



# Efficacy and Utilization trends of adjuvant chemotherapy for stage I, II, and III breast cancer in the elderly population: A National Cancer Database Analysis

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## Disclosure

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## Background:

- Estimated new cases diagnosed in 2018 – 266,120 (15.3% of all cancers)
- Around 90% of them are diagnosed with local or regional disease
- Median age at diagnosis is 62
- Standard of Care:
  - Surgery with neoadjuvant or adjuvant chemotherapy. Followed by RT +/- hormonal therapy
- Data for elderly patient is limited in clinical trials

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## Background: Adjuvant chemo in the elderly

<p>• Mixed • Metaplastic</p> <p>Node positive (1 or more ipsilateral metastases &gt;2 mm)</p> <p><sup>f</sup>See Principles of HER2 Testing (BINV-A).</p> <p><sup>g</sup>Mixed lobular and ductal carcinoma should be graded based on the ductal component and treated based on this grading. For metaplastic carcinoma, the prognostic value of the histologic grading is uncertain. However, when a specific histologic subtype of metaplastic carcinoma is present and accounts for more than 10% of the tumor, the subtype is an independent prognostic variable.</p> <p><sup>h</sup>Consider adjuvant bisphosphonate therapy in postmenopausal (natural or induced) patients receiving adjuvant therapy.</p> <p><sup>ii</sup>Evidence supports that the magnitude of benefit from surgical or radiation ovarian ablation in premenopausal women with hormone receptor-positive breast cancer is similar to that achieved with CMF alone. See <a href="#">Adjuvant Endocrine Therapy (BINV-J)</a>.</p> <p><sup>bb</sup>Chemotherapy and endocrine therapy used as adjuvant therapy should be given sequentially with endocrine therapy following chemotherapy. Available data suggest that sequential or concurrent endocrine therapy with radiation therapy is acceptable. See <a href="#">Adjuvant Endocrine Therapy (BINV-J)</a> and <a href="#">Preoperative/Adjuvant Therapy Regimens (BINV-K)</a>.</p> <p><sup>cc</sup>There are limited data to make chemotherapy recommendations for those &gt;70 y of age. See <a href="#">NCCN Clinical Practice Guidelines for Older Adult Oncology</a>.</p> <p><small>Note: All recommendations are category 2A unless otherwise indicated. Clinical Trials: NCCN indicates that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.</small></p>	<p>Adjuvant chemotherapy<sup>bb,cc</sup> with trastuzumab<sup>dd</sup> (category 1) and endocrine therapy<sup>aa,ff</sup> or Adjuvant chemotherapy<sup>bb,cc</sup> with trastuzumab<sup>dd</sup> + pertuzumab and endocrine therapy<sup>aa,ff</sup></p> <p><sup>dd</sup>The prognosis of patients with T1a and T1b tumors that are node negative is uncertain even when HER2 is amplified or overexpressed. This is a population of breast cancer patients that was not studied in the available randomized trials. The decision for use of trastuzumab therapy in this cohort of patients must balance the known toxicities of trastuzumab, such as cardiac toxicity, and the uncertain, absolute benefits that may exist with trastuzumab therapy.</p> <p><sup>ee</sup>Adjuvant chemotherapy with weekly paclitaxel and trastuzumab (Tolaney et al. NEJM 2015) can be considered for T1 N0 M0, HER2-positive cancers, particularly if the primary cancer is ER negative. The absolute benefit of HER2-based systemic chemotherapy is likely negligible in patients with ER-positive cancers and tumor size bordering on T1mic (&lt;1 mm), when the estimated recurrence risk is less than 5% and endocrine therapy remains a viable option for systemic treatment.</p> <p><sup>ff</sup>Consider extended adjuvant neratinib following adjuvant trastuzumab-containing therapy for patients with HR-positive, HER2-positive disease with a perceived high risk of recurrence. The benefit or toxicities associated with extended neratinib in patients who have received pertuzumab is unknown.</p>
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**Preoperative/Adjuvant Therapy Regimens (BINV-K)**  
<sup>cc</sup>There are limited data to make chemotherapy recommendations for those >70 y of age. See [NCCN Clinical Practice Guidelines for Older Adult Oncology](#).

