Aktuelle Therapiestandards in der neoadjuvanten Behandlung 2025

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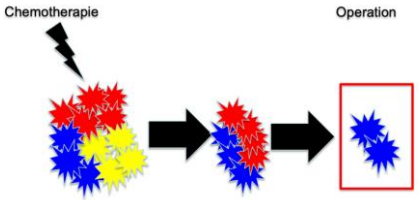
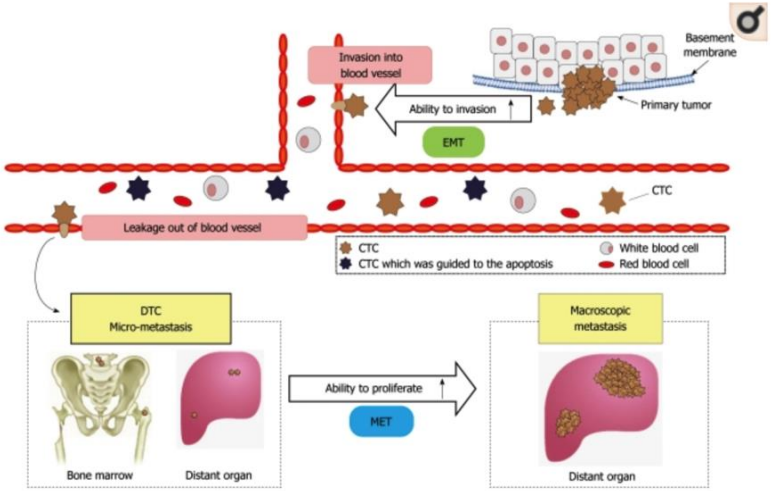
Conflict of Interest

- **Vortragshonorare:** Amgen, Roche, Teva, Clovis, Tesaro, MSD, Novartis, Pfizer, Lilly, GSK, Gilead, Astra Zeneca, Daiichi Sankyo, Stemline, Seagen
- **Beratertätigkeit:** Amgen, MSD, Tesaro, Roche, Pfizer, Lilly, Myriad, Esai, GSK, Gilead, Daiichi Sankyo, Roche, Astra Zeneca
- **Reisekosten:** Pfizer, Clovis, Seagen, Pharma mar, MSD, Celgene, Roche, Astra Zeneca, Gilead, Daiichi Sankyo, Stemline

Neoadjuvante Systemtherapie

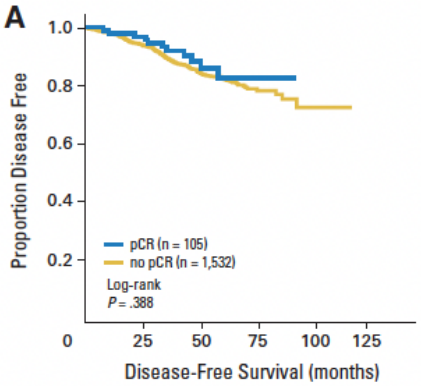
- Möglichkeit der BET/Operabilität
- Axilläres Downstaging
- Prognoseeinschätzung
- Prognoseverbesserung durch individualisierte Postneoadjuvanz
- Deeskalation
- Genetische Testung
- In-vivo Testung (innovativer) Substanzen



