

Grundsätze der neoadjuvanten Therapie und Updates 2026

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HOCH Health Ostschweiz

Brustzentrum Kantonsspital St.Gallen



Neoadjuvante systemische Chemotherapie – Klinischer Benefit

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in der DGGG e.V.
sowie
in der DKG e.V.

Guidelines Breast
Version 2025.1D

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**FORSCHEN
LEHREN
HEILEN**

	Oxford	
	LoE	GR
▪ Ermöglicht eine Prognoseverbesserung durch Individualisierung der neoadjuvanten und post-neoadjuvanten Behandlung	1b	A
▪ Überleben ist gleich nach neoadjuvanter (präoperativer, primärer) und adjuvanter systemischer Therapie (bei gleichem Regime und gleicher Zyklenzahl, wenn die postneoadjuvante Therapie nicht anhand des pathologischen Ansprechens stratifiziert wird)	1a	A
▪ Pathologische Komplettremission ist mit einem besseren Überleben assoziiert	1b	A
▪ Der RCB Score und die RCB Klasse sind subtypen-unabhängige Prognosefaktoren	2a	B
▪ Kann Operabilität bei primär inoperablen Tumoren erreichen	1b	A
▪ Verbessert die Optionen für eine brusterhaltende Operation	1b	A
▪ Senkt die Rate an axillären Lymphonodektomien	2b	B
▪ Erlaubt Individualisierung der Therapie nach dem Interims-Ansprechen	1b	B

162. In a woman eligible to breast conservative surgery should neo-adjuvant chemotherapy and anti-HER2 therapy be the preferred option for **HER2-positive EBC** patients in stage II-III?

Yes
94,1%

168. In a woman eligible to breast conservative surgery should neo-adjuvant chemotherapy be a preferred option for **TN EBC** patients?

Yes
92,5%

If chemotherapy is indicated
systemic treatment before surgery (neoadjuvant) should be preferred



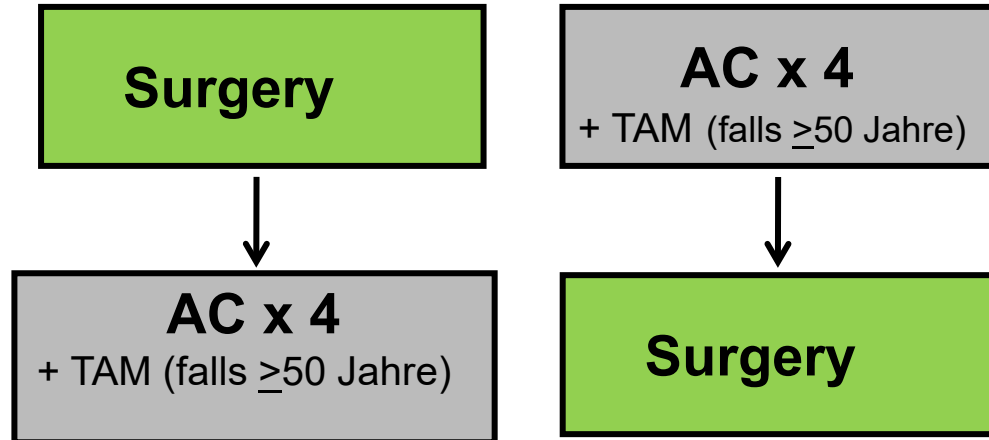
NSABP B-18

Operables Mammakarzinom

(T1: 28%, T2: 58%, T3: 13%; N0: 74%)

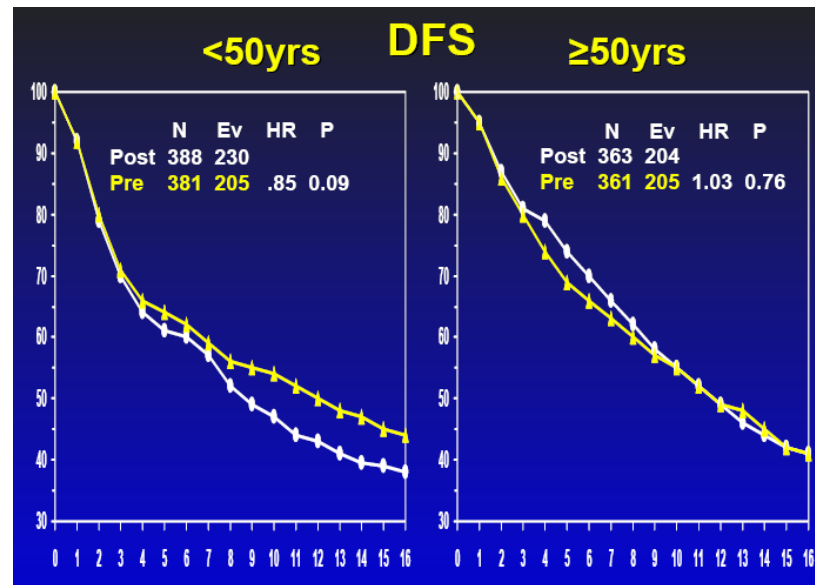
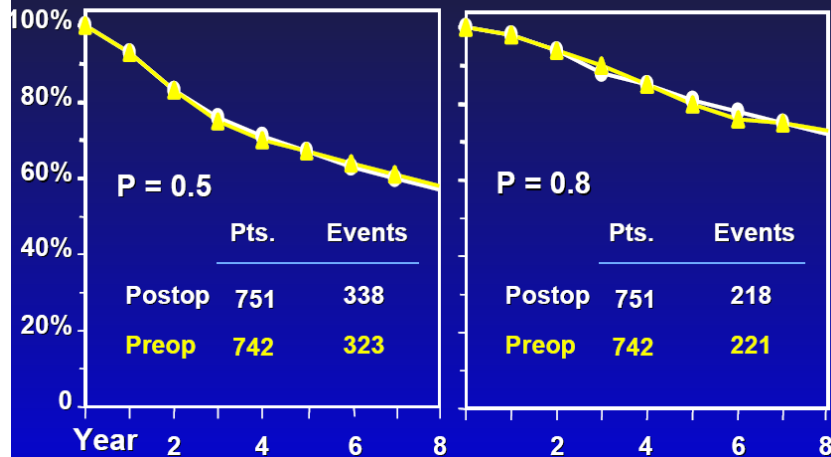
N = 1523

