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# LIVE-Stream Aufzeichnung vom ASCO 2019: Brustkrebs Deutschland Round Table - Moderation: Renate Haidinger, Brustkrebs Deutschland e.V., München, mit:

**Christoph Thomssen; Michael Untch; Renate Haidinger; Nadia Harbeck; Christian Jackisch; Wolfgang Janni**

## Im Live Stream besprochene Studien

***Erweiterte adjuvante antihormonelle Therapie:***

John Bartlett, Dennis Sgroi, Kai Treuner, Yi Zhang, et al.

Trans-aTTom: Breast Cancer Index for prediction of endocrine benefit and late distant recurrence (DR) in patients with HR+ breast cancer treated in the adjuvant tamoxifen—To offer more? (aTTom) trial.

**Conclusions:** These data provide further validation and establish level 1B evidence for BCI as a predictive biomarker for preferential benefit from EET in HR+ breast cancer.

*Lucia Del Mastro, Mauro Mansutti, Giancarlo Bisagni, Riccardo Ponzone, et al.*

Benefit from letrozole as extended adjuvant therapy after sequential endocrine therapy: A randomized, phase III study of Gruppo Italiano Mammella (GIM).

**Conclusions:** After 2-3 years of adjuvant tam, extended treatment with 5 years of letrozole resulted in significant improvement in DFS compared to the standard duration of 2-3 years of letrozole. Clinical trial information: NCT01064635

***Neoadjuvante Therapie:***

*Sara A. Hurvitz, Miguel Martin, Kyung Hae Jung, Chiun-Sheng Huang, et al.*

Neoadjuvant trastuzumab (H), pertuzumab (P), and chemotherapy versus trastuzumab emtansine (T-DM1) and P in human epidermal growth factor receptor 2 (HER2)-positive breast cancer (BC): Final outcome results from the phase III KRISTINE study.

**Conclusions:** EFS numerically favors TCHP due to locoregional progression events with T-DM1+P prior to surgery. T-DM1+P was associated with fewer grade ≥3 AEs but increased treatment discontinuation. Clinical trial information: NCT02131064

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| | TCHP (n = 221) | T-DM1+P (n = 223) |
|---|---|---|
| EFS events, n (%) | 13 (5.9) | 31 (13.9) |
| Locoregional progression before surgery | 0 (0) | 15 (6.7) |
| Invasive disease recurrence | 11 (5.0) | 11 (4.9) |
| Non-invasive recurrence (DCIS) | 0 (0) | 3 (1.3) |
| Death without prior EFS event | 2 (0.9) | 2 (0.9) |
| 3-yr IDFS in patients with pCR (95% CI) | 97.5% (94.7–100.0) | 96.7% (93.0–100.0) |
| 3-yr IDFS in patients without pCR (95% CI) | 84.2% (72.5–96.0) | 89.4% (83.1–95.6) |
| Grade ≥3 AEs, n (%) | 148 (67.6) | 71 (31.8) |

45 (20.2)

*Otto Metzger Filho, Giuseppe Viale, Lorenzo Trippa, Tianyu Li, et al.*

HER2 heterogeneity as a predictor of response to neoadjuvant T-DM1 plus pertuzumab: Results from a prospective clinical trial.

**Conclusions:** ITH-HER2 assessed by routine pathology evaluation is a strong predictor of pCR to a dual-HER2 targeted therapy regimen. If validated, ITH-HER2 may need to be considered in selection of pts for HER2-targeted regimens without chemotherapy in the curative setting. Clinical trial information: NCT02326974

*Peter A. Fasching, Christian Jackisch, Kerstin Rhiem, Andreas Schneeweiss, et al.*

GeparOLA: A randomized phase II trial to assess the efficacy of paclitaxel and olaparib in comparison to paclitaxel/carboplatin followed by epirubicin/cyclophosphamide as neoadjuvant chemotherapy in patients (pts) with HER2-negative early breast cancer (BC) and homologous recombination deficiency (HRD)

**Conclusions:** GeparOla could not exclude a pCR rate of ≤55% in the PwO arm. Subgroup analysis is hypothesis generating and need further confirmation.

| | Olaparib+Paclitaxel<br>pCR rate (90%CI) | Carboplatin+Paclitaxel<br>pCR rate (90%CI) |
|---|---|---|
| HR+ patients (n = 29) | 52.6% (32.0%, 72.6%) | 20.0% (3.7%, 50.7%) |
| HR- patients (n = 77) | 56.0% (43.4%, 68.0%) | 59.3% (41.7%, 75.2%) |
| Patients age < 40 (n = 32) | 76.2% (56.3%, 90.1%) | 45.5% (20.0%, 72.9%) |
| Patients age ≥ 40 (n = 74) | 45.8% (33.4%, 58.6%) | 50.0% (32.7%, 67.3%) |

Clinical trial information: NCT02789332

William M. Sikov, Mei-Yin Polley, Erin Twohy, Charles M. Perou, et al.