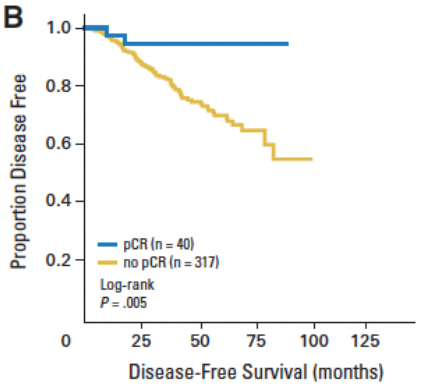


Park Y et al. World J Clin Oncol. 2011;2(8):303-310

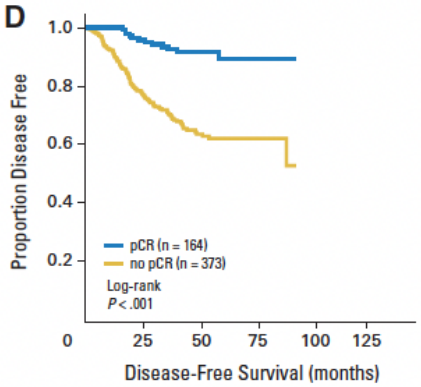
Luminal A like



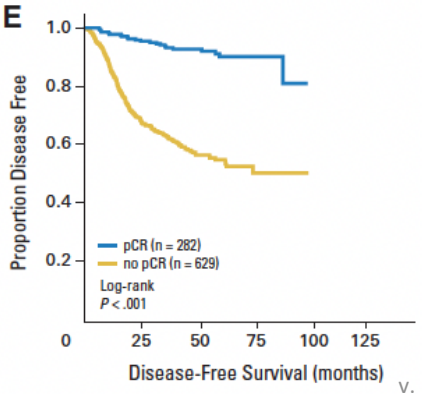
Luminal B like



Her2

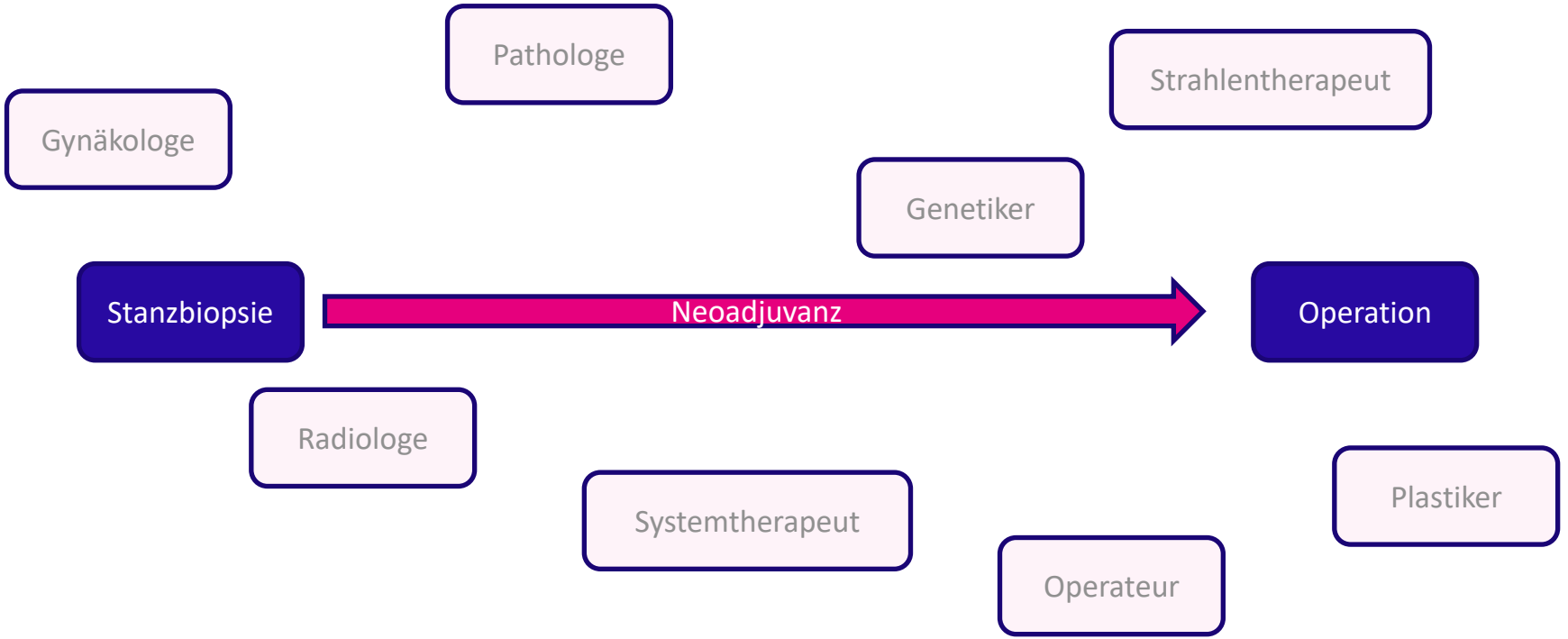


TNBC

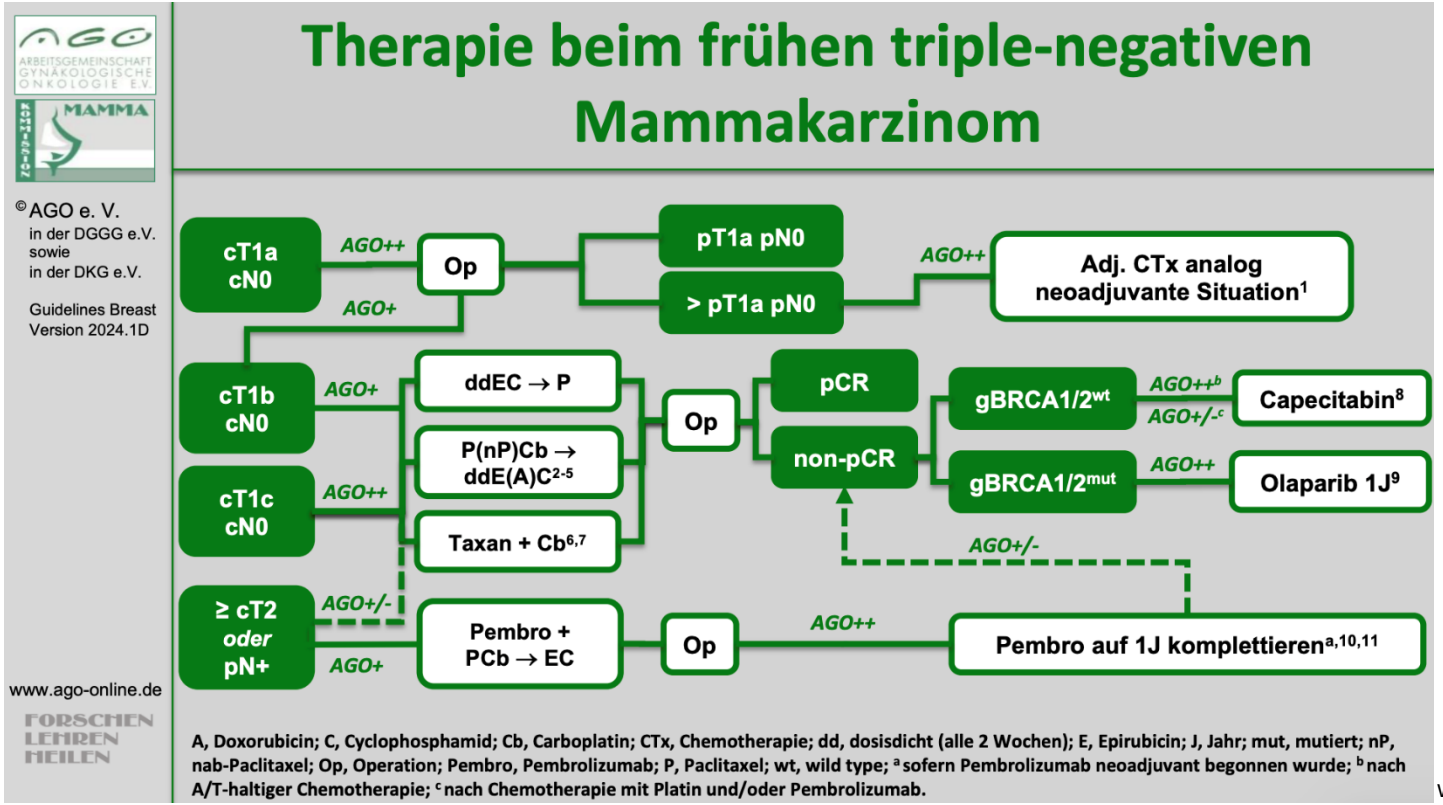


v. Minckwitz G et al. J Clin Oncol 2012;30:1796-1804

Neoadjuvanz als Paradebeispiel einer multidisziplinären Zusammenarbeit



TNBC



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(Neo-)Adjuvante Chemotherapie: bei kleinen, nodal-negativen Tumoren (T1)

	Oxford		
	LoE	GR	AGO
▪ **Indikation zur Chemotherapie bei**			
▪ **TNBC**			
▪ > 10 mm neoadjuvant bevorzugt	2b	B	++
▪ > 5–10 mm neoadjuvant oder adjuvant	2b	B	+
▪ ≤ 5 mm adjuvant	2b	B	+/-
▪ **HER2+ in Kombination mit Trastuzumab**			
▪ > 10 mm neoadjuvant oder adjuvant	1a	A	++
▪ > 5–10 mm adjuvant	2b	B	+
▪ ≤ 5 mm adjuvant	2b	B	+/-

