
# Adjuvant chemotherapy for breast cancer limitations and results

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**German Breast Group**


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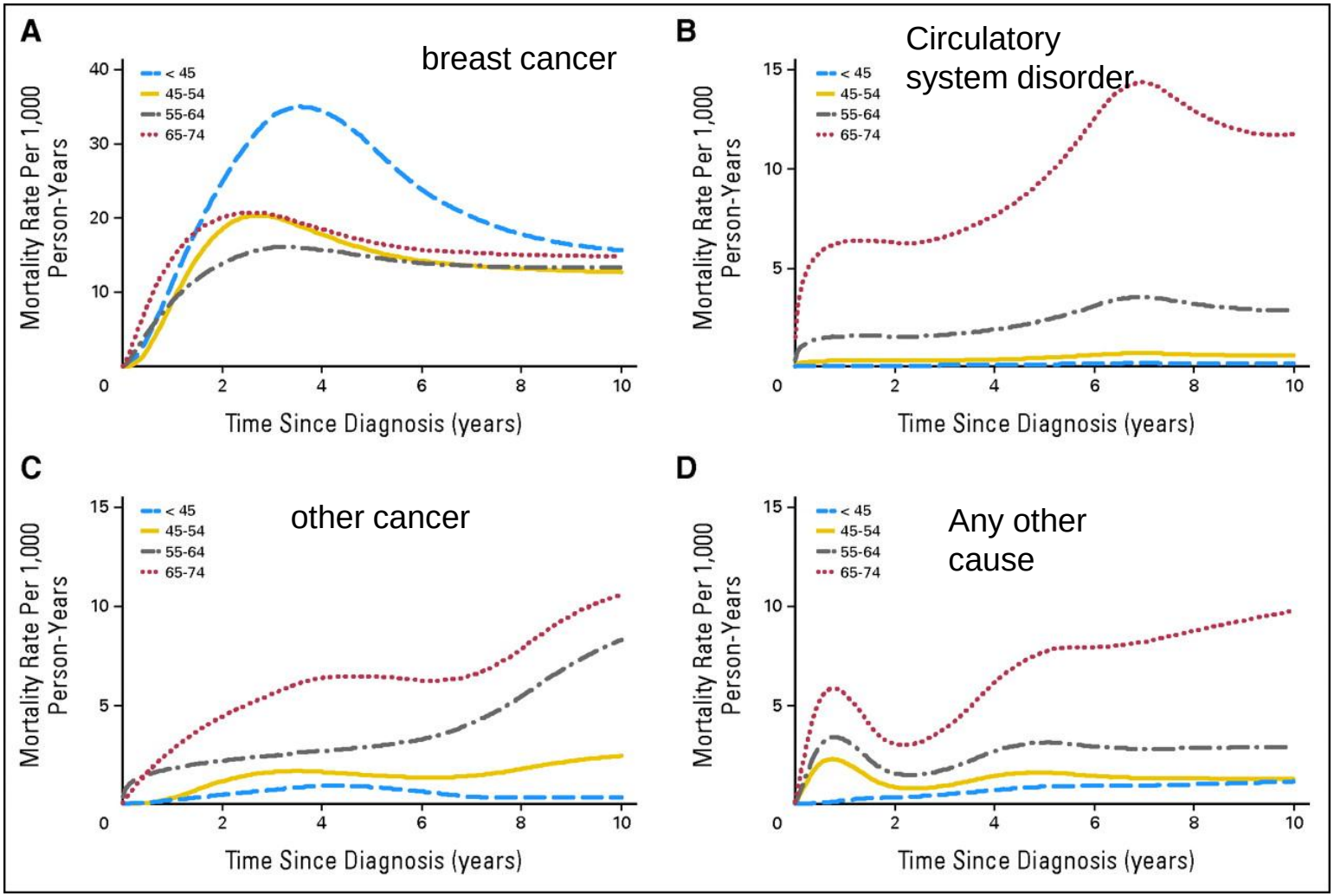
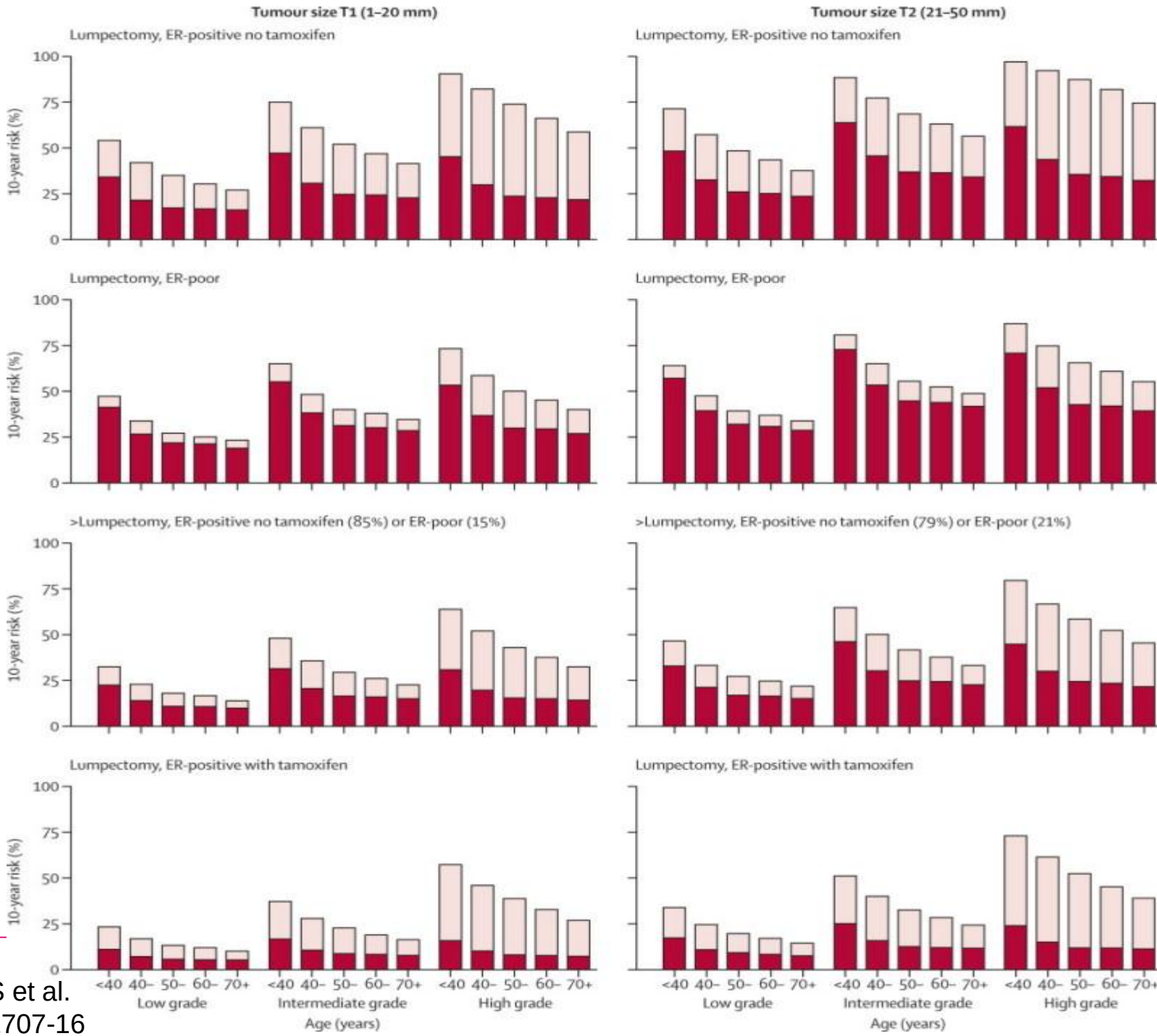
**Estimated mortality rates within 10 years of diagnosis in women with breast cancer younger than 75 years of age diagnosed between 1990 and 2006 (mortality rates estimated from flexible parametric survival models with age as only covariate.**