Enrollment: 10/88-4/93



NSABP B-18

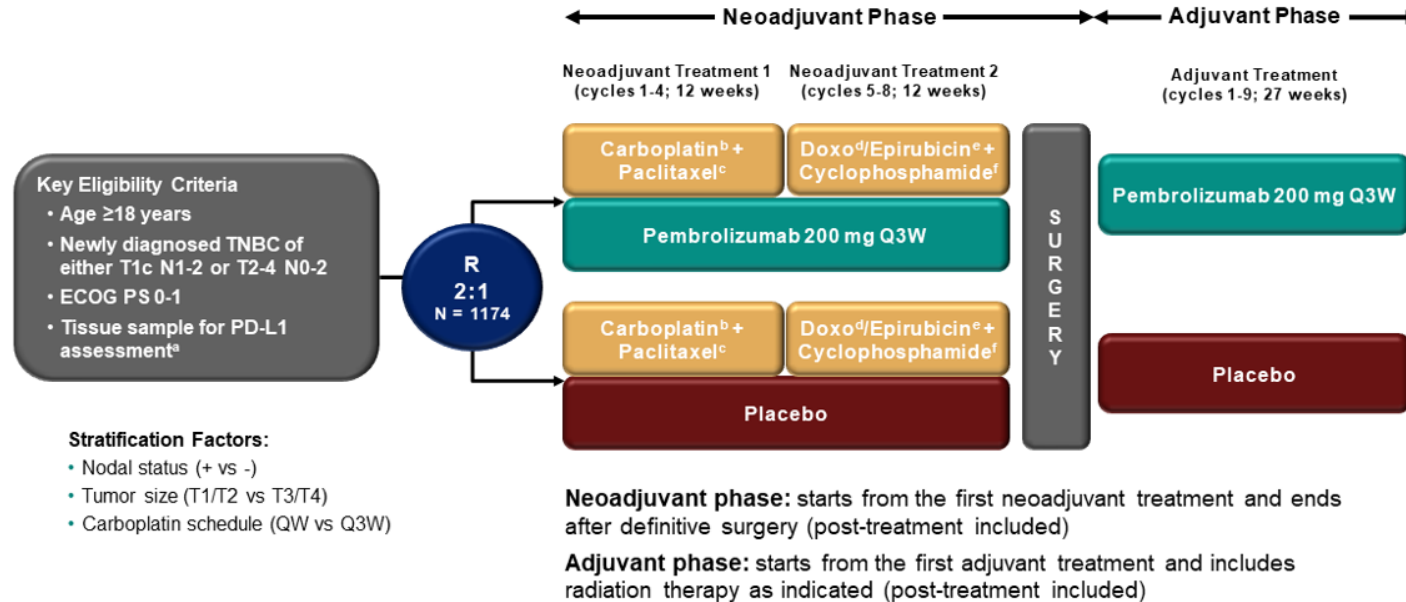
B-18 DFS and Survival



TNBC – Stadium 2 und 3



Keynote 522 – Immuntherapie neoadjuvant und adjuvant

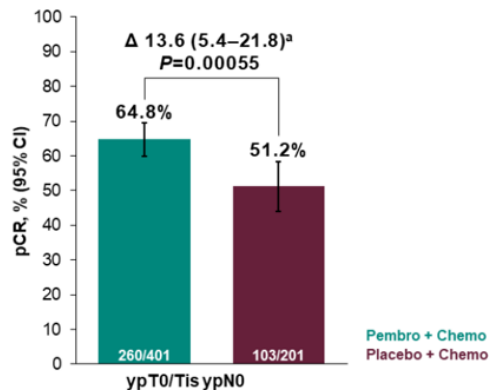


^aMust consist of at least 2 separate tumor cores from the primary tumor. ^bCarboplatin dose was AUC 5 Q3W or AUC 1.5 QW. ^cPaclitaxel dose was 80 mg/m² QW. ^dDoxorubicin dose was 60 mg/m² Q3W.

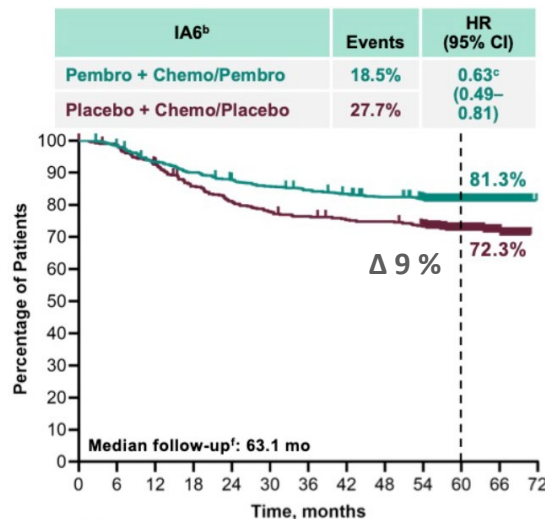
^eEpirubicin dose was 90 mg/m² Q3W. ^fCyclophosphamide dose was 600 mg/m² Q3W.