CALGB (Alliance) 40603: Long-term outcomes (LTOs) after neoadjuvant chemotherapy (NACT) +/- carboplatin (Cb) and bevacizumab (Bev) in triple-negative breast cancer (TNBC).

**Conclusions:** As expected, regardless of treatment arm pCR was associated with markedly better LTOs, and pts with any residual disease had significantly worse outcomes. The addition of Cb or Bev to standard NACT for TNBC did not improve LTOs in this trial, although it should be noted that the trial was not powered for this endpoint. Omission of chemotherapy doses may result in poorer outcomes, especially among Cb-treated pts, which may warrant further evaluation. Support: U10CA180821; U10CA180882; Genentech; https://acknowledgments.alliancefound.org; NCT00861705 Clinical trial information: NCT00861705

T*essa Gerjanne Steenbruggen, Mette S. Van Ramshorst, Erik van Werkhoven, Vincent O. Dezentjé, et al.*

Adjuvant chemotherapy in small node-negative triple-negative breast cancer (TNBC).

**Conclusions:** Adjuvant chemotherapy is associated with higher OS and BCSS in small node negative TNBC. Benefit is most evident in grade 3 tumors and tumors > 1cm and not evident in tumors ≤1cm and grade 1-2.

| | aHR OS | 95% CI | aHR BCSS | 95% CI |
|---|---|---|---|---|
| all patients | 0.55 | 0.44-0.69 | 0.55 | 0.42-0.73 |
| pT1ab | 1.52 | 0.80-2.90 | 1.17 | 0.55-2.49 |
| pT1c | 0.53 | 0.41-0.67 | 0.57 | 0.43-0.76 |
| grade 1-2 | 1.03 | 0.63-1.67 | 0.99 | 0.57-1.71 |
| grade 3 | 0.50 | 0.39-0.65 | 0.54 | 0.40-0.74 |

***Metastasiertes Mammakarzinom: Triple Negativ***

*Peter Schmid, Sylvia Adams, Hope S. Rugo, Andreas Schneeweiss, et al.*

IMpassion130: updated overall survival (OS) from a global, randomized, double-blind, placebo-controlled, Phase III study of atezolizumab (atezo) + nab-paclitaxel (nP) in previously untreated locally advanced or metastatic triple-negative breast cancer (mTNBC).

**Conclusions:** The 2nd IMpassion130 interim OS analysis was consistent with the 1st analysis, confirming clinically meaningful OS benefit with atezo + nP in previously untreated PD-L1+ mTNBC. Clinical trial information: NCT02425891

| | Atezo + nP | Placebo + nP |
|---|---|---|
| ITT population, events/pts, n/n (%) | 255/451 (57%) | 279/451 (62%) |
| HR (95% CI); log-rank *P* | 0.86 (0.72, 1.02); 0.078[a] | — |
| Median OS (95% CI), mo | 21.0 (19.0, 22.6) | 18.7 (16.9, 20.3) |
| 2-year OS (95% CI), % | 42 (37, 47) | 39 (34, 44) |
| Median follow-up duration, mo | 18.5 | 17.5 |
| PD-L1+ population,[b] events/pts, n/n (%) | 94/185 (51%) | 110/184 (60%) |
| HR (95% CI) | 0.71 (0.54, 0.93) | — |
| Median OS (95% CI), mo | 25.0 (19.6, 30.7) | 18.0 (13.6, 20.1) |
| 2-year OS (95% CI), % | 51 (43, 59) | 37 (29, 45) |

HRs estimated per stratified Cox model. [a] Not significant. [b] PD-L1 on IC ≥ 1% (VENTANA SP142 IHC assay).

*Charles McCrea, Robert Hettle; AstraZeneca, Cambridge, United Kingdom*

Indirect treatment comparison of the efficacy and safety of olaparib 300 mg tablets BID and talazoparib 1 mg once daily in the treatment of patients with germline BRCA-mutated (gBRCA) HER2-negative metastatic breast cancer.