TNBC

T1mic

T1a

T1b

T1c

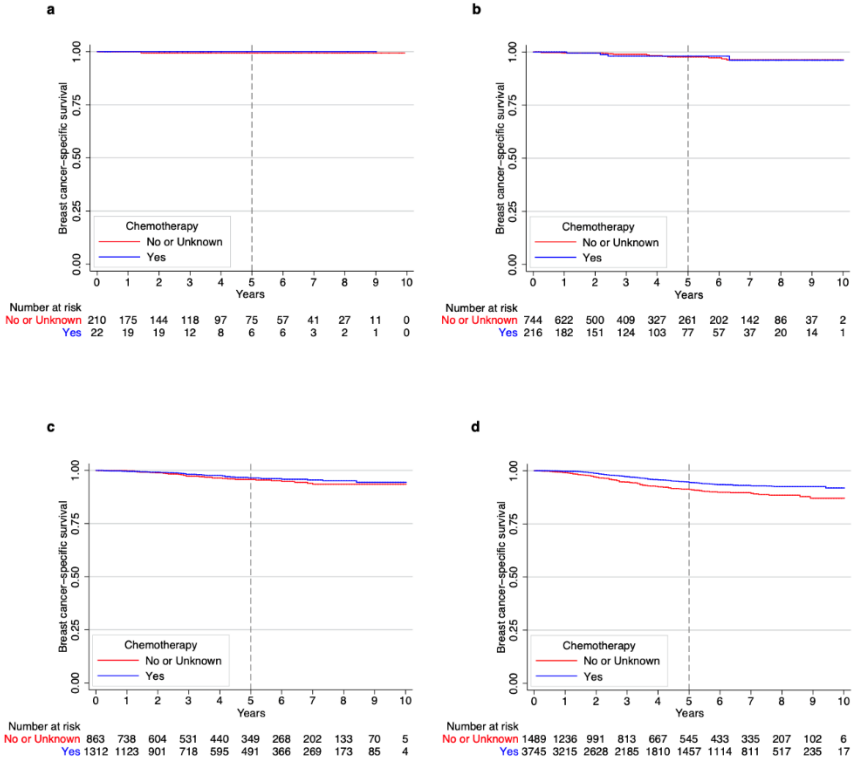


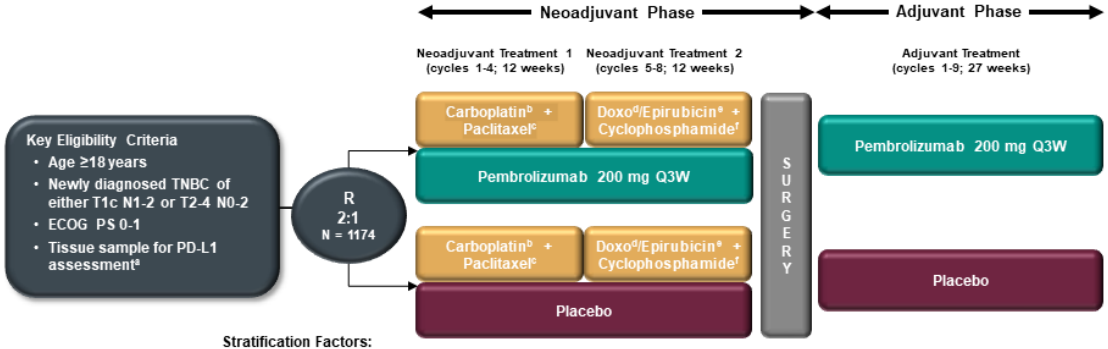
Fig. 1 | Breast cancer-specific survival (BCSS) in women with stage IA triple-negative breast cancer. BCSS in **a**) patients with T1mic disease; **b**) patients with T1a disease; **c**) patients with T1b disease; and **d**) patients with T1c disease.

Tarantino, P., Leone, J., Vallejo, C.T. *et al.* Prognosis and treatment outcomes for patients with stage IA triple-negative breast cancer. *npj Breast Cancer* **10**, 26 (2024). https://doi.org/10.1038/s41523-024-00634-6

TNBC- KEYNOTE-522

Schmid KN522 ESMO Virtual Plenary 2021

KEYNOTE-522 Study Design (NCT03036488)



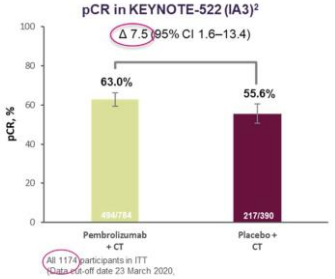
Stratification Factors:
- Nodal status (+ vs -)
- Tumor size (T1/T2 vs T3/T4)
- Carboplatin schedule (QW vs Q3W)

Neoadjuvant phase: starts from the first neoadjuvant treatment and ends after definitive surgery (post treatment included)

Adjuvant phase: starts from the first adjuvant treatment and includes radiation therapy as indicated (post treatment included)

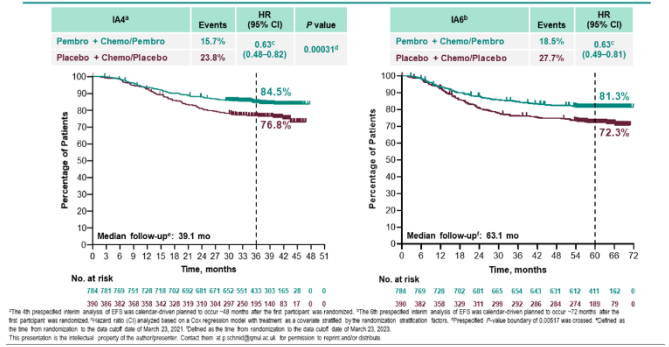
[a]Must consist of at least 2 separate tumor cores from the primary tumor.
[b]Carboplatin dose was AUC 5 Q3W or AUC 1.5 QW.
[c]Paclitaxel dose was 80 mg/m² QW.
[d]Doxorubicin dose was 60 mg/m² Q3W.
[e]Epirubicin dose was 90 mg/m² Q3W.
[f]Cyclophosphamide dose was 600 mg/m² Q3W.