Colzani E et al. JCO 2011;29:4014-4021

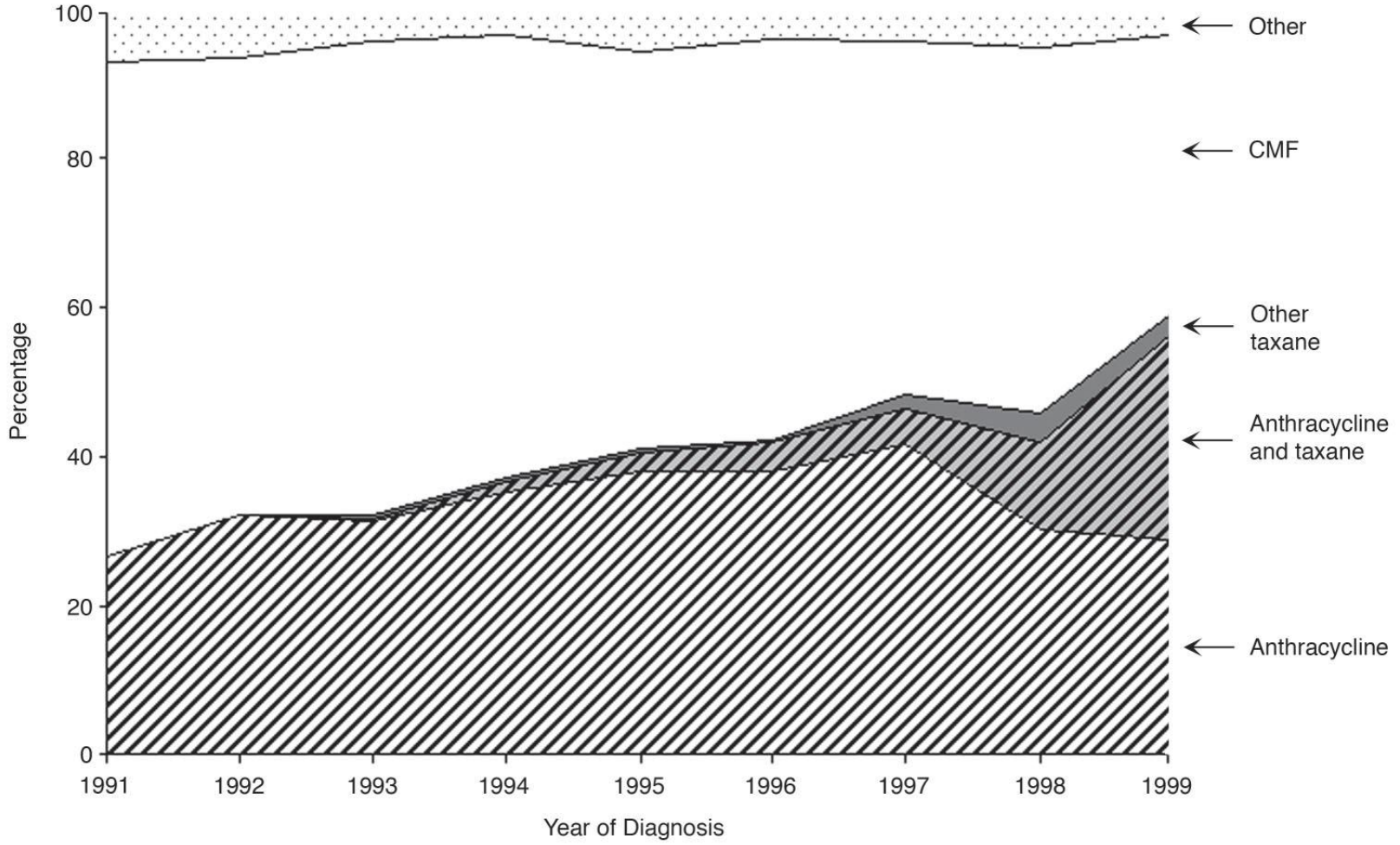


JOURNAL OF CLINICAL ONCOLOGY




EBCTCG, Darby S et al. Lancet 2011;378:1707-16

# Use of regimen in elderly




Giordano S; J Clin Oncol 2006; 24:2750-2756

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ICE II
INVESTIGATIONAL CHEMOTHERAPY ELDERLY PATIENTS

**Tab. 1 Auswahl einiger Studien zu Therapiemodalitäten bei älteren Brustkrebspatientinnen**

| Autor (Jahr, Land) | Studienart | Patientinnen | | Art der Untertherapie | Effekt der Untertherapie |
|---|---|---|---|---|---|
| | | Anzahl (n) | Alter | | |
| Bouchardy [4] (2003, Schweiz) | Populationsbasiert | 407 | ≥80 | 53% insgesamt (12% keine Therapie, 32% Tamoxifen alleine) | Mortalität steigt bei Patientinnen mit vs. ohne Untertherapie |
| Eaker [9] (2006, Schweden) | Populationsbasiert | 3271 | ≥70 | >38% Untertherapie | Mortalität steigt |
| Gajdos [17] (2001, USA) | Retrospektiv | 206 | ≥70 | 57% Untertherapie | Rezidivrisiko steigt |
| Giordano [18] (2006, USA) | Populationsbasiert | 41390 | ≥65 | 75–79 Jahre 4-mal seltener CT, ≥80 Jahre 20mal seltener CT | Mortalität steigt |
| Muss [30] (2005, Multinational) | Retrospektiv | 542<br>159 | ≥65<br>≥70 | Untertherapie der Chemotherapie | Erhöhtes Rezidivrisiko, Mortalität steigt |
| Smith [39] (2006, USA) | Populationsbasiert | 3409 | >65 | 51% ohne Radiotherapie | Rezidivrisiko steigt |

Hancke et al., Gynäkologe 2009; 42: 675-80

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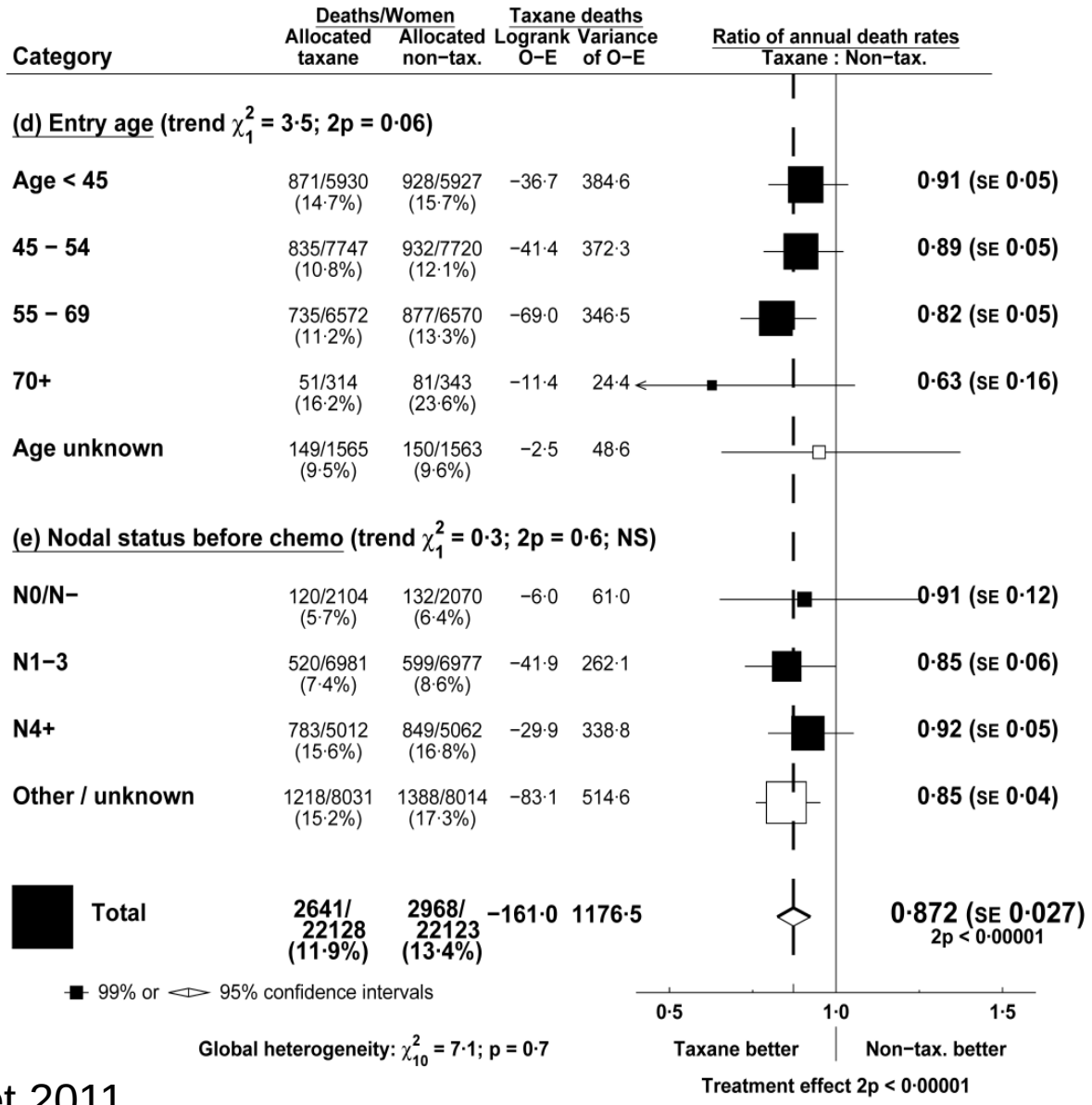
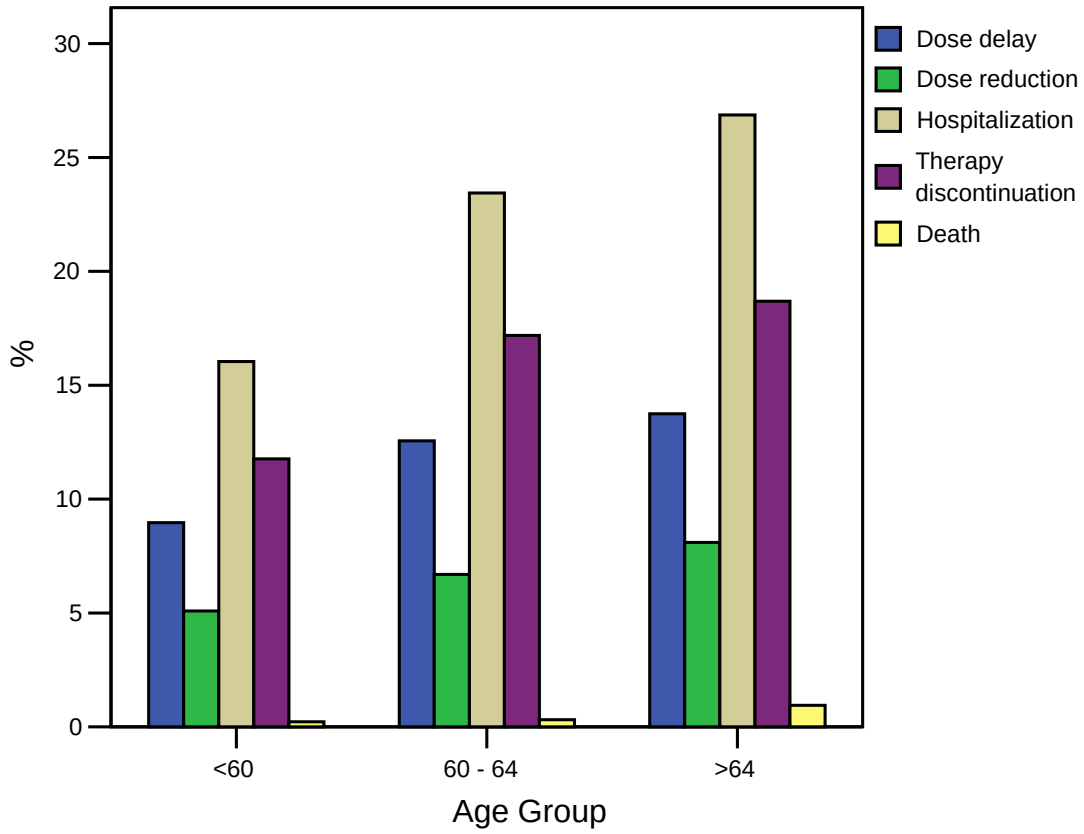
# Breast cancer mortality ratio in taxane trials, by AGE and STAGE




