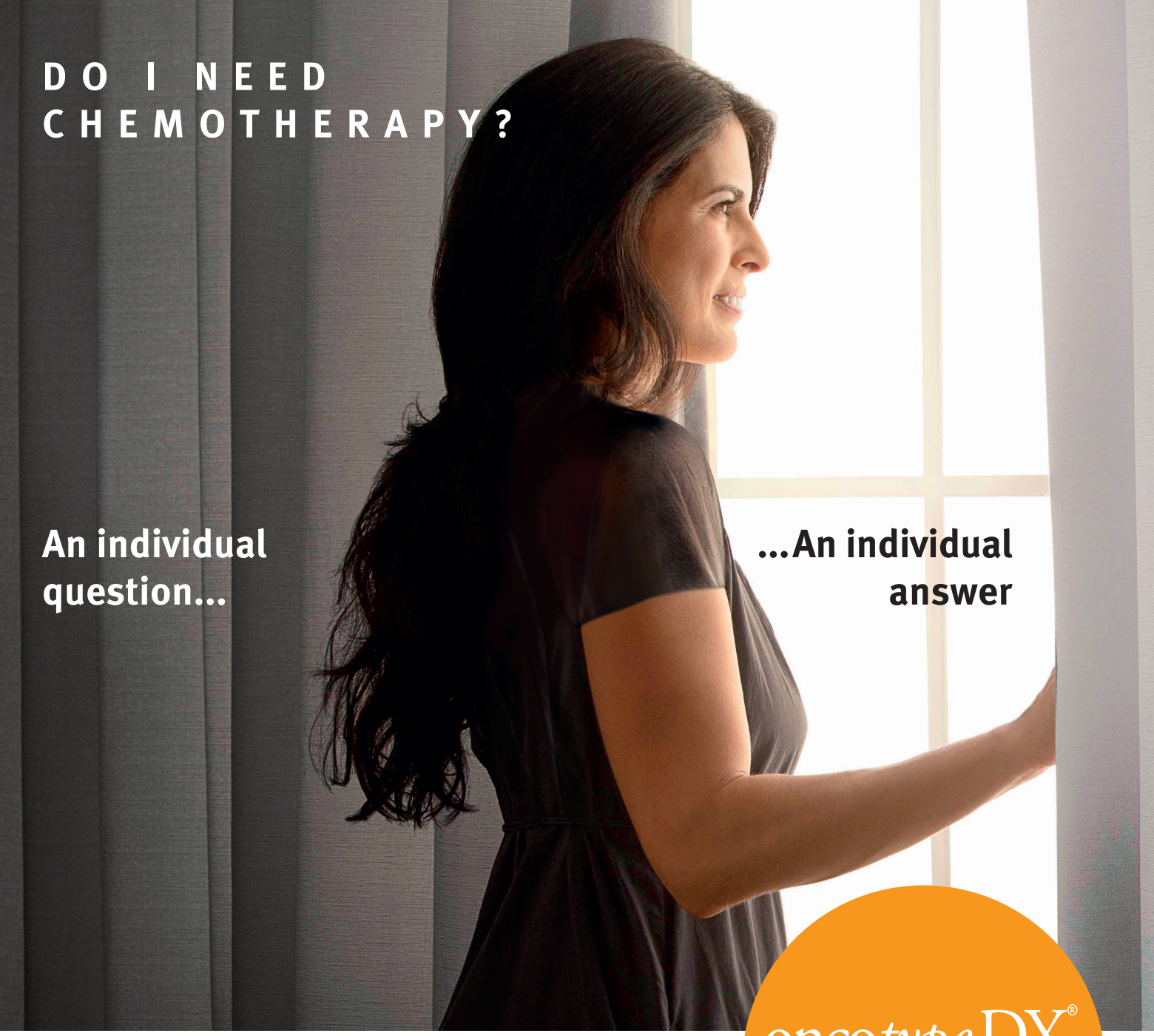
T

*Page numbers for abstracts are followed by the abstract number(s) in parentheses.

*Page numbers for abstracts are followed by the abstract number(s) in parentheses.

Authors are responsible for content and language quality of their abstracts

*Page numbers for abstracts are followed by the abstract number(s) in parentheses.



oncotype DX® Breast Cancer Assay

INFORMING LIFE DECISIONS

- The ONLY multi-gene assay that helps to identify patients at risk of distant recurrence[1,2] and patients who are likely, or unlikely, to benefit from chemotherapy[3,4]
- Intended for newly diagnosed patients with early-stage, ER-positive, HER2-negative invasive breast cancer that is node negative or with 1-3 positive nodes[1,2]

Visit us at **www.oncotypeDX.com**

Genomic Health®

References

1. Paik S et al. *N Engl J Med* 2004; 351: 2817-2826; **2.** Dowsett M et al. *J Clin Oncol* 2010; 28: 1829-1834; **3.** Paik S et al. *J Clin Oncol* 2006; 24: 3726-3734; **4.** Albain KS et al. *Lancet Oncol* 2010;11: 55-65.

GHI10448_0215_EN_INT