KEYNOTE-522 (IA3)*[2]
Pembrolizumab + CT vs placebo + CT in early TNBC



San Antonio Breast Cancer Symposium®, December 5–9, 2023

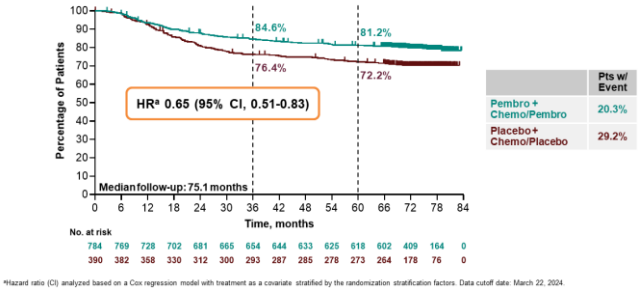
EFS at IA4 and IA6



Schmid et al. KN522 ESMO Virtual Plenary 2021

TNBC- KEYNOTE-522

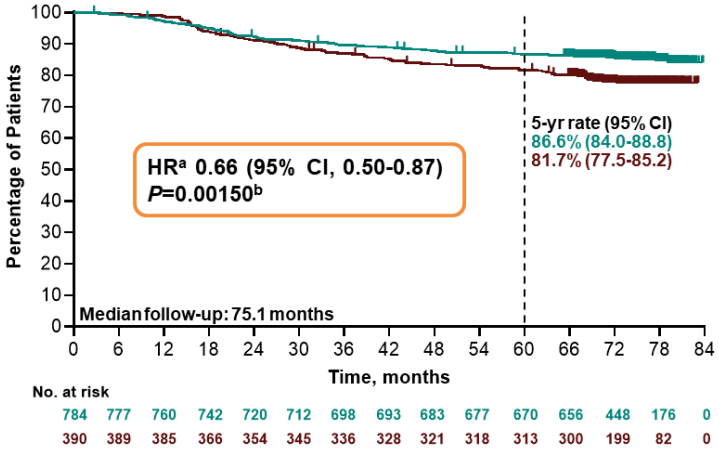
Updated Event-Free Survival



	Pts w/ Event
Pembro + Chemo/Pembro	20.3%
Placebo + Chemo/Placebo	29.2%

[a]Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. Data cutoff date: March 22, 2024.

Key Secondary Endpoint: Overall Survival



	Pts w/ Event
Pembro + Chemo/Pembro	14.7%
Placebo + Chemo/Placebo	21.8%

[a]The unstratified piecewise HR was 0.87 (95% CI, 0.57-1.32) before the 2-year follow-up and 0.51 (95% CI, 0.35-0.75) afterwards. The weighted average HR with weights of number of events before and after 2-year follow-up was 0.66. With 200 events (67.3% information fraction), the observed *P*-value crossed the prespecified nominal boundary of 0.00503 (1-sided) at this interim analysis. Data cutoff date: March 22, 2024.

Schmid et al. KN522 LBA4 ESMO 2024

TNBC

12xPaclitaxel+Carboplatin
4x Epirubicin/Cyclophosphamid
Pembrolizumab

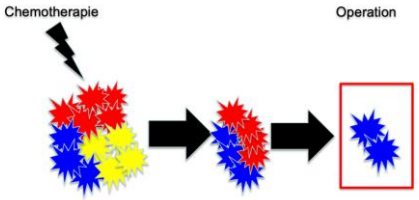
Parallel?

Sequentiell?

pCR

9 Gaben
Pembrolizumab

Studie



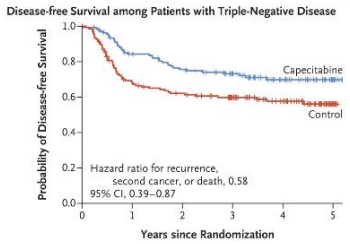
Non-pCR

Pembrolizumab

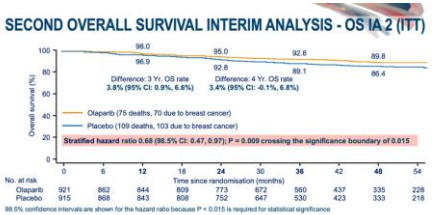
Capecitabin

Olaparib

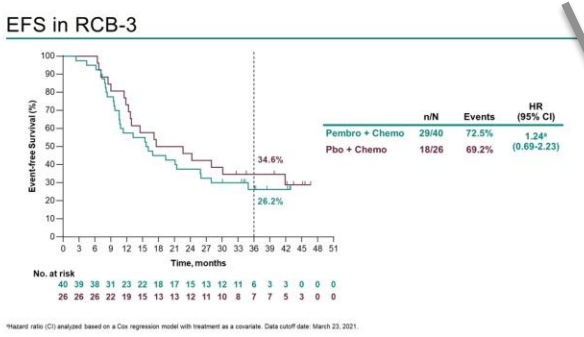
Studie



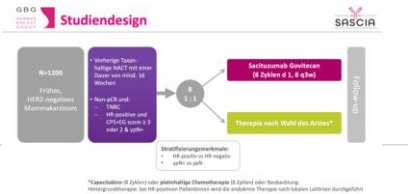
Masuda N et al. N Engl J Med 2017; 376:2147-2159