Keynote – 522 pCR und Outcome

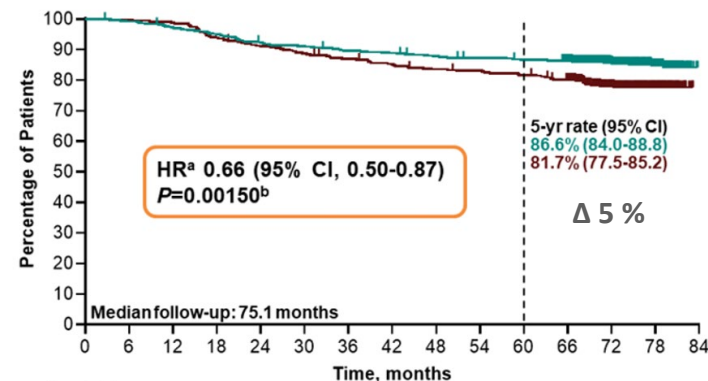
pCR



EFS

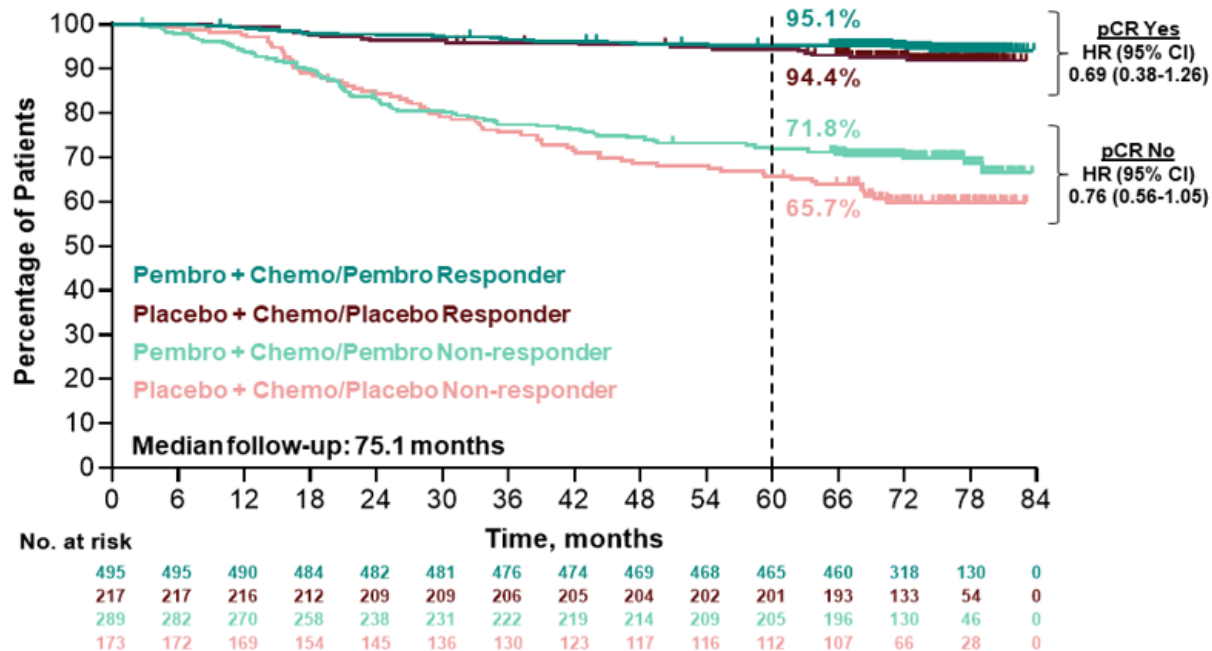


OS

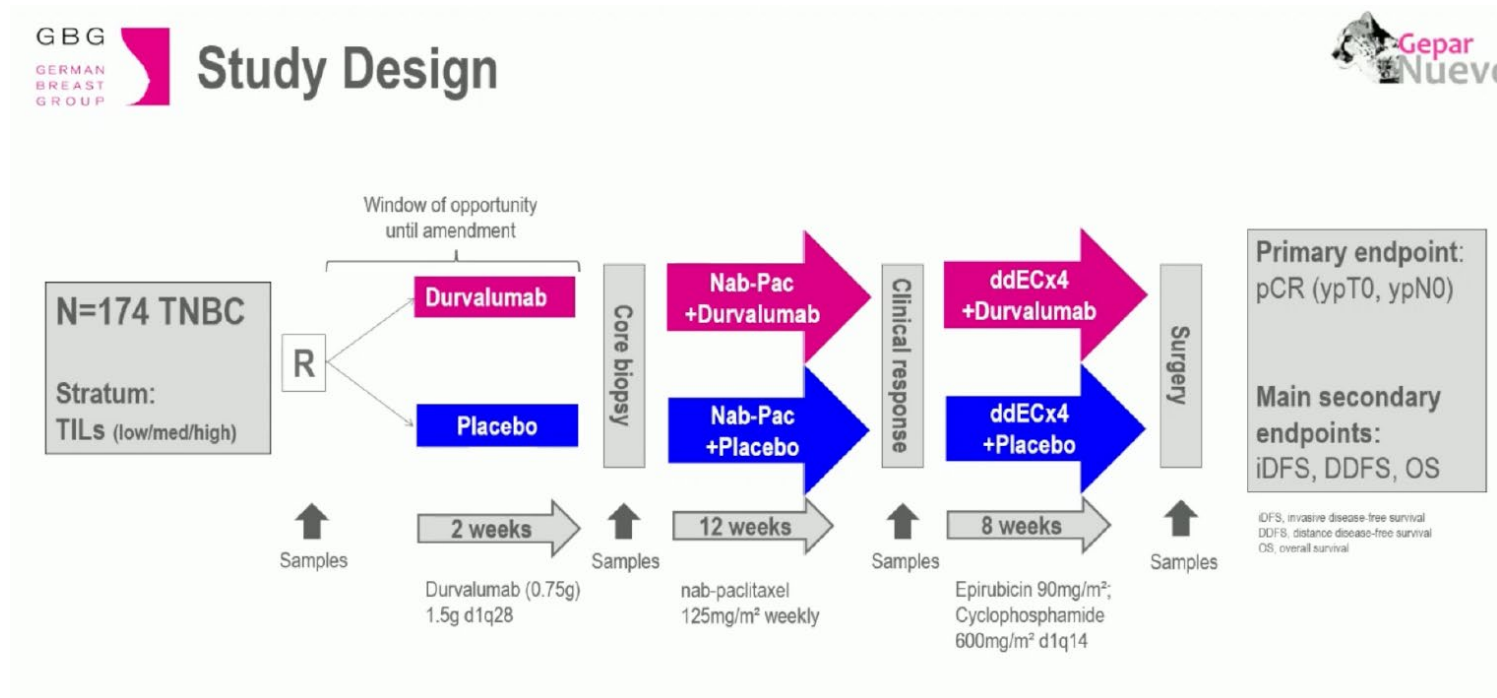


Keynote – 522 Update OS

Overall Survival by Pathologic Complete Response (yp T0/Tis ypN0)



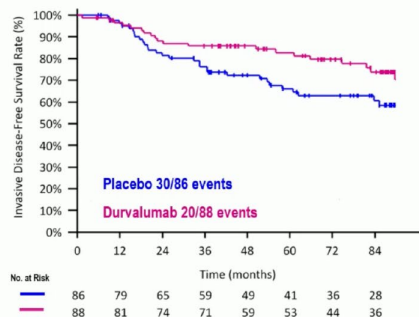
GeparNuevo – Immuntherapie nur neoadjuvant



GeparNuevo - Outcome

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Updated Results: iDFS

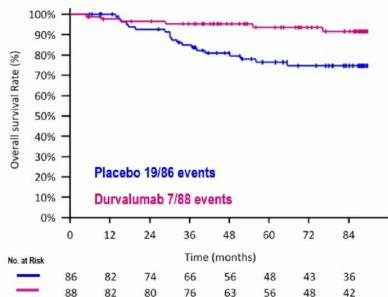


Median follow-up 86.4 (range 4.9-103) months

	Placebo	Durvalumab
6-year iDFS (95% CI)	62.8% (50.7%, 72.8%)	79.6% (68.7%, 87.1%)
7-year iDFS (95% CI)	60.7% (48.2%, 71.0%)	73.7% (61.4%, 82.6%)
HR 0.56 (0.32-0.99) Log-rank p=0.043		

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7-year Overall Survival

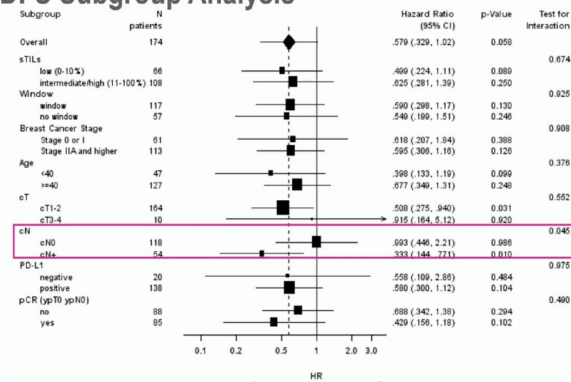


Median follow-up 86.4 (range 4.9-103) months

	Placebo	Durvalumab
6-year iDFS (95% CI)	74.7% (63.0%, 83.1%)	93.6% (85.2%, 97.3%)
7-year iDFS (95% CI)	74.7% (63.0%, 83.1%)	91.6% (81.8%, 96.2%)
HR 0.33 (0.14-0.79) Log-rank p=0.009		