EBCTCG, Lancet 2011

# Compliance in (neo)adjuvant taxane treatment




Loibl S et al. Breast Cancer Res. 10:R77; 2008

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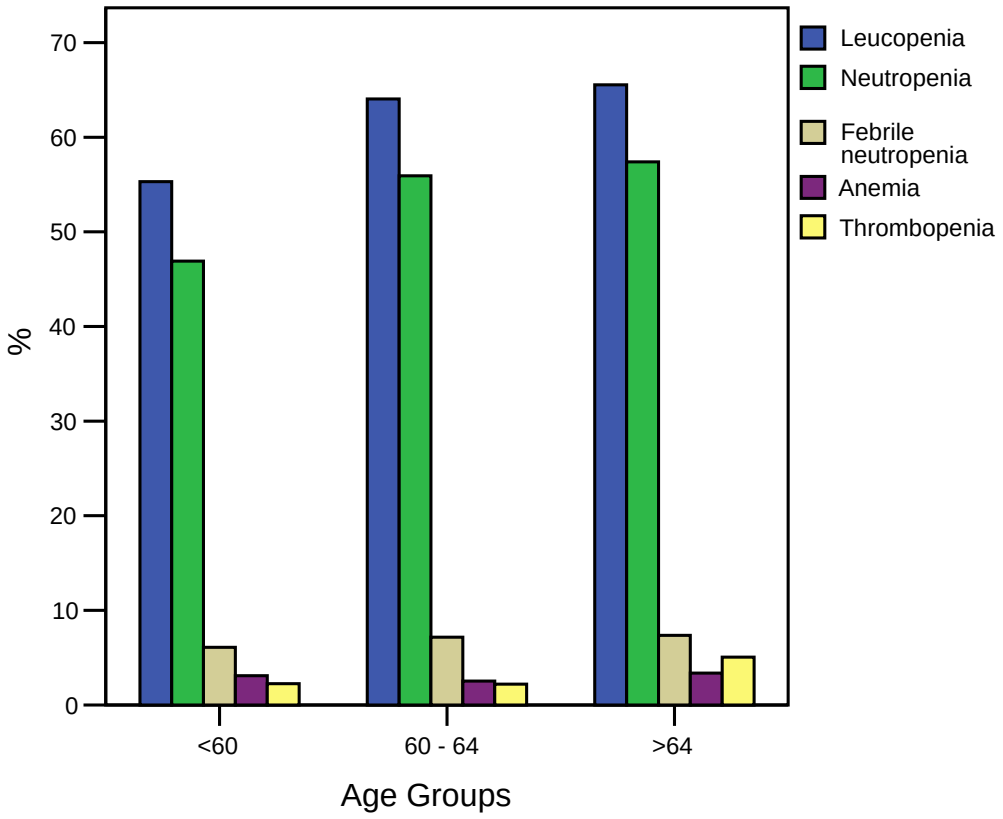
# Haematologioc Toxicity




Loibl S et al. Breast Cancer Res. 10:R77; 2008

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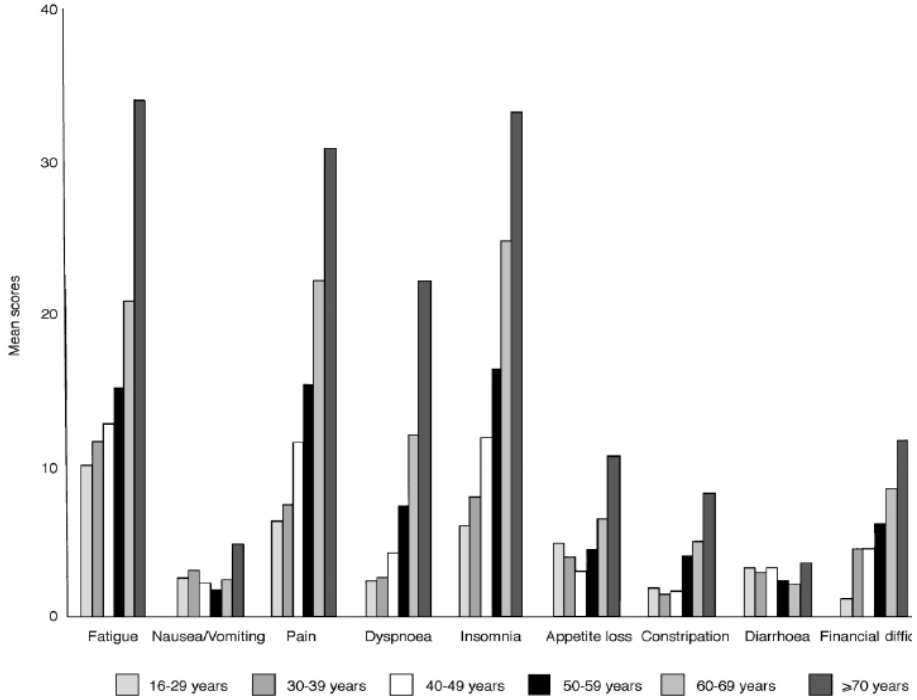
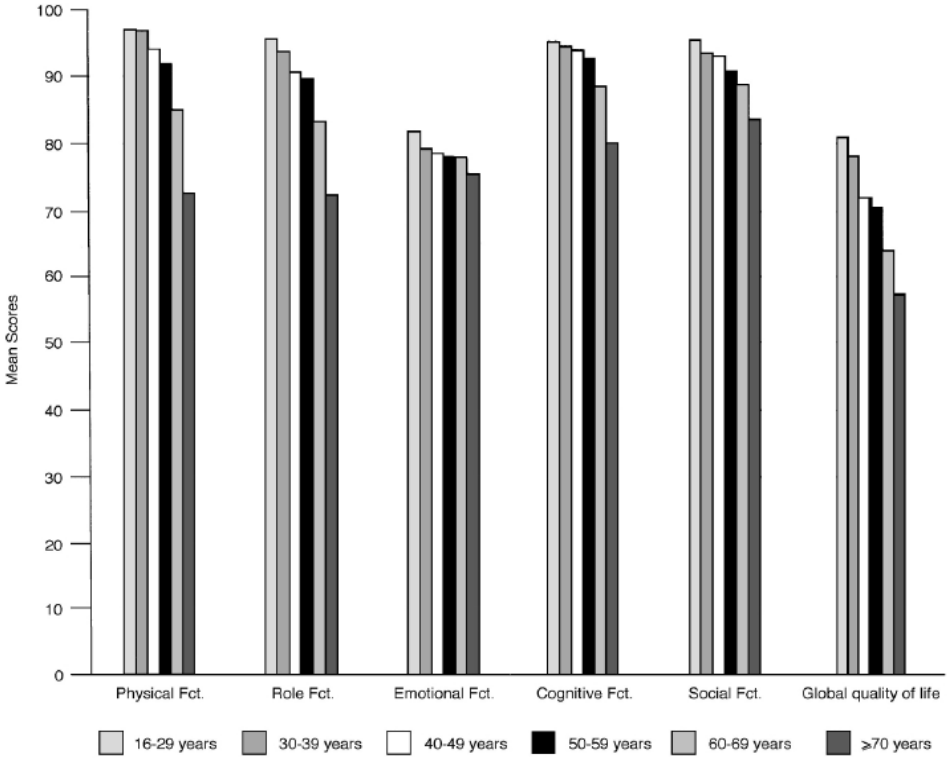
# Quality of Life in different age groups