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## Background:

### Adjuvant Chemotherapy in Older Women with Early-Stage Breast Cancer

Hyman B. Muss, M.D., Donald A. Berry, Ph.D., Constance T. Cirincione, M.S., Maria Theodoulou, M.D., Ann M. Mauer, M.D., Alice B. Kornblith, Ph.D., Ann H. Partridge, M.D., M.P.H., Lynn G. Dressler, Ph.D., Harvey J. Cohen, M.D., Heather P. Becker, Patricia A. Karcheske, B.S., Judith D. Wheeler, M.P.H., Edith A. Perez, M.D., Antonio C. Wolff, M.D., Julie R. Gralow, M.D., Harold J. Burstein, M.D., Ph.D., Ahmad A. Mahmood, M.D., Gustav Magrinal, M.D., Barbara A. Parker, M.D., Ronald D. Hart, M.D., Dobijani Grenier, M.D., Larry Norton, M.D., Clifford A. Hudis, M.D., and Eric P. Winer, M.D. for the CALGB Investigators: University of Vermont, Burlington (H.B.M.); the M.D. Anderson Cancer Center, Houston (D.A.B.); the Cancer and Leukemia Group B (CALGB) Statistical Center, Duke University Medical Center (C.T.C., P.A.K.) and Duke University Medical Center (H.J.C., J.D.W., A.A.M.) — both in Durham.

- CALGB 49907 – 2009
  - Patients age >65 yo with stage I-III breast cancer (n = 600)
  - Randomized to CMF or AC VS. Capecitabine
  - Non-inferiority study
  - Result: Standard adjuvant chemotherapy is superior to Capecitabine

Muss HB, Berry DA et.al. Adjuvant Chemotherapy in Older Women with Early-Stage breast Cancer. N Engl J Med. 2009 May 14; 360(20):2055-2065.

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## Background:

- ICE trial: Phase III trial presented at SABCS 2014
  - Patient population 64-88 yo (n = 1,358)
  - Capecitabine + Ibandronate VS. Ibandronate alone
  - Result: No difference in DFS or OS
- 2017 Retrospective study by Yan-Shuang et.al.
  - Patients >60 yo (n = 251)
  - Adjuvant Capecitabine vs no chemotherapy
  - Result: DFS was improved with adjuvant therapy
  - No difference in OS

1. Von Monckwitz G et.al. S3-04; General Session 3  
2. Li, Yan-Shuang et.al. Mol Clin Oncol. 2017 Oct; 7(4)

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## Objectives:

- To identify factors associated with the use of adjuvant chemotherapy in the elderly population (age  $\geq 65$ )
- To analyze the overall survival outcomes in the elderly women with stage I to III HR positive or negative breast cancer who received adjuvant chemotherapy compared to those who did not

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## Method:



- Source of Data:
  - National Cancer Database (NCDB) – Clinical oncology database
    - Sourced from hospital registry data, collected from >1,500 Commission-on-cancer-accredited facilities.
    - It is used to analyze and track patients with malignant neoplastic diseases, their treatment, and outcomes.
    - US based database
    - Inpatient and outpatient information
    - Incorporates information for >70% of newly diagnosed cancers

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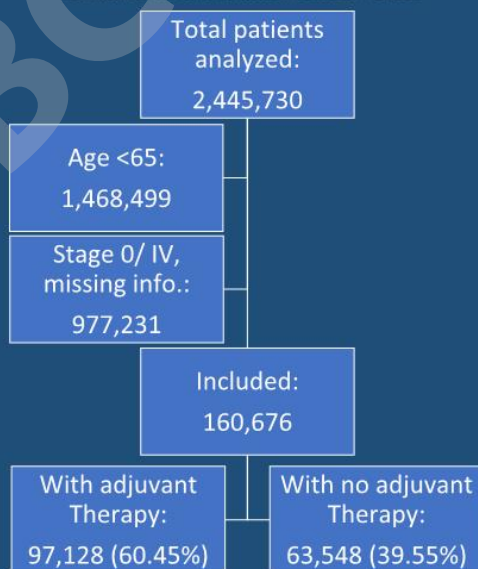