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iDFS Subgroup Analysis



Sibylle Lohr

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longer iDFS with Durvalumab
longer iDFS with Placebo

AGO-B
BREAST STUDY GROUP

ESMO congress

Loibl S et al ESMO 2025

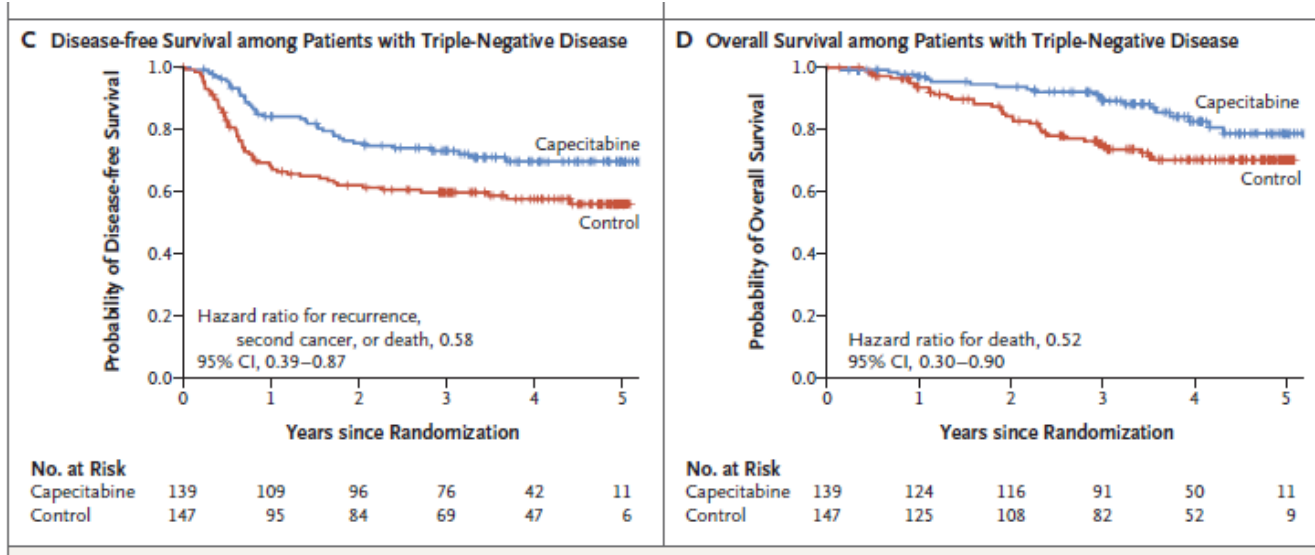
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Create X- Studie Capecitabine vs nichts postneoadjuvant

Wenn keine pCR – TNBC



69.8% vs. 56.1%
(Δ 13.7%)

78.8% vs 70.3%
(Δ 8.5%)

Nach Keynote – keine pCR



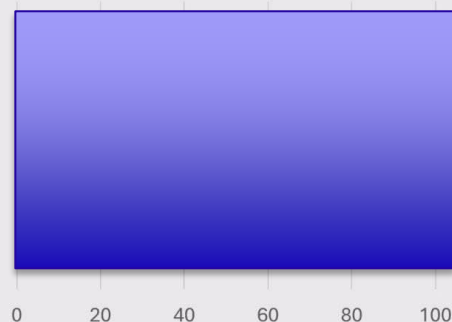
19TH ST.GALLEN INTERNATIONAL BREAST CANCER CONFERENCE 2025

12 – 15 March 2025, Vienna / Austria

submitted by
a delegate

You are treating a patient with stage 2 TNBC. She received neoadjuvant TCb/AC/pembrolizumab (ala KN522) with a good clinical response, but was found at surgery to have residual disease constituting less than 1 cm tumor in the breast with negative lymph nodes. You would recommend which of the following in adjuvant therapy?

- Ongoing pembrolizumab
- Ongoing pembrolizumab and capecitabine
- Capecitabine alone



Total votes: 66

64



Harold J. Burstein
USA

Nach Keynote – keine pCR

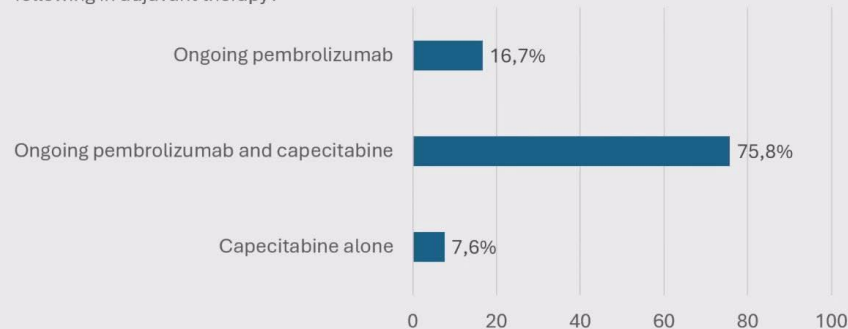


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Total votes: 66

64



Harold J. Burstein
USA

TNBC – Neue postneoadjuvante Studien

OptimICE-PCR

(N=1295)

OPT-PEMBRO

(N=2639)

(2'597'427 CHF saved /year/60 Pat)

pCR

nach

CHT-Pembro

S
U
R
G
E
R
Y

Pembro

OBSERVATION

Ascent 05

Keine pCR

nach

CHT ± Immuntherapie

S
U
R
G
E
R
Y

8 x SG + Pembro

8 x Pembro
8 x Pembro + Cap

Immuntherapie – Low dose Pembro

Methods

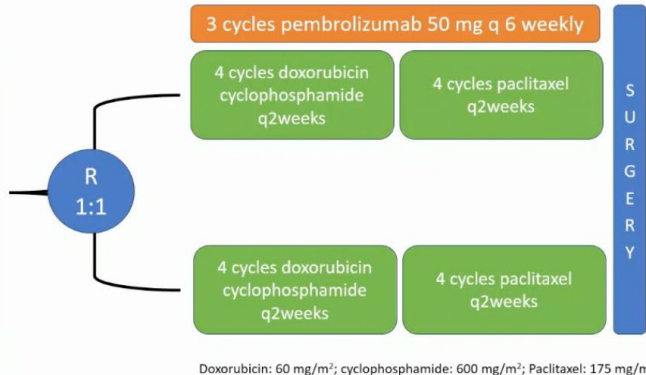
PLANeT Trial: CTRI/2024/01/062088

Pembrolizumab Low-dose in Addition to Neoadjuvant chemotherapy in Triple negative breast cancer