Schwarz + Hinz; Eur J Cancer 2001

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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 14, 2009 VOL. 360 NO. 20

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

Hyman B. Muss, M.D., Donald A. Berry, Ph.D., Constance T. Cirrincione, 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. Kartcheske, 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., Gutav Magrinat, M.D., Barbara A. Parker, M.D., Ronald D. Hart, M.D., Debjani Grenier, M.D., Larry Norton, M.D., Clifford A. Hudis, M.D., and Eric P. Winer, M.D., for the CALGB Investigators*

Muss et al., N Engl J Med 2009; 360: 2055-65

# CALGB 49907

N= 633 Pat.
Alter ≥ 65
$T_{1–3}$, $N_1$
$T_3$, $N_0$
$T_2$, $N_0$ , ER/PR–
T ≥ 3cm

**R**

AC x 4
or
CMF x 6

Capecitabine x 6

ER/PR +: Tamoxifen 5 yrs

Muss H et al. New Engl J Med 2009

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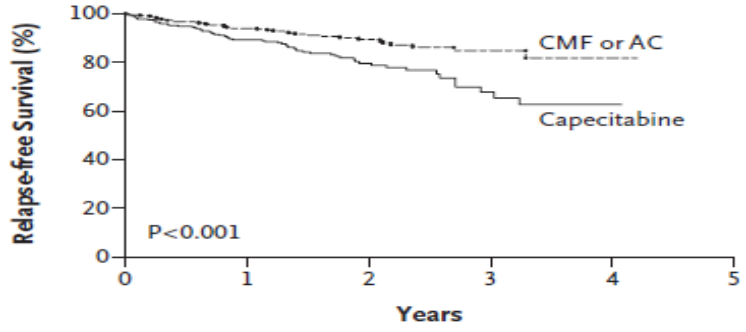
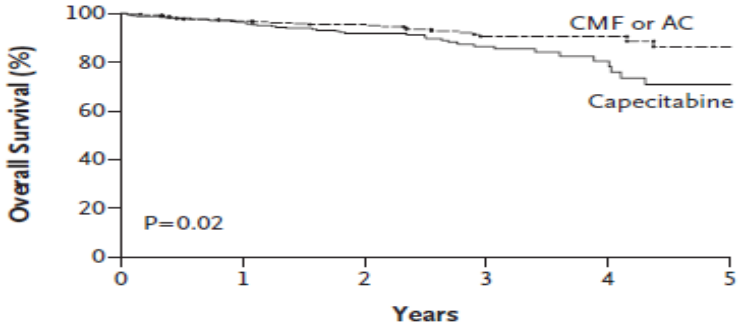
**A All Patients**



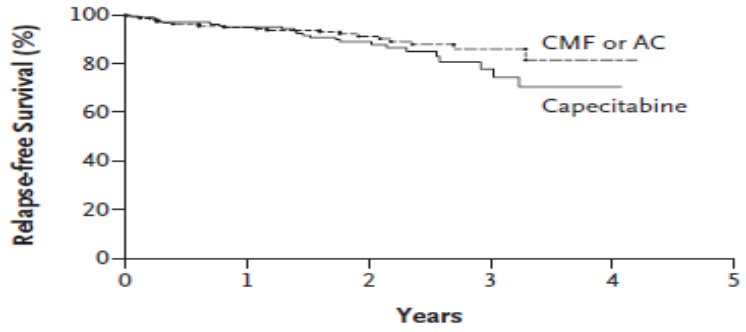

| No. at Risk | | | | | | |
|---|---|---|---|---|---|---|
| CMF or AC | 326 | 254 | 124 | 46 | 2 | 0 |
| Capecitabine | 307 | 237 | 96 | 29 | 1 | 0 |

**B All Patients**



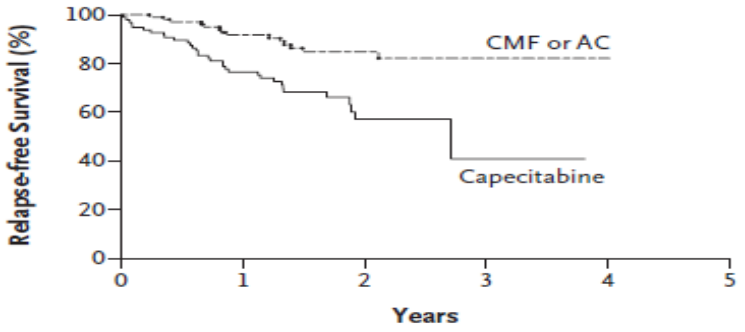

| No. at Risk | | | | | | |
|---|---|---|---|---|---|---|
| CMF or AC | 326 | 297 | 216 | 117 | 58 | 7 |
| Capecitabine | 307 | 279 | 180 | 90 | 36 | 8 |

**C Patients with Hormone-Receptor–Positive Tumors**



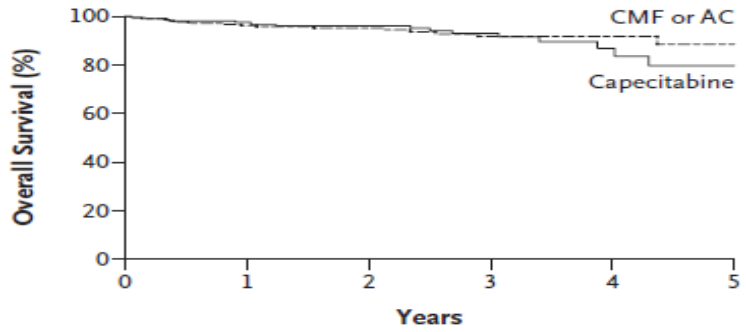

| | No. of Patients at Risk | No. of Events |
|---|---|---|
| CMF or AC | 218 | 21 |
| Capecitabine | 209 | 26 |

**D Patients with Hormone-Receptor–Negative Tumors**



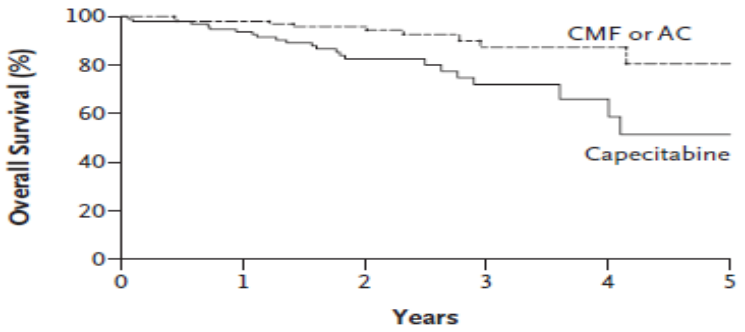

| | No. of Patients at Risk | No. of Events |
|---|---|---|
| CMF or AC | 106 | 14 |
| Capecitabine | 97 | 34 |