**Conclusions:** Results of the ITC suggest that olaparib and talazoparib are equally efficacious on PFS, and differ in AE risk profile, with olaparib predicted to have fewer common hematological and alopecia events, but an increased risk of nausea and vomiting versus talazoparib. Observed differences require confirmation in comparative studies. Limitations of the analysis include heterogeneity in study design, reporting of AEs, and mix of chemotherapies used in the control arm of the studies.

| Any grade AE | OR (95% credible interval) olaparib vs talazoparib |
|---|---|
| Anemia | 0.37 (0.18, 0.78) |
| Thrombocytopenia | 0.23 (0.06, 0.90) |
| Neutropenia | 0.54 (0.28, 1.06) |
| Alopecia | 0.22 (0.07, 0.66) |
| Fatigue | 1.00 (0.49, 2.06) |
| Headache | 0.82 (0.36, 1.90) |
| Diarrhea | 1.15 (0.53, 2.53) |
| Nausea | 2.39 (1.23, 4.64) |
| Vomiting | 2.13 (0.96, 4.92) |

*Joshua James Gruber,* Anosheh *Afghahi, Alyssa Hatton, Danika Scott, et al.*

Talazoparib beyond BRCA: A phase II trial of talazoparib monotherapy in BRCA1 and BRCA2 wild-type patients with advanced HER2-negative breast cancer or other solid tumors with a mutation in homologous recombination (HR) pathway genes.

**Conclusions:** In this proof-of-concept phase II study, single agent talazoparib demonstrated activity in HER2-negative advanced breast cancer pts with a HR pathway mutation beyond *BRCA1/2*. Further evaluation of talazoparib in this population is warranted. Clinical trial information: NCT02401347

***Metastasiertes Mammakarzinom: HER2-Positiv***

*Sandra M. Swain, David Miles, Sung-Bae Kim, Young-Hyuck* Im*, et al.*

**End-of-study analysis from the phase III, randomized, double-blind, placebo** (Pla)**-controlled CLEOPATRA study of first-line (1L) pertuzumab (P), trastuzumab (H), and docetaxel (D) in patients (pts) with HER2-positive metastatic breast cancer (MBC).**

**Conclusions:** The OS improvement with 1L P + H + D v Pla + H + D for pts with HER2-positive MBC was maintained after an additional 4 years of long-term follow-up, as were the safety and cardiac safety profiles. Clinical trial information: NCT00567190

***Metastasiertes Mammakarzinom: Hormon Sensitiv***

*Yeon Hee Park, Tae Yong Kim, Gun Min Kim, Kyung Hae Jung, et al.*

A randomized phase II study of palbociclib plus exemestane with GNRH agonist versus capecitabine in premenopausal women with hormone receptor-positive metastatic breast cancer (KCSG-BR 15-10, NCT02592746).

**Conclusions:** Exemestane plus palbociclib with ovarian suppression showed clinical benefit in terms of PFS compared with capecitabine in patients with premenopausal ER-positive MBC. Clinical trial information: NCT02592746

**Abstract LBA1008: Phase III** MONALEESA**- 7 trial of premenopausal patients withHR+/HER2– advanced breast cancer (ABC) treated with endocrine therapy ± ribociclib: Overall survival (OS) results.**

**Conclusions:** RIB + ET demonstrated a clinically and statistically significant longer OS than ET alone in premenopausal pts with HR+/HER2− ABC. This is the first time that a CDK4/6 inhibitor or any targeted agent + ET has demonstrated significantly longer OS vs ET alone as initial endocrine-based therapy. Clinical trial information: NCT02278120

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*Joseph A. Sparano, Robert James Gray, Della F. Makower, Tracy G. Lively, et al.*

Impact of clinical risk category on prognosis and prediction of chemotherapy benefit in early breast cancer (EBC) by age and the 21-gene recurrence score (RS) in TAILORx.

**Conclusions:** Clinical risk stratification provides additional prognostic information to the 21-gene RS, but not prediction of CT benefit in the overall TAILORx population or those > 50y, and facilitates more refined estimates of absolute CT benefit for women ≤50y with a RS 16-25. (Funded by National Cancer Institute, Komen Foundation, Breast Cancer Research Foundation). Clinical trial information: **NCT00310180**.