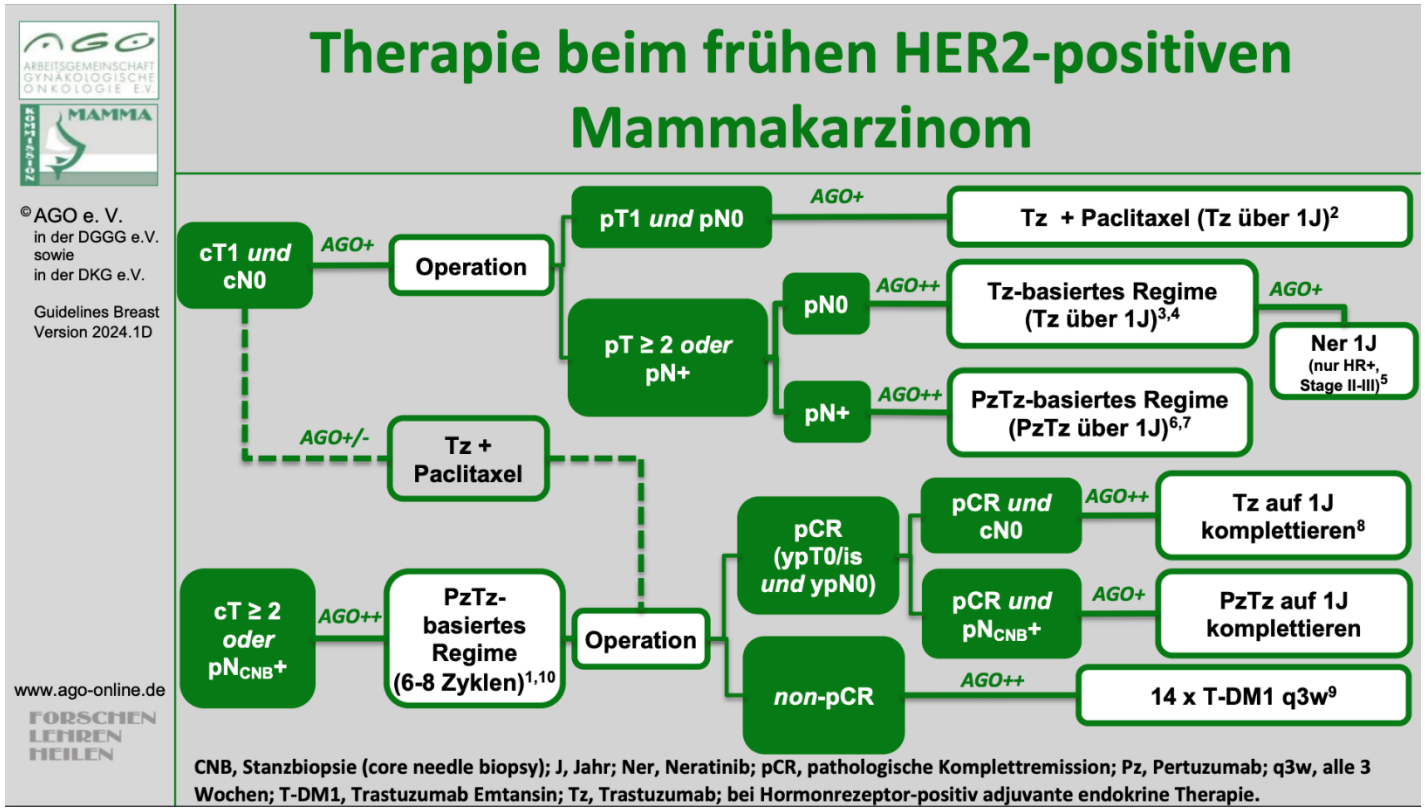
Tutt et al. ESMO Virtual Plenary 03/2022 VP1



Keynote522.Lajos Pusztai. Abstract 503



HER2+



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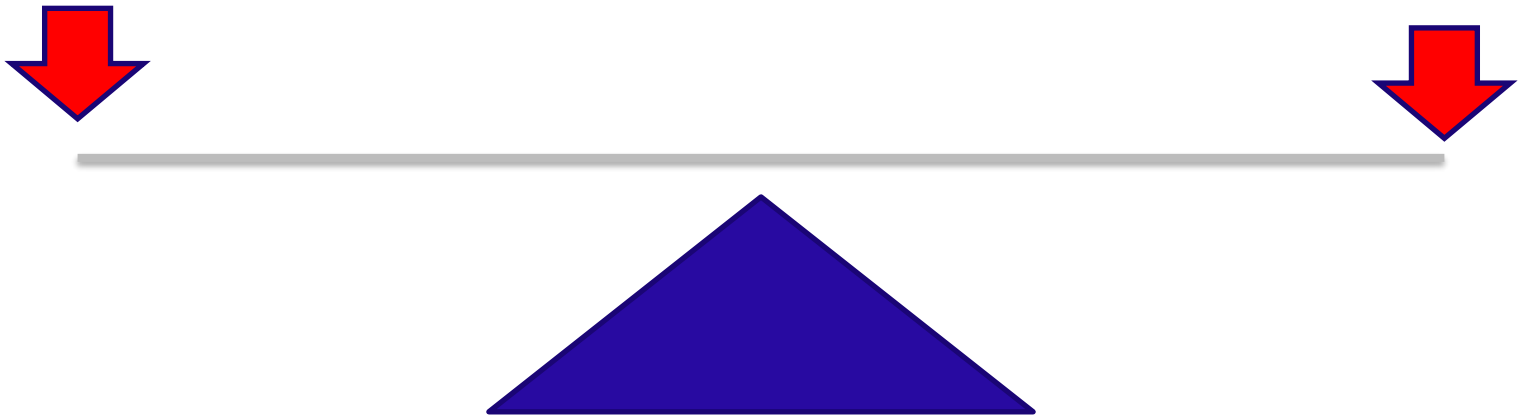
HER2+ Anthrazyklin?!?