Participants (n=160)

- Stage II-III TNBC
- No access to pembrolizumab
- ECOG PS 0-1
- Age ≥ 18 years
- No active autoimmune condition
- Not on systemic steroids
- No prior treatment with ICI

Stratification factor
Nodal involvement (yes v no)

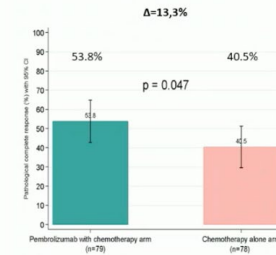


Primary Endpoint
Complete pathological response (ypT0N0)

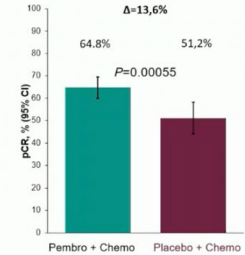
Secondary Endpoints

- IDFS
- RCB
- QOL
- Safety

PLANeT: Modified Intention-to-treat, N=157



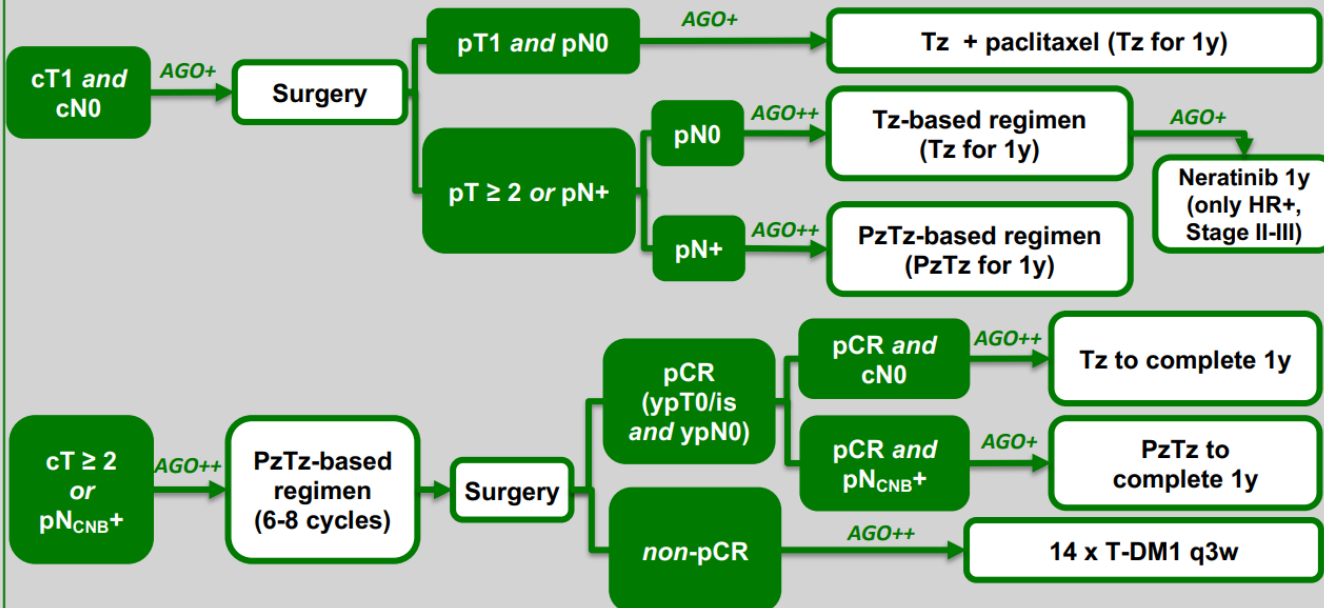
KN-522: Definitive pCR analysis, N=602



A Arora et al Ann Oncol 2025

HER2+ Stadium 2 und 3

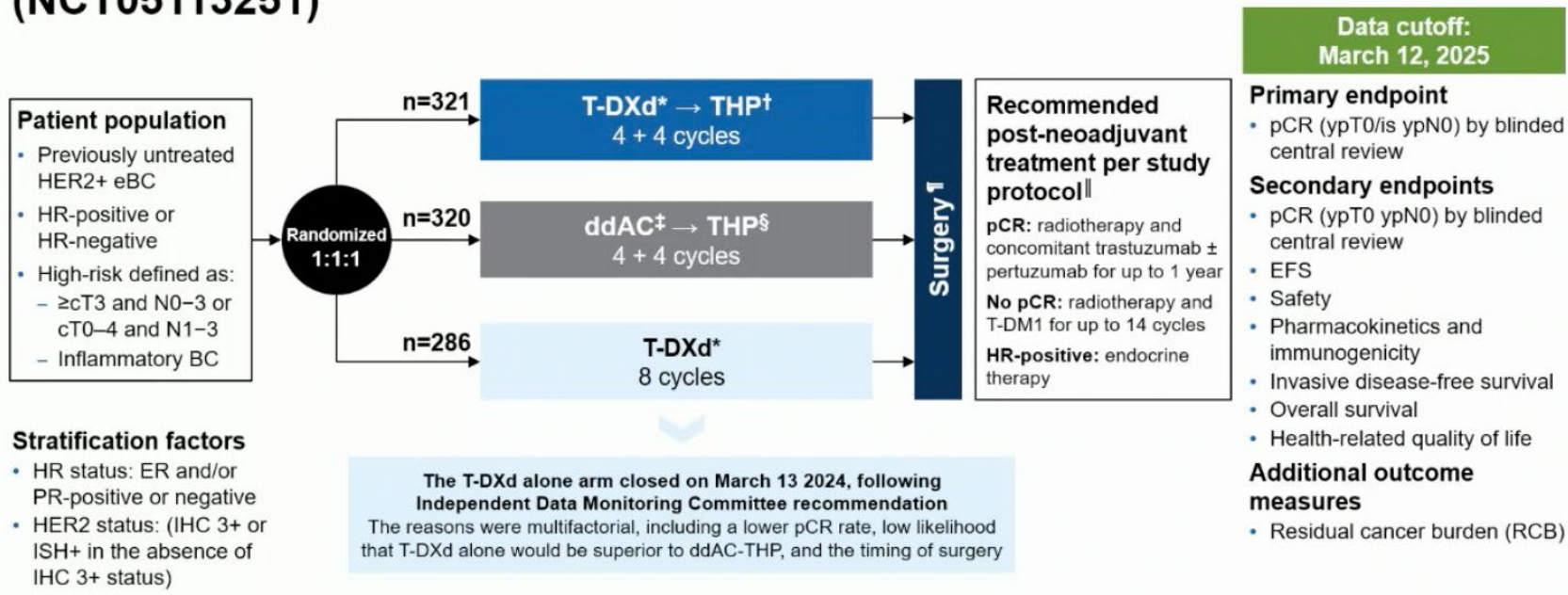
Therapy of HER2-positive Early Breast Cancer