**E Patients with Hormone-Receptor–Positive Tumors**



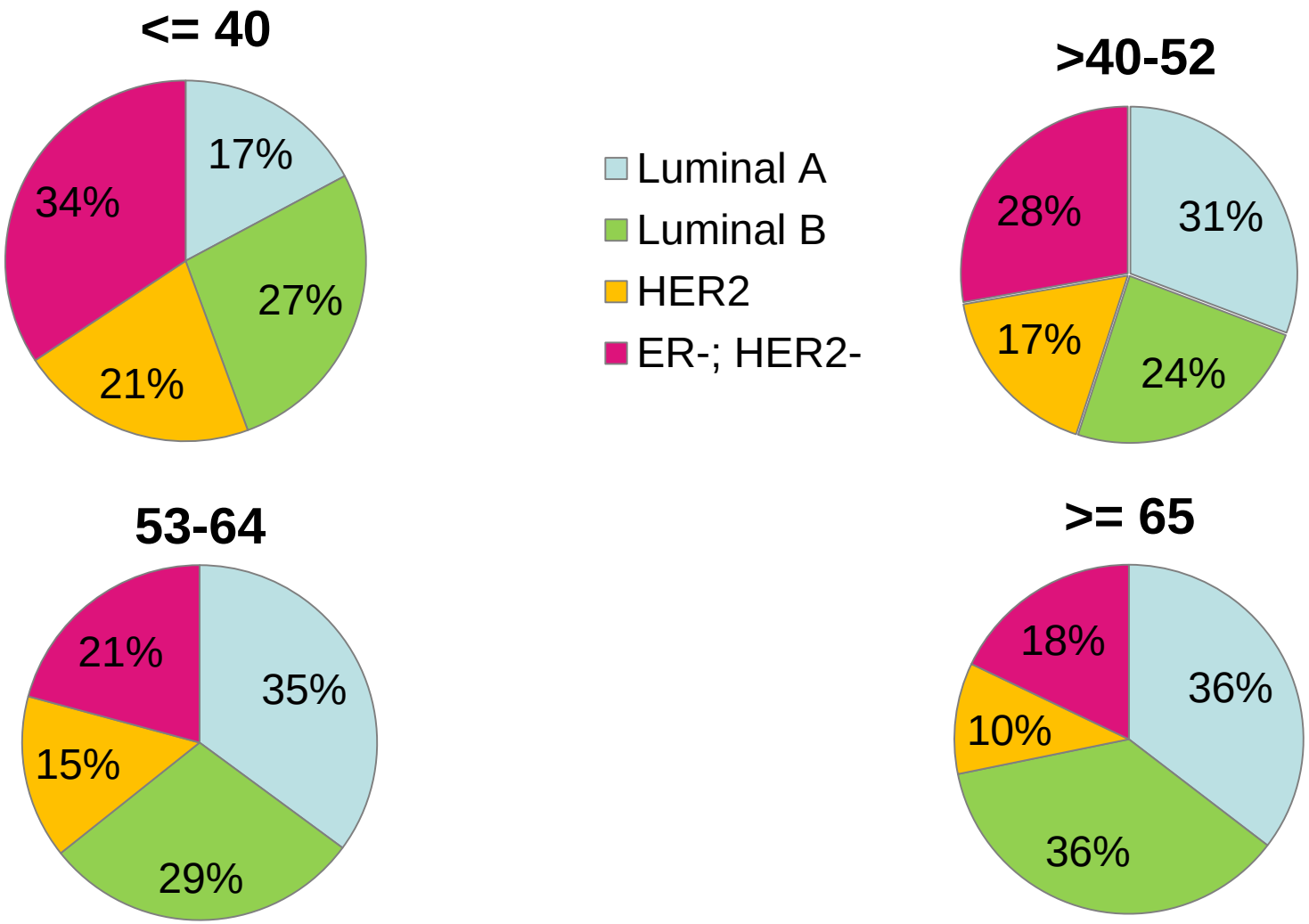

| | No. of Patients at Risk | No. of Events |
|---|---|---|
| CMF or AC | 218 | 15 |
| Capecitabine | 209 | 16 |

**F Patients with Hormone-Receptor–Negative Tumors**




| | No. of Patients at Risk | No. of Events |
|---|---|---|
| CMF or AC | 106 | 9 |
| Capecitabine | 97 | 22 |

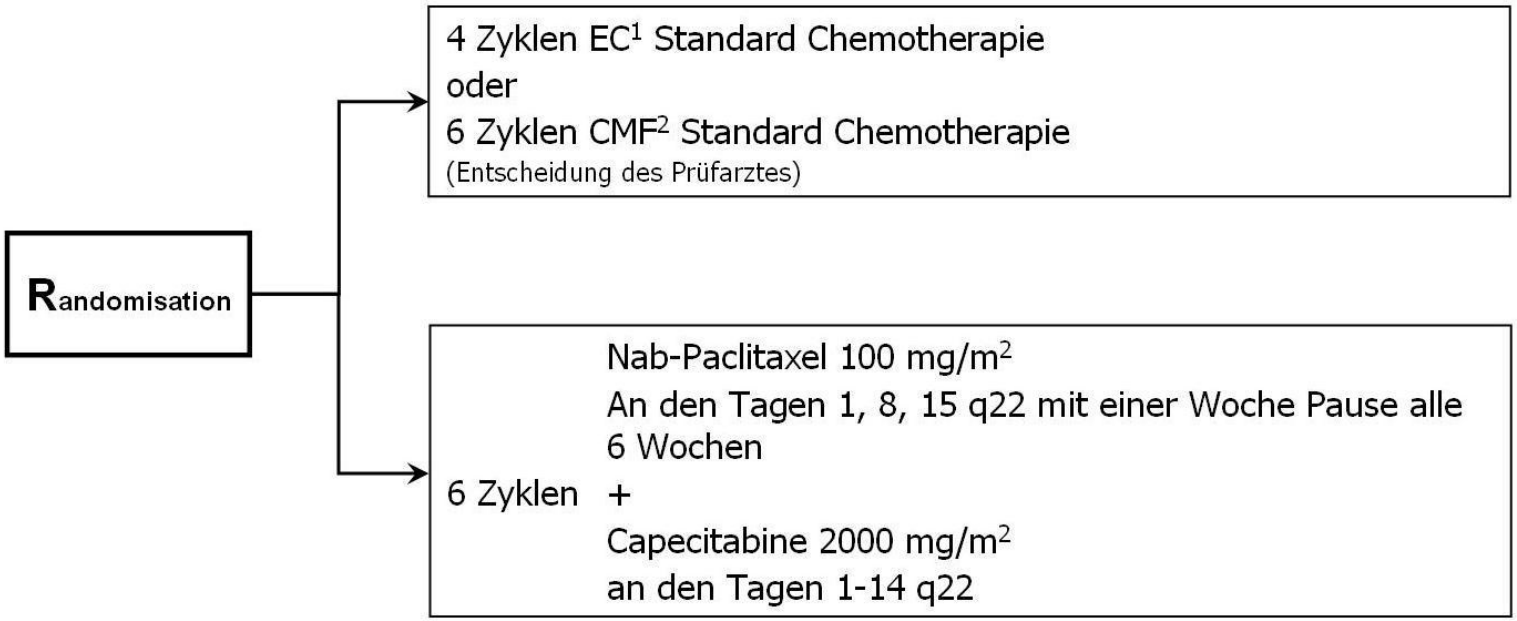
# Breast Cancer Subtypes According to Age