## Methods: Patient Selection -

- Data from 2004 – 2015
  - Age  $\geq 65$  yo
  - Stage I, II, III breast cancer
  - ER/PR +/-
- 
- Any HER-2 neu status – data not available from before 2010

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## Methods:



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## Statistical Methods:

- Adjusted Odds Ratio calculated from Logistic regression
  - Utilization was adjusted for histology, stage, grade, age, charlson-deyo comorbidity index, race, hormonal status.
- Univariate Cox analysis to estimate hazard ratios
- Multivariate Cox regression analysis used for OS:
  - Adjusted for histology, stage, grade, age, charlson-deyo comorbidity index, race, hormonal status.
- Kaplan Meier Estimates for Overall Survival

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## Factors associated with utilization:

Odds Ratio (adjusted) Estimates and Wald Confidence Intervals				
Variables	Odds Ratio	95% confidence Limits		P-value
Grade 2 vs 1 / 3 vs 1	1.88/3.51	1.82/3.37	1.95/3.65	<0.0001/<0.0001
ER-/PR- vs ER+/PR+	2.72	2.62	2.81	<0.0001
ER+/PR- vs ER+/PR+	1.70	1.64	1.76	<0.0001
Stage 1 vs 3 / 2 vs 3	0.23/0.56	0.22/0.54	0.24/0.59	<0.0001/<0.0001
	0.105	0.100	0.109	<0.0001
Race: Black vs white	0.99	0.96	1.04	0.9275
Private vs Medicaid	1.40	1.26	1.56	<0.0001
Private vs. Medicare	1.20	1.61	1.25	<0.0001
Lumpectomy vs Mastectomy	0.82	0.73	0.92	0.0011
RT vs No RT	2.55	2.47	2.64	<0.0001
Academic vs Community program	0.93	0.89	0.97	0.0007
CDCC Score >=3 vs 0	0.38	0.34	0.43	<0.0001

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## Average Age:

- Average age with chemotherapy: 70.7 yo
- Average age without chemotherapy: 75.5 yo

Age Range	Percent population
65-70 yo	46.5%
71-75 yo	24.6%
76-80 yo	15.4%
81-85 yo	8.8%
86-90 yo	4.8%

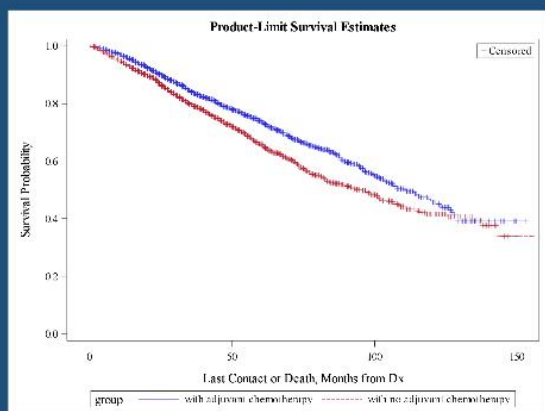
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## Median Overall Survival Data:

	With Chemo (in months)	Without Chemo (in months)	P-value	HR (adjusted)
Overall:	144.9	112.6	<0.0001	0.617
ER+/PR+	145.5	119.8	<0.0001	0.649
ER+/PR-	143.1	104.9	<0.0001	0.609
ER-/PR-	140.4	81.2	<0.0001	0.547
Stage 1	152.1	94.8	<0.0001	0.801
Stage 2	148.1	94.8	<0.0001	0.608
Stage 3	97.3	45.2	<0.0001	0.666