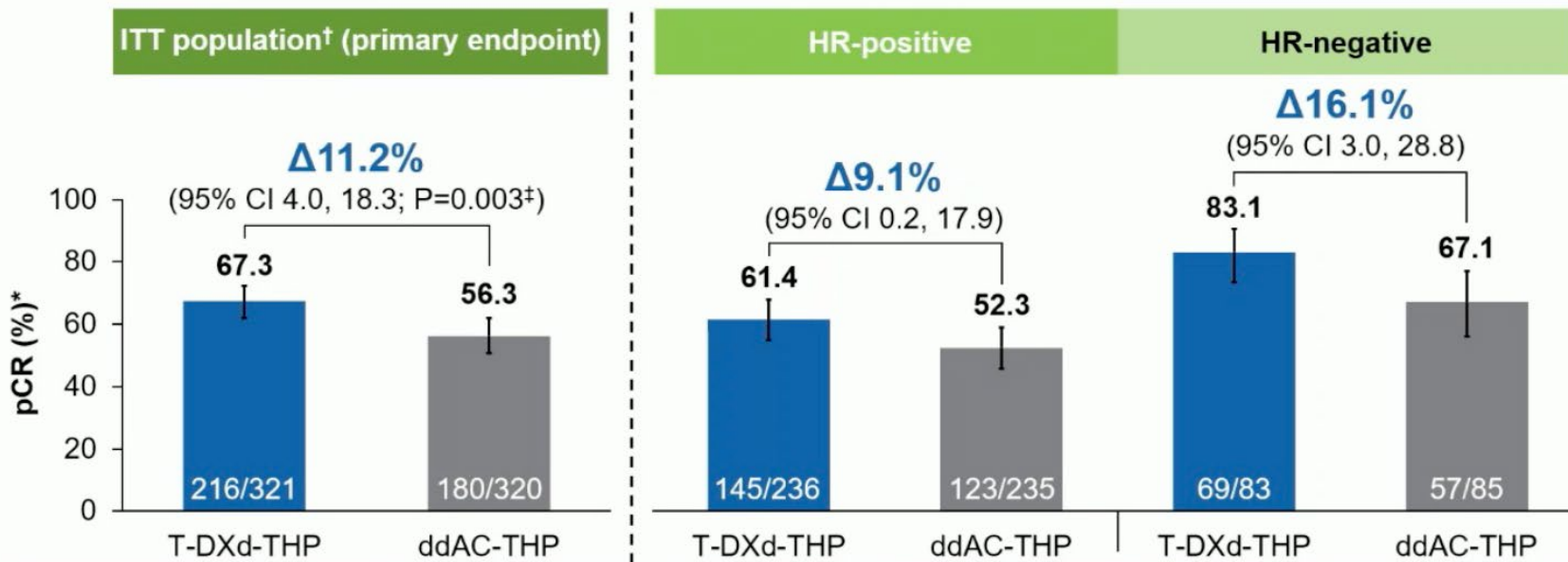
CNB, core needle biopsy; HR, hormone receptor; pCR, pathological complete response; Pz, Pertuzumab; q3w, every 3 weeks; T-DM1, Trastuzumab emtansine; Tz, Trastuzumab; y, year; if HR+ additional adjuvant endocrine therapy.

DESTINY-Breast11 study design

A randomized, global, multicenter, open-label, Phase 3 study
(NCT05113251)



pCR (ypT0/is ypN0): primary endpoint



Neoadjuvant T-DXd-THP demonstrated a statistically significant and clinically meaningful improvement in pCR vs ddAC-THP
Improvement was observed in both the HR-positive and HR-negative subgroups

Platin beim HER2 + MACA

neoCARHP Study Design (NCT04858529)

Aged ≥ 18 , untreated, staged II-III, HER2-positive breast cancer

Stratification

- Hormone status
- Nodal status

R (1:1)
N=774

THP×6 Q3W (n=387)
(Investigator-selected taxane* + Trastuzumab IV 6 mg/kg, loading dose 8 mg/kg + Pertuzumab IV 420 mg, loading dose 840mg)

TCbHP×6 Q3W (n=387)
(Investigator-selected taxane* + Carboplatin IV AUC 6 mg/mL/min + Trastuzumab IV 6 mg/kg, loading dose 8 mg/kg + Pertuzumab IV 420 mg, loading dose 840mg)

* Docetaxel, Paclitaxel or Nab-paclitaxel

Surgery

- Primary endpoint: pCR (ypT0/is ypN0)
- Secondary endpoints: Safety, clinical response during neoadjuvant therapy, EFS, DFS, OS

	THP (n=382)	TCbHP (n=384)
Age (median [IQR], years)	52 (45-58)	51 (44-56)
Menopausal status, n (%)		
Premenopausal	191 (50.0%)	200 (52.1%)
Postmenopausal	191 (50.0%)	184 (47.9%)
T stage, n (%)		
T1-2	311 (81.4%)	302 (78.6%)
T3-4	71 (18.6%)	82 (21.4%)
Nodal status, n (%)		
Negative	137 (35.9%)	138 (35.9%)
Positive	245 (64.1%)	246 (64.1%)
Disease stage, n (%)		
Stage II	294 (77.0%)	275 (71.6%)
Stage III	88 (23.0%)	109 (28.4%)
Taxane therapy, n (%)		
Nab-paclitaxel	170 (44.5%)	171 (44.5%)
Docetaxel	137 (35.9%)	141 (36.7%)
Paclitaxel	75 (19.6%)	72 (18.8%)

THP was considered non-inferior if the lower bound of the two-sided 95% CI (Newcombe–Wilson score method) for the pCR difference exceeded the prespecified -10% non-inferiority margin.