nach Azim H et al. Clinical Cancer Res 2011

ICE II
INVESTIGATIONAL CHEMOTHERAPY ELDERLY PATIENTS

# Study Design




***Wenn HER2+: Trastuzumab Behandlung gemäß der AGO Leitlinien***

***Wenn ER und/oder PR+: Endokrine Behandlung gemäß der AGO Leitlinien***

***Bisphosphonat Behandlung gemäß der AGO Leitlinien***

**[1] EC: Epirubicin (90 mg/m²) + Cyclophosphamide (600 mg/m²) an Tag 1 q22**

**[2] CMF: Cyclophosphamide (75 mg/m²) + Methotrexat (40 mg/m²) + 5-Fluorouracil (600 mg/m²) an Tag 1 and 8 q29**

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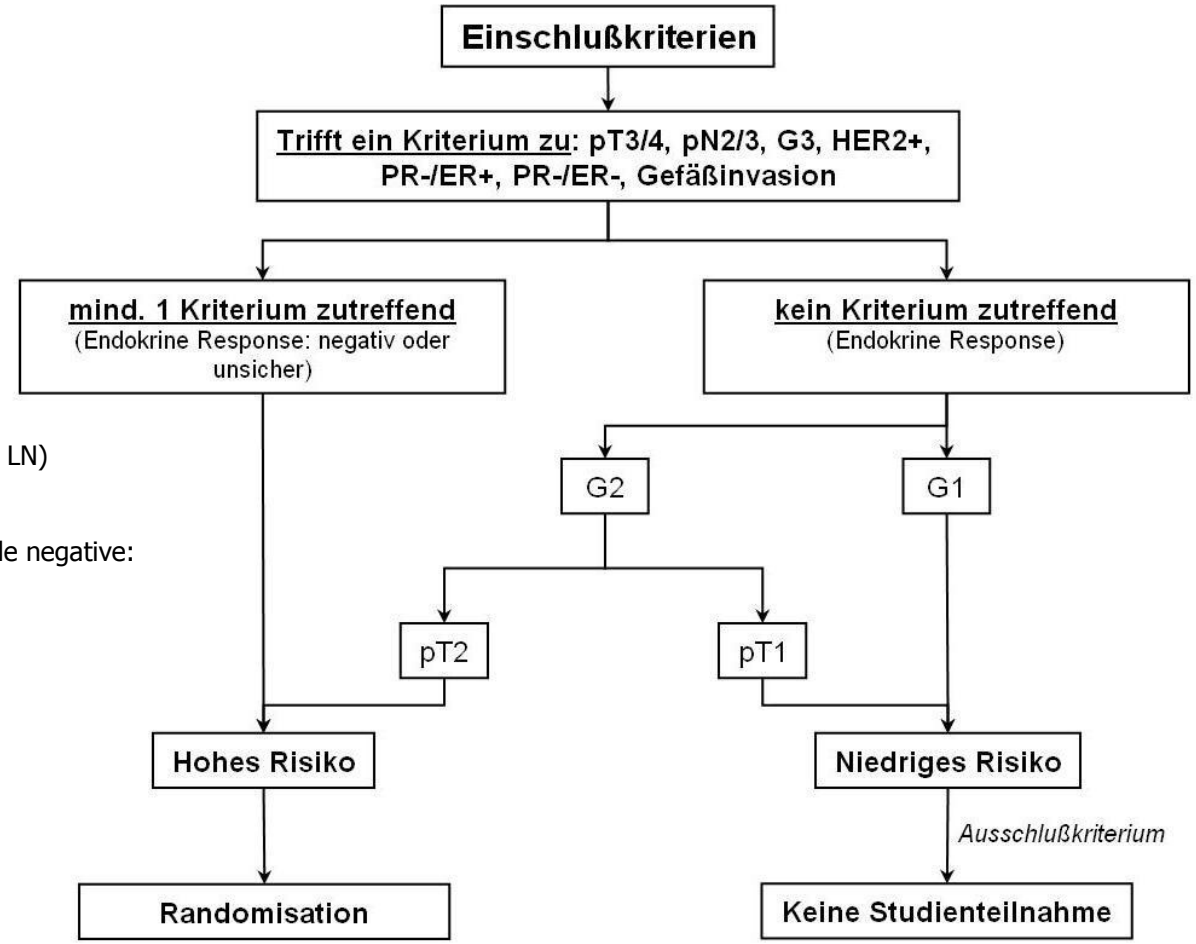
# Clinico-pathological Risk assessment

- node positive patients N2-N3 (≥ 4 positive LN) Independent of additional risk factors

- node positive (N1: 1-3 positive LN) or node negative: Need additional risk factors

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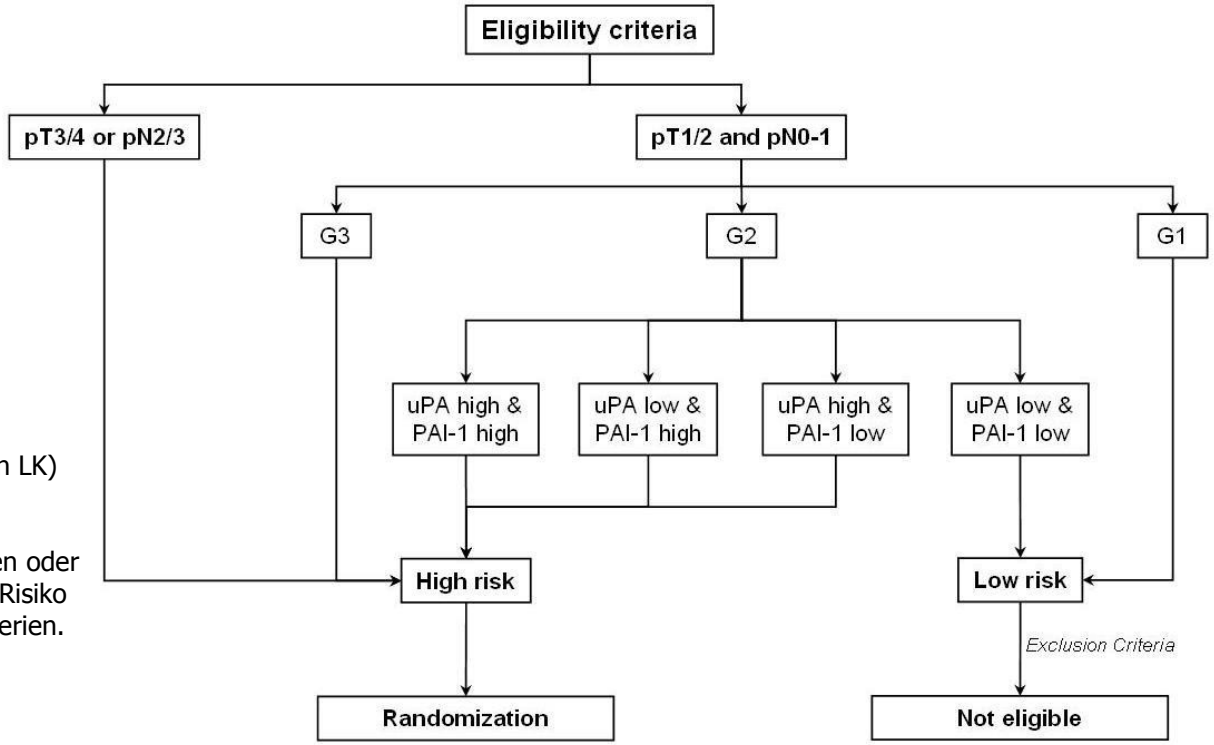
# Biological risk assessment

- Nodal positive Patientinnen N2-N3 (≥ 4 befallenen LK) unabhängig von zusätzlichen Risikofaktoren

- Nodal-positive (N1: 1-3 befallene LK) Patient/innen oder nodal-negativen Patient/innen mit einem erhöhten Risiko gemäß der histopathologischen oder uPA/PA11 Kriterien.




| | |
|---|---|
| ***uPA high: uPA ≥ 3 ng/mg*** | ***uPA low: uPA < 3 ng/mg*** |
| ***PAI-1 high: PAI-1 ≥ 14 ng/mg*** | ***PAI-1 low: PAI-1 < 14 ng/mg*** |

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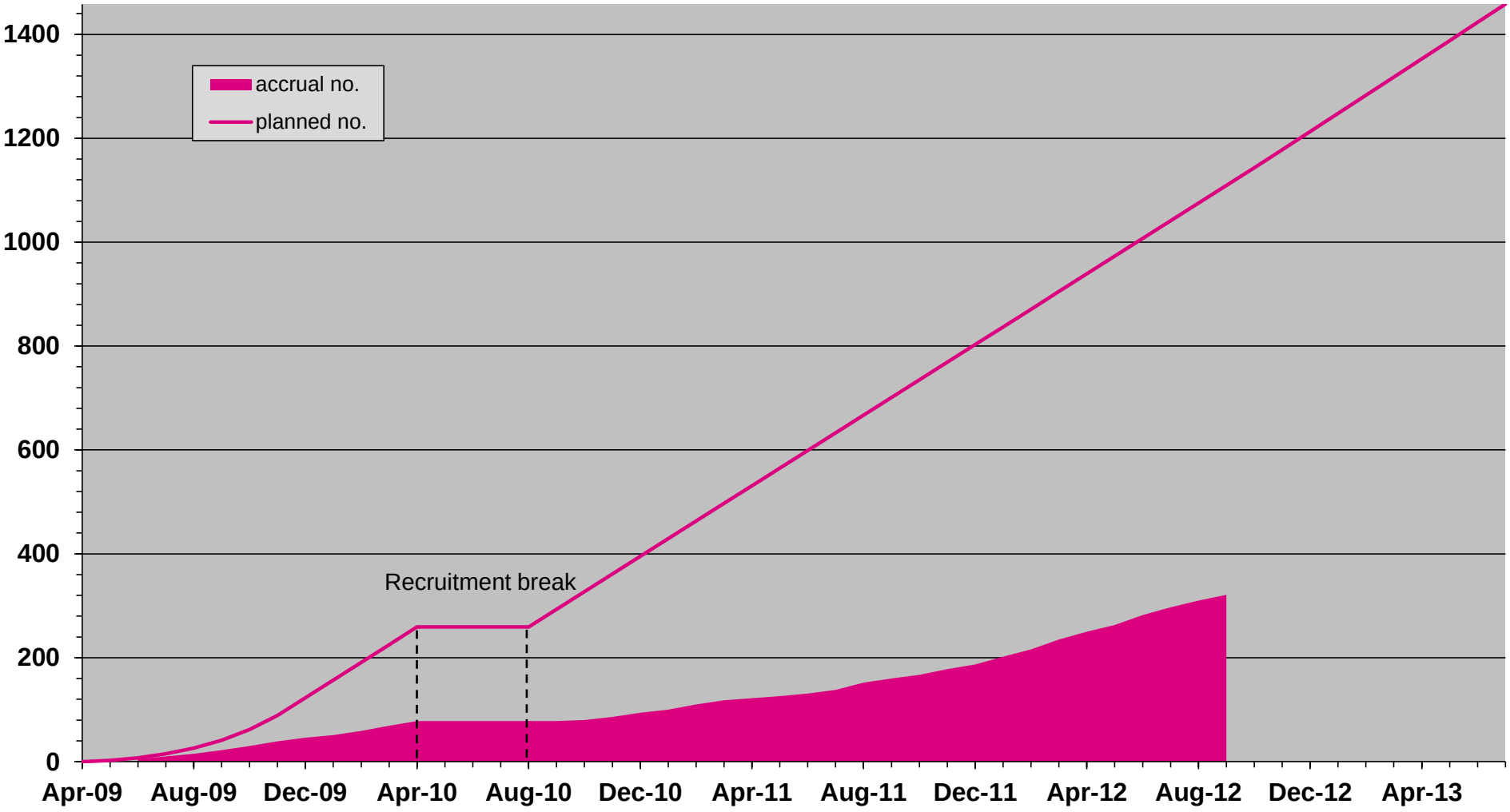
# ICE II - Recruitment on 01.09.2012
# n = 321