RISIKO

NUTZEN

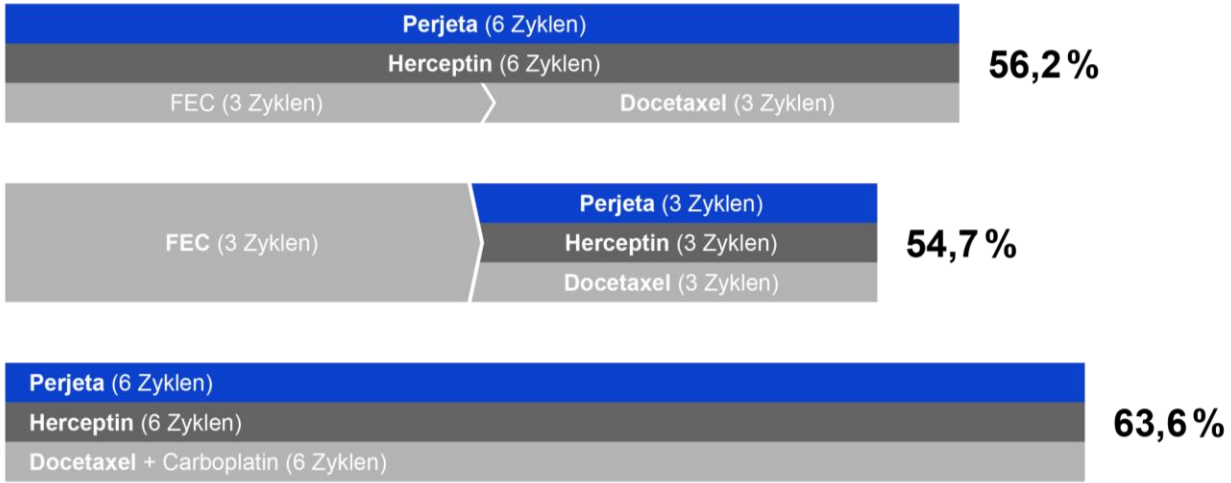


HER2+ TRYPHAENA

R

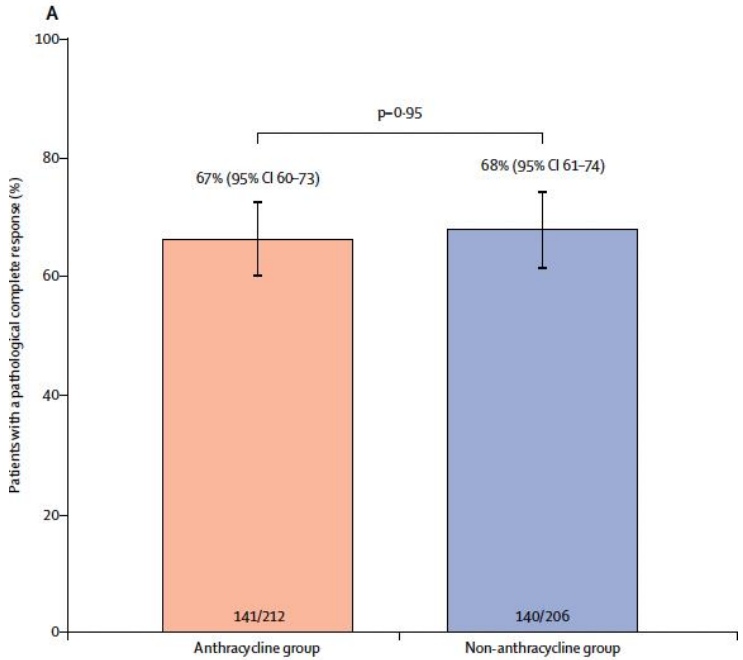
- 3xFEC-> 3 xT+H+P
- 3xFEC+T+P-> 3 xT+H+P
- 6 x TCHP

Rate pathologischer Komplettremission in Brust und Axilla (ypT0/is ypN0):



Schneeweiss A et al. Annals of Oncology 24: 2278–2284, 2013

HER2+ TRAIN2



	Anthracycline group (n=212)	Non-anthracycline group (n=206)	Odds ratio (95% CI)
Hormone receptor status			
ER-positive and/or PR-positive	64/125 (51%)	64/116 (55%)	1·17 (0·71–1·95)
ER-negative and PR-negative	77/87 (89%)	76/90 (84%)	0·71 (0·30–1·68)
Age			
<50 years	79/116 (68%)	78/110 (71%)	1·14 (0·65–2·01)
≥50 years	62/96 (65%)	62/96 (65%)	1·00 (0·55–1·81)
Tumour stage			
0–2	96/141 (68%)	99/145 (68%)	1·01 (0·61–1·66)
3–4	45/71 (63%)	41/61 (67%)	1·18 (0·58–2·43)
Node status			
Negative	59/79 (75%)	54/75 (72%)	0·87 (0·43–1·78)
Positive	82/133 (62%)	86/131 (66%)	1·19 (0·72–1·96)
Disease stage			
II	89/133 (67%)	98/142 (69%)	1·10 (0·66–1·83)
III	52/79 (66%)	42/64 (66%)	0·99 (0·49–1·99)
Tumour grade			
1–2	65/102 (64%)	66/102 (65%)	1·04 (0·59–1·85)
3	68/98 (69%)	66/72 (72%)	1·12 (0·60–2·09)
All patients	**141/212 (67%)**	**140/206 (68%)**	**1·07 (0·71–1·61)**

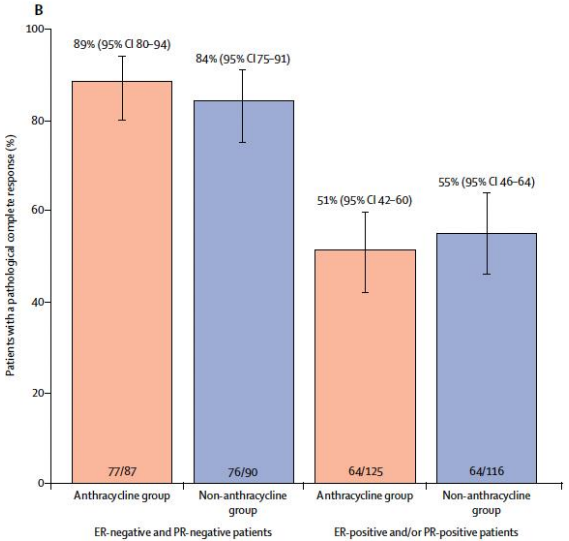
Figure 3: **Pathological complete responses by subgroup**
Disease stage II includes one patient with stage I disease in the non-anthracycline group. Disease stage III includes one patient with stage IV disease in the anthracycline group. Tumour grade and disease stage were post-hoc analyses. All other subgroup analyses were prespecified as stratification factors. ER=oestrogen receptor. PR=progesterone receptor.

Van Ramshorst MS et al. Lancet Oncol 2018; 19: 1630–40

HER2+ Spielt der HR-Status eine Rolle?