Platin beim HER2 + MACA

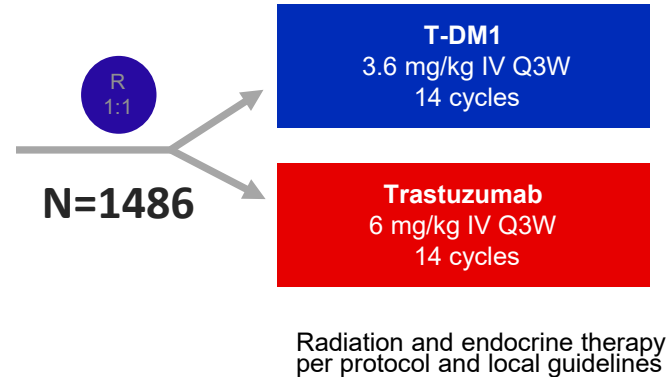
Trial	pCR Overall	pCR in ER-positive	pCR in ER-negative
neoCARHP-TCHPx6	66%	59%	78%
neoCARHP-THPx6	64%	56%	78%

Safety:

- Increased grade 3/4 adverse events in TCHP arm: neutropenia (16.4% vs 6.8%), febrile neutropenia (2.6% vs. 1.3%), thrombocytopenia (4.2% vs. 0.3%), anemia (6.6% vs. 2.1%)
- Higher all grade nausea, vomiting, increased creatinine

Katherine Studie – Postneoadjuvante Therapie

- **cT1-4/N0-3/M0 at presentation** (cT1a-b/N0 excluded)
- Centrally confirmed HER2-positive breast cancer
- **Neoadjuvant therapy** must have consisted of
 - **Minimum von 6 Zyklen Chemotherapie**
 - Minimum von 9 Wochen ein Taxan
 - Anthracycline und Alkylantien waren erlaubt
 - All chemotherapy prior to surgery
 - **Minimum von 9 Wochen Trastuzumab**
 - Second HER2-targeted agent allowed
- **Invasive Residuen in der Mamma oder axillären LK**
- Randomization within 12 weeks of surgery



Characteristics:

- HR pos
72%
- Vorthherapie mit Trastuzumab / Pertuzumab
18%
- ypT1a, ypT1b or ypT1mic and ypN0
21%

v Minckwitz G al. NEJM 2019
Geyer C et al NEJM 2025

Katherine Studie - Outcome

	T-DM1	Trastuzumab	Δ	HR	P-Wert
3 y-IDFS (%)	88.3	77	11	0.5	$P<0.0001$
7 y-IDFS (%)	80.8	67.1	14	0.54	$P<0.0001$
3 y-OS (%)	94.3	92.5	1.8	0.7	$P=0.0848$
7 y- OS (%)	89.1	84.4	5	0.66	$P=0.0027$

Therapieeffekt in allen Subgruppen:
 - Pertuzumab-Vorthherapie
 - Residual disease < 1cm and ypN0

!

v Minckwitz G al. NEJM 2019
 Geyer C et al NEJM 2025

DESTINY-Breast05 study design

A global, multicenter, randomized, open-label, phase 3 trial (NCT04622319)

Key Eligibility Criteria

- Residual invasive disease in the breast and/or axillary lymph nodes after neoadjuvant chemotherapy with HER2-directed therapy (NAT)^a
- High-risk defined as presentation prior to NAT with:
 - Inoperable eBC (cT4,N0-3,M0 or cT1-3,N2-3,M0) OR
 - Operable eBC (cT1-3,N0-1,M0) with axillary node-positive disease (ypN1-3) after NAT
- Centrally confirmed HER2+ (IHC 3+ or ISH+) eBC
- ECOG PS 0 or 1

Stratification factors

- Extent of disease at presentation (inoperable, operable)
- HER2-targeted NAT (single, dual)
- Hormone receptor status (positive, negative)
- Post-NAT pathologic nodal status (positive, negative)

N ≅ 1600

R
1:1

T-DXd 5.4 mg/kg IV Q3W
for 14 cycles
N ≅ 800

T-DM1 3.6 mg/kg IV Q3W
for 14 cycles
N ≅ 800

40-day safety follow-up

Primary endpoint

- IDFS

Key secondary endpoint

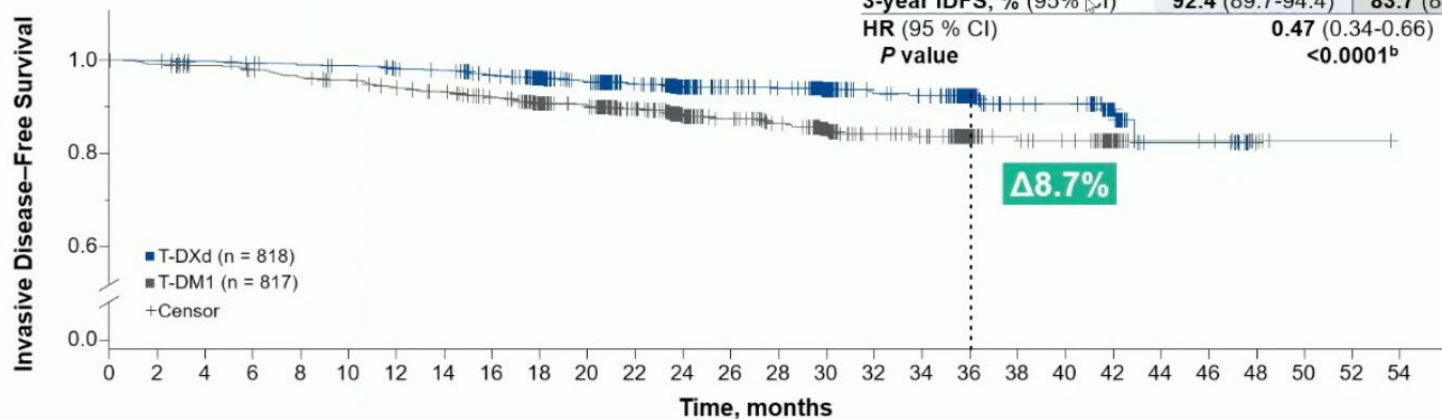
- DFS

Other secondary endpoints

- OS
- BMFI
- DRFI
- Safety

^aNAT is defined as ≥16 weeks' NAT with ≥9 weeks trastuzumab ± pertuzumab and ≥9 weeks taxane-based chemotherapy.

Primary endpoint: IDFS^a



	T-DXd n = 818	T-DM1 n = 817
Patients with events, n (%)	51 (6.2)	102 (12.5)
3-year IDFS, % (95% CI)	92.4 (89.7-94.4)	83.7 (80.2-86.7)
HR (95 % CI)	0.47 (0.34-0.66)	
P value	<0.0001 ^b	

Number at Risk:

T-DXd	818	788	781	776	771	768	758	753	731	684	634	544	440	380	370	275	218	212	129	92	90	46	14	14	0	0	0	0
T-DM1	817	781	769	760	745	734	719	708	687	632	599	527	417	355	337	233	186	177	120	84	79	38	14	13	4	1	1	0

53% reduction in the risk of invasive disease recurrence or death for T-DXd compared with T-DM1

Postneoadjuvante Studien HER2-Positiv nach neoadjuvanter Therapie

DESTINY-Breast05

T-DM1 vs T-DXd

Astefania trial

T-DM1 + Placebo vs T-DM1 + Atezolizumab

CompassHER2 RD Trial

T-DM1 vs T-DM1 + Tucatinib

Zusammenfassung

TNBC Stadium 2 und 3:

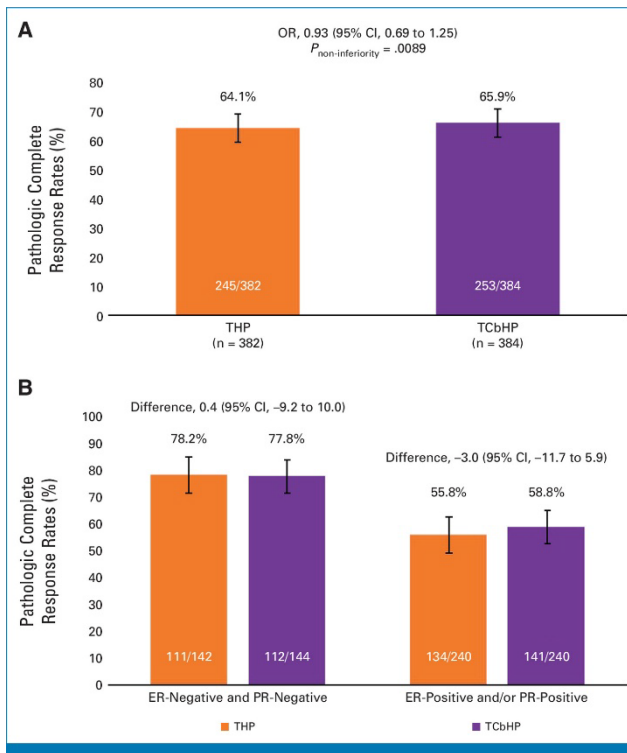
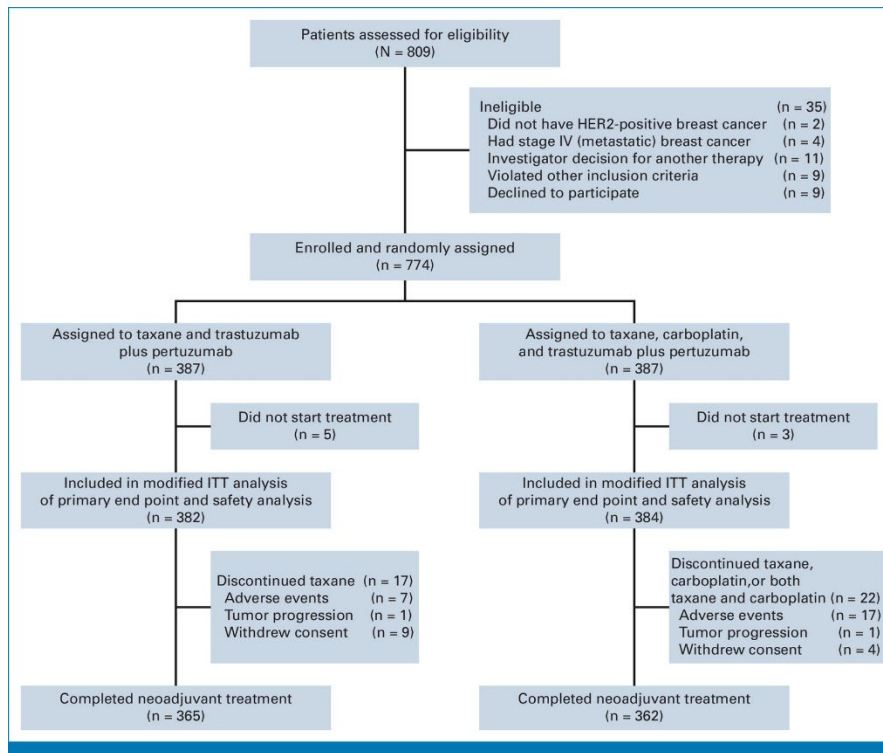
- Standard Regime: Chemo-Immuntherapie (Keynote 522 Schema)
- Adjuvant:
 - Wertigkeit der adjuvanten Immuntherapie?
 - Rolle der ADCs ?

HER2+ Stadium 2 und 3:

- Standard: anti-HER2 Therapie mit Trastuzumab und Pertuzumab
- Chemo-Backbone?
 - Anthrazyklin-Taxan
 - Platin-Taxan
 - Taxan
 - T-DXd - Taxan
- Adjuvant
T-DM1 und T-DXD, je nach Risikoprofil



HER2+ neoCARHP



HER2+ TRAIN2

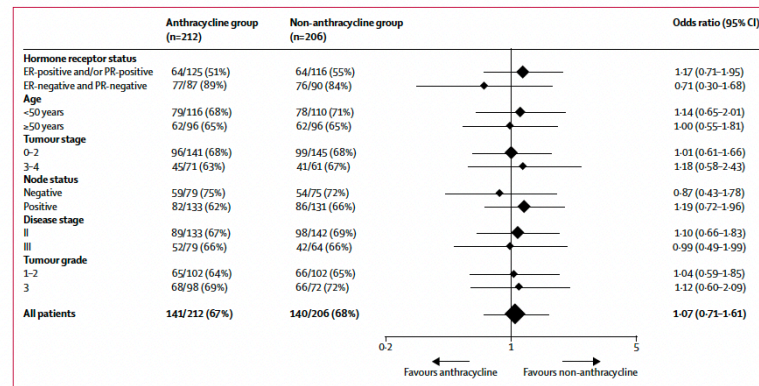
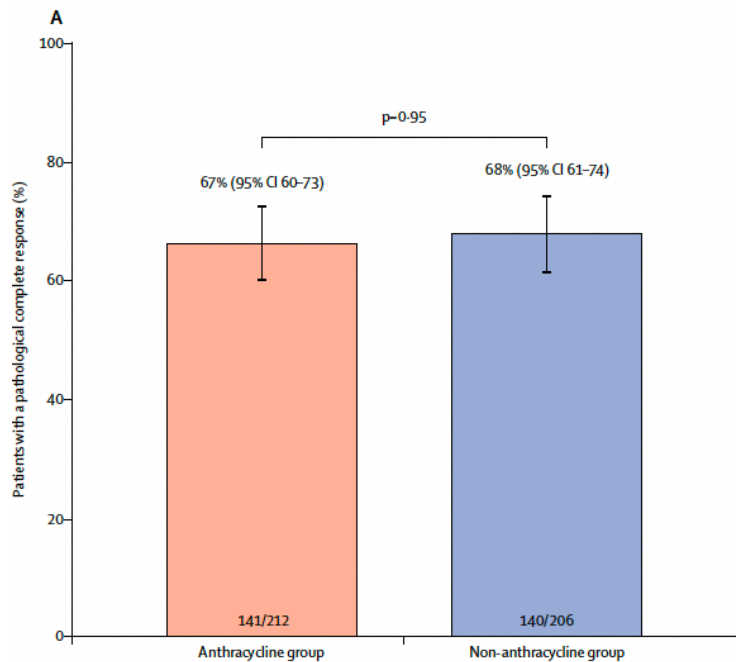


Figure 3: Pathological complete responses by subgroup

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=estrogen receptor, PR=progesterone receptor.

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

OS, TNBC