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# Baseline Characteristics

| | Anzahl 250 | | | | | |
|---|---|---|---|---|---|---|
| **Sex** | **female** | **male** | | | | |
| | 246 | 4 | | | | |
| **Therapy** | **EC** | **CMF** | **PX** | | | |
| | 117 | 9 | 124 | | | |
| **Risik** | **pT3/4; N2/3** | **uPA; PAI** | **Clinico-pathological** | | | |
| | 74 | 20 | 156 | | | |
| **Age** | **65-69** | **70-74** | **75-80** | **>80** | | |
| | 67 | 113 | 64 | 6 | | |
| **Prognostic faktors** | **HER2+** | **HER2-** | **N+** | **N-** | **ER+** | **ER-** |
| | 43 | 207 | 138 | 112 | 183 | 67 |

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# ICE - Studie

N=1400 R

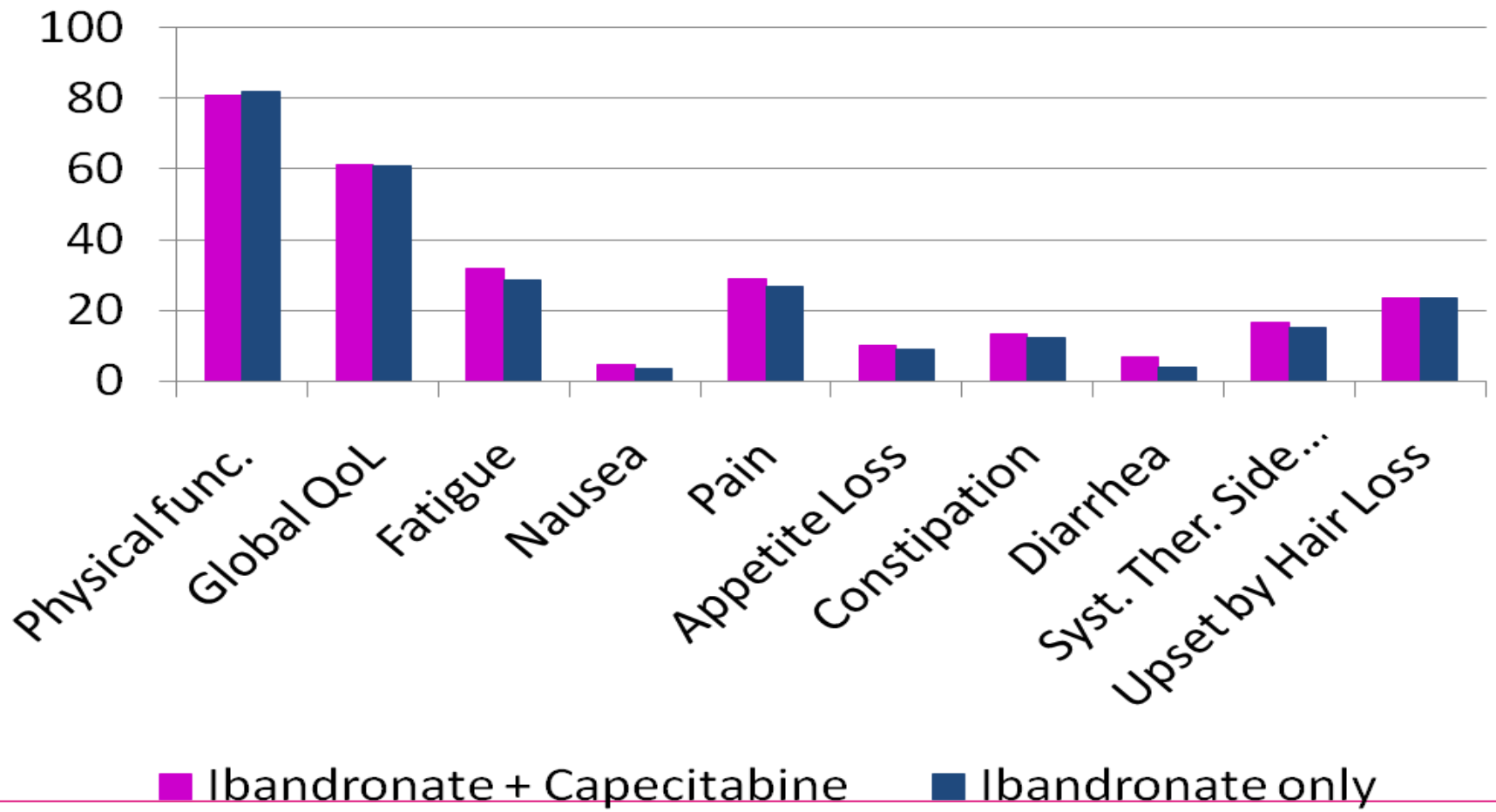
**Ibandronate 2 years**
**50 mg p.o. or 6 mg i.v.**