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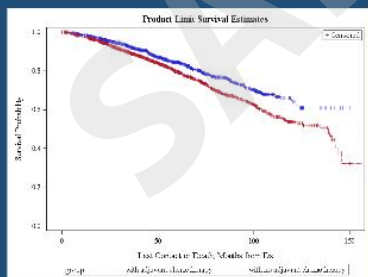
## Results:



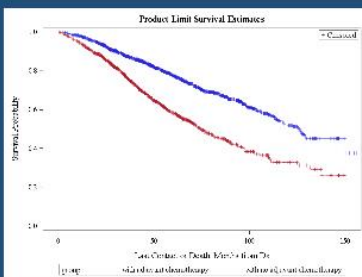
- P-value: <0.0001
- HR: 0.617
- OS at 120 months:
  - 59.5%
  - 46.7%

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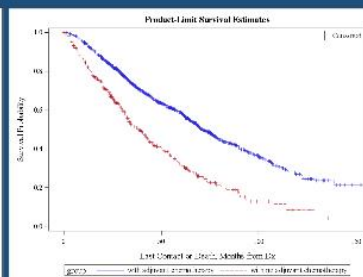
## OS based on Stage:



Stage I  
P-value: <0.0001  
HR: 0.801



Stage II  
P-value: <0.0001  
HR: 0.608

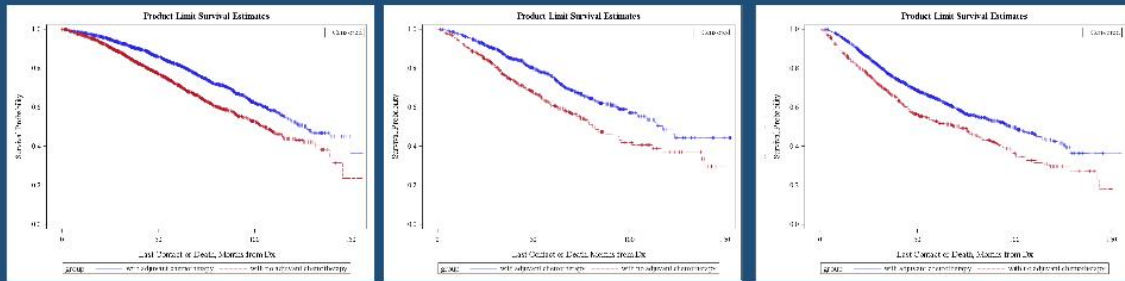


Stage III  
P-value: <0.0001  
HR: 0.666

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## OS based on hormonal status:



ER+/PR+  
P: <0.0001  
HR: 0.673

ER+/PR-  
P: <0.0001  
HR: 0.609

ER-/PR-  
P: <0.0001  
HR: 0.547

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## Limitations:

- Hospital based data - retrospective study
- HER-2 neu population not well defined
  - Data not available from before 2010
- Study population does not represent everyone:
  - COC-accredited programs only
- Genotype Prediction scores were not taken into account

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## Tailoring your therapy:

- Chemotherapy toxicity prediction calculator
  - Cancer and Aging Research Group (CARG)
  - Moffitt Cancer Center Senior Adult Oncology Program Tools
- Genetic-based assays
  - OncoType Dx
  - Mammaprint

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## Geriatric Assessment Score:

- Assessment of comorbidities
- Cognitive assessment
- Medication management and polypharmacy
- Social issues and QOL
- Assessment of physical function
- Falls
- Functional, Nutritional, and psychological status
- ✓ CARG score or CRASH score

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## Conclusions:

- Factors predicting utilization of chemotherapy included a higher grade, CDCC score, stage, administration of radiation, hormonal status, facility type, having private insurance
  - Race had no bearing on it
- Getting adjuvant chemotherapy is associated with increased overall survival in patients with stage I – III breast cancer
  - Across all stage and hormonal status
- Geriatric Assessment tools have shown accuracy in predicting the risk of chemotherapy

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