TRAIN2

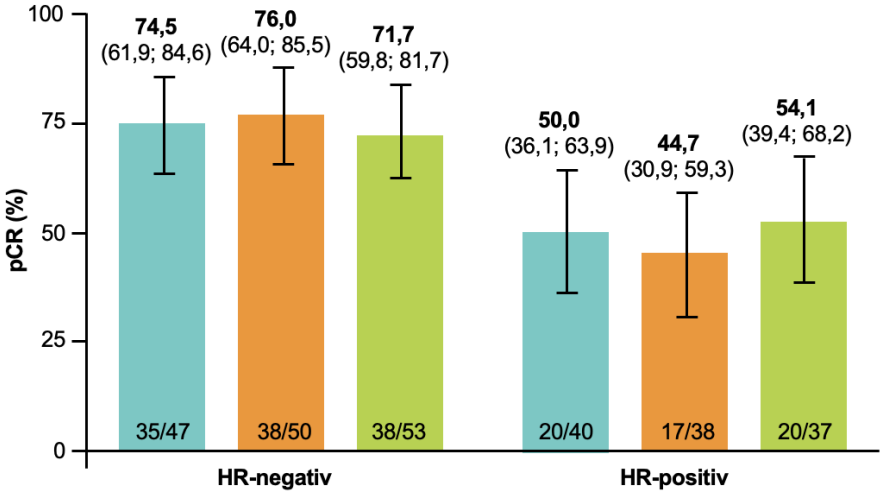
HR- HR+



Van Ramshorst MS et al. Lancet Oncol 2018; 19: 1630–40

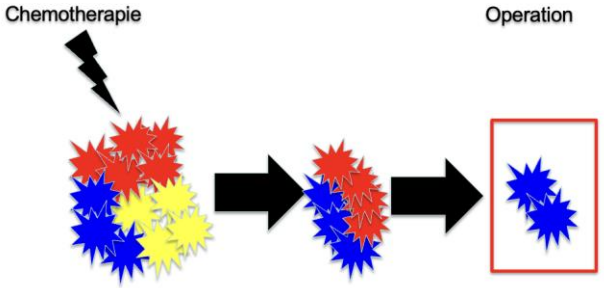
FASCINATE-N

HR- HR+



Li et al. 2024 SABCS, GS1-04

HER2+ Postneoadjuvanz



KATHERINE

Studiendesign

Phase-III-Studie

Haupteinschlusskriterien
- Vorherige neoadjuvante Therapie musste enthalten:
  - Mindestens 6 Zyklen Chemotherapie
  - Mindestens 9 Wochen Trastuzumab
    - Zweite HER2-gerichtete Substanz erlaubt
- Invasiver Rest-Tumor in der Brust oder axillären Lymphknoten
- Randomisierung innerhalb 12 Wochen nach OP

R 1:1

T-DM1
3,6 mg/kg i.v. alle 3 Wochen, 14 Zyklen

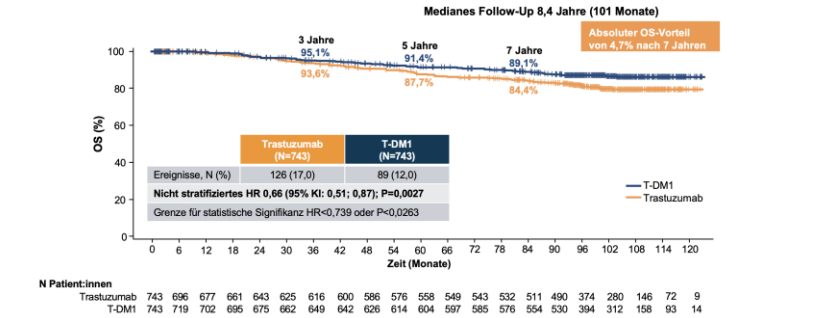
Trastuzumab
6 mg/kg i.v. alle 3 Wochen, 14 Zyklen

- Bestrahlung und endokrine Therapie nach Protokoll und lokalen Leitlinien
- Wechsel zu Trastuzumab war erlaubt, wenn T-DM1 aufgrund von UE abgesetzt wird

- **Primärer Endpunkt:** iDFS
- **Sekundäre Endpunkte:** iDFS einschließlich zweites primäres Nicht-Mammakarzinom, DFS, OS, DRFI, Sicherheit und QoL
- **Stratifikationsfaktoren:** Klinisches Stadium bei der Vorstellung (inoperabel vs operabel), HR-Status, präoperative HER2-Therapie, pathologischer Lymphknotenstatus nach präoperativer Therapie

KATHERINE

2. OS-Interimsanalyse*



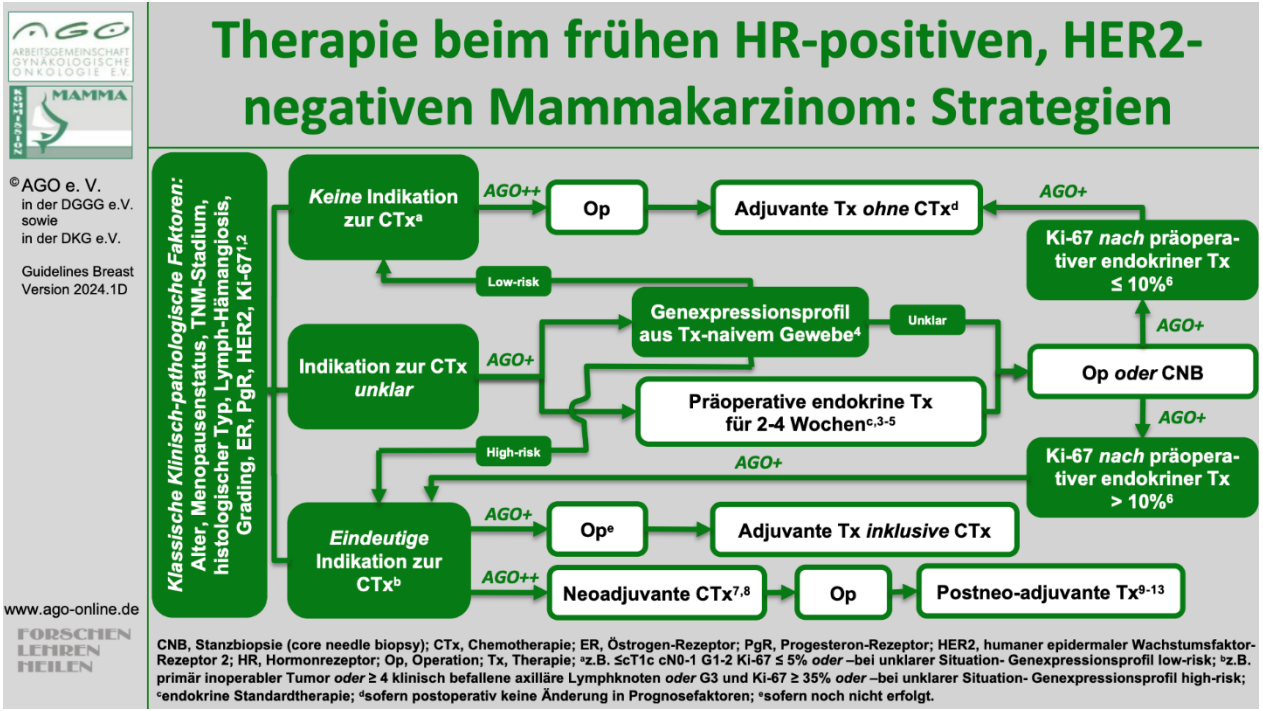
T1-DM1 verringerte das Sterberisiko signifikant um 34%

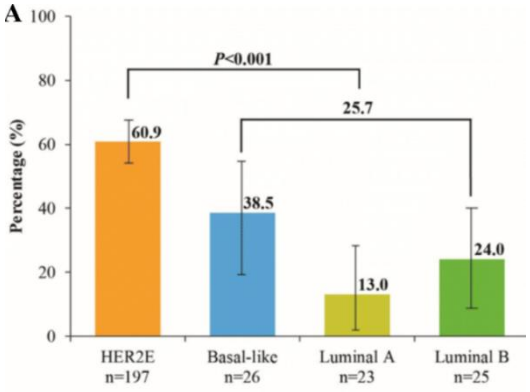
*Medianer Follow-Up: 8,4 Jahre (101 Monate).
T-DM1: Trastuzumab Emtansin.

Loibl et al. | 2023 SABCS | GS03-12

HR+/HER2-

HR+/HER2-





Swain et al. Breast Cancer Research and Treatment volume 178, pages 389–399 (2019)

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HR+/HER2-

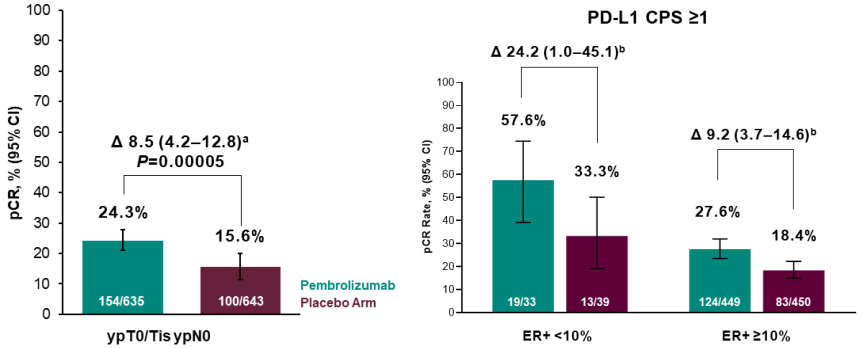
KN-756

R → Pembrolizumab
R → Placebo

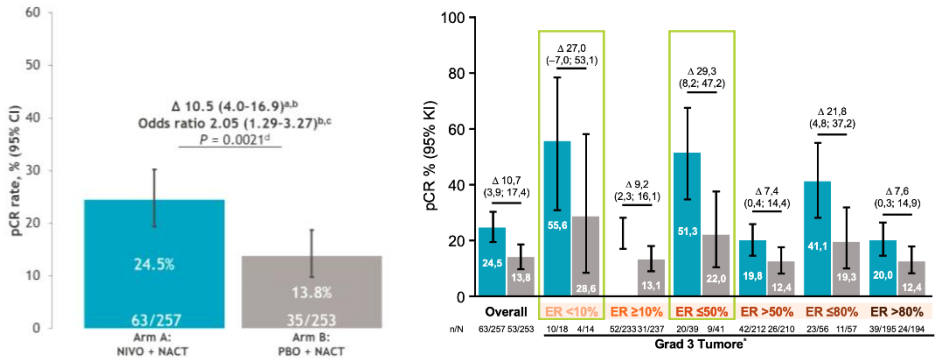
Pacli weekly->Anthrazylkin

Checkmate-7FL

R → Nivolumab
R → Placebo



F. Cardoso. KN-756, ESMO2023



Checkmate7FL, Loi S, ESMO2023

Welche Patientin hat trotz non-pCR einen Ereignis-freien Verlauf?

Welche Patientin erleidet trotz pCR ein Rezidiv/Metastasierung?

npj | breast cancer

www.nature.com/npjbcancer

OS, TNBC

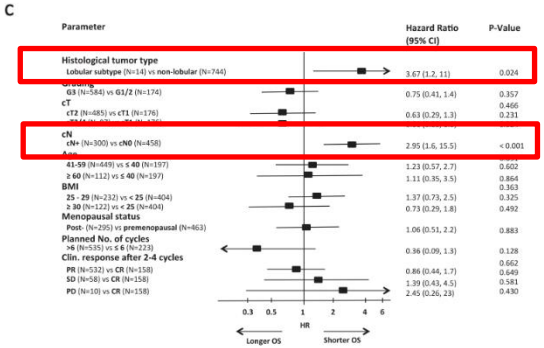


Fig. 2 Multivariate Cox regression models for disease-free survival (a), distant disease-free survival (b) and overall survival (c) in TNBC cohort. Error bars represent the 95%CI. HR hazard ratio, CI confidence interval, HER2 human epidermal growth factor receptor 2, TNBC triple-negative breast cancer.

ARTICLE OPEN

Check for updates

Identifying breast cancer patients at risk of relapse despite pathological complete response after neoadjuvant therapy

Jens Huober[1,2,18], Marion van Mackelenbergh[3,18✉], Andreas Schneeweiss[4], Fenja Seither[5], Jens-Uwe Blohmer[6], Carsten Denkert[7], Hans Tesch[8], Claus Hanusch[9], Christoph Salat[10], Kerstin Rhiem[11], Christine Solbach[12], Peter A. Fasching[13], Christian Jackisch[14], Mattea Reinisch[15], Bianca Lederer[5], Keyur Mehta[5], Theresa Link[16], Valentina Nekljudova[5], Sibylle Loibl[5✉] and Michael Untch[17]

OS, Her2

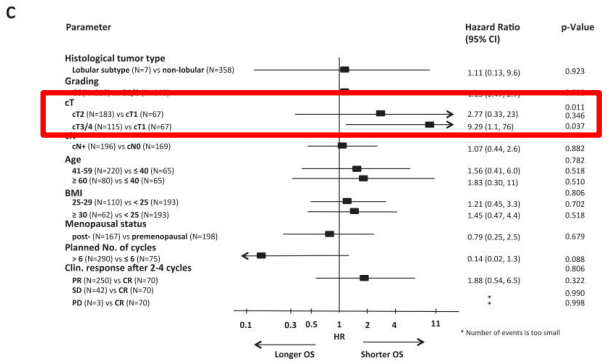


Fig. 3 Multivariate Cox regression models for disease-free survival (a), distant disease-free survival (b) and overall survival (c) in HER2 + / HR- cohort. Error bars represent the 95%CI. HR hazard ratio, CI confidence interval, HER2 human epidermal growth factor receptor 2, TNBC triple-negative breast cancer.

Huober et al. npj Breast Cancer (2023) 9:23

Vielen Dank für Ihre Aufmerksamkeit!

22. ASM
FRANKFURT /MAIN

...it mattered later

A Patient Turned Doctor`s Perspective on Fertility Loss

Dr. Magaret Cupit-Link

JCO Cancer Stories- The Art of Oncology

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