**Capecitabine 2000 mg/m² x 6**
**Ibandronate 2 J. p.o. or i.v.**

**ER/PR +: Anastrozol 1mg / 5 J. (sequentiell zu X)**

Reimer et al. ESMO 2009

# QoL Baseline




Reimer et al. ESMO 2009

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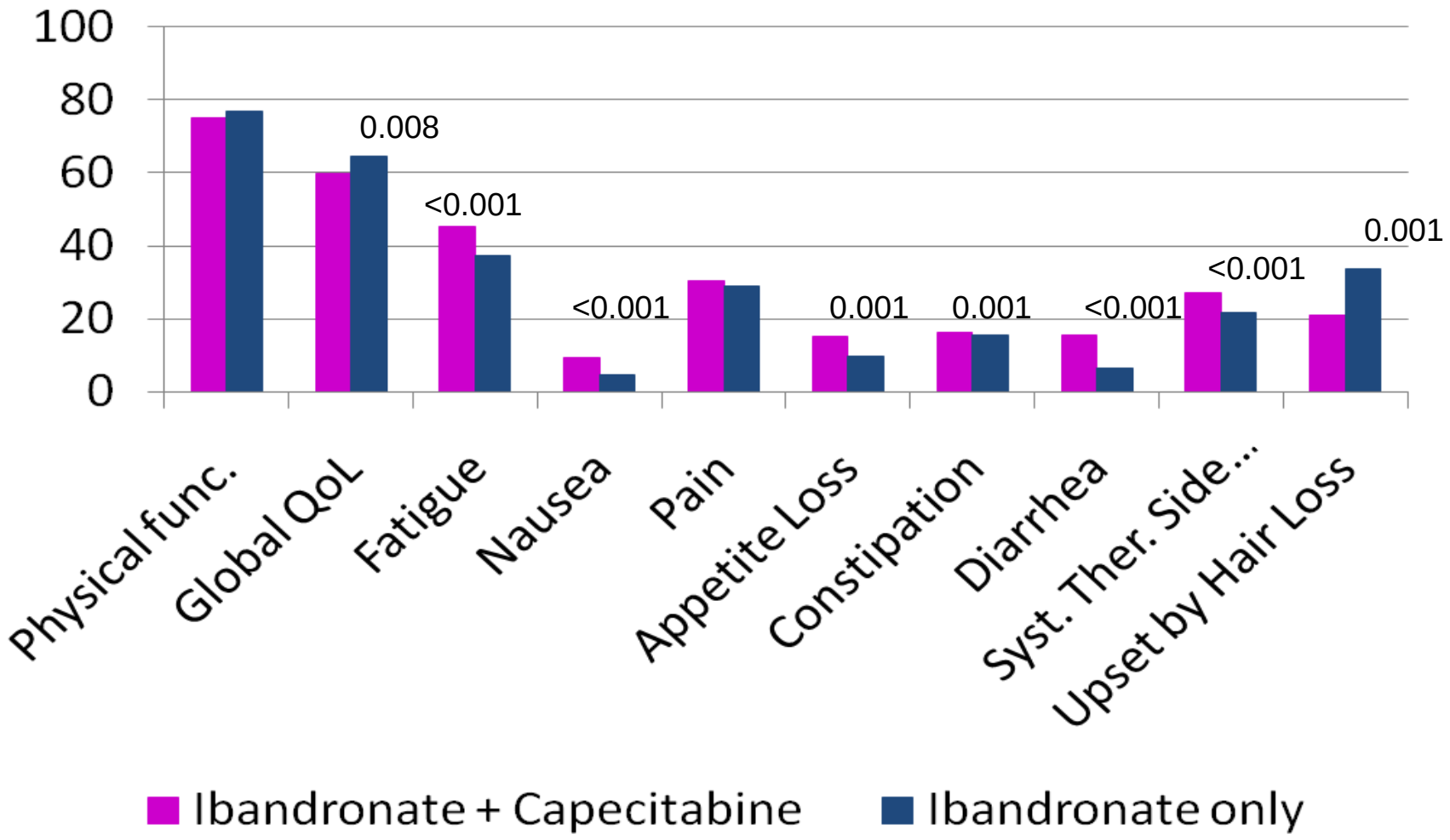
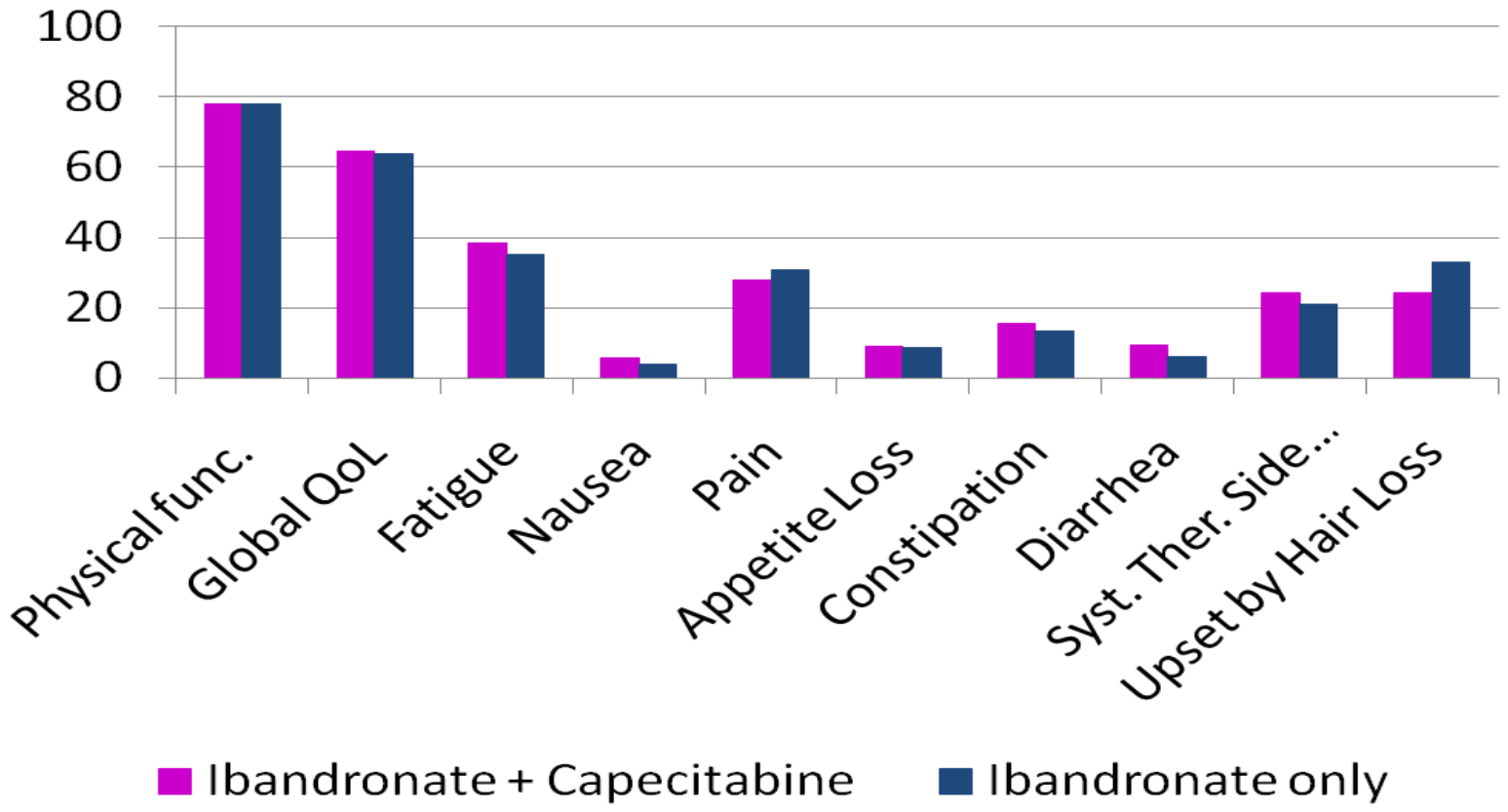
# QoL at the end of chemotherapy




Reimer et al. ESMO 2009

# QoL 6 months after end of chemotherapy




Reimer et al. ESMO 2009

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# Treatment for Fit Elderly Patients

## (Life Expectancy > 5 yrs and Acceptable Comorbidities)



Guidelines Breast
Version 2012.1

www.ago-online.de

Further Information

References

FORSCHEN
LEHREN
HEILEN

| | Oxford / AGO LoE / GR | | |
|---|---|---|---|
| ➢ **Geriatric assessment** | 2b | B | ++ |
| ➢ **Treatment according to standard** | 2a | C | ++ |
| ➢ **Surgery similar to „younger“ age** | 2b | B | ++ |
| ➢ **Endocrine treatment (endocrine resp.)** | 1a | A | ++ |
| ➢ **Chemotherapy** | | | |
| ➢ **< 70 years** | 1a | A | + |
| ➢ **> 70 years (especially N+, ER/PgR-)** | 2a | C | +* |
| ➢ **Radiotherapy** | 2b | C | + |
| ➢ **Omit Radiotherapy after BCT In low risk** | 2b | B | +/- |
| **ER + population > 70 y if Tam is planned (CAVEAT: increased risk local recurrence)** | | | |
| ➢ **Trastuzumab** *Study participation recommended | 2b | C | + |

# Treatment for Frail Patients
## (Life Expectancy <5 yrs, Substantial Comorbidities)



Guidelines Breast
Version 2012.1

| | Oxford / AGO LoE / GR |
|---|---|
| ➢ **Reduced standard treatment** | 2b C ++ |
| ➢ **Options extrapolated from trials in elderly:** | |
| ➢ No breast surgery (consider endocrine options) | 2b C + |
| ➢ No axillary clearing (≥ 60 y, cN0, Rec pos) | 2b B + |
| ➢ No radiotherapy ( ≥ 70 y, pT1, pN0, Rec pos) | 2b C + |
| ➢ Hypofractionated radiotherapy | 2b C + |
| ➢ No chemotherapy >70 years and negative risk-benefit analysis | 2b C + |

www.ago-online.de

Further Information

References

# Management of elderly patients with breast cancer: updated recommendations of the International Society of Geriatric Oncology (SIOG) and European Society of Breast Cancer Specialists (EUSOMA).

"...Despite competing causes of death, breast cancer is the cause of death in a substantial number of older patients. In women ≥80 years at diagnosis, up to 40% die from breast cancer. Underestimation of life expectancy and fitness for therapy may result in age-related under-treatment, itself a risk factor for breast cancer recurrence and death."

Biganzoli L, et al. Lancet Oncol. 2012 ;13:e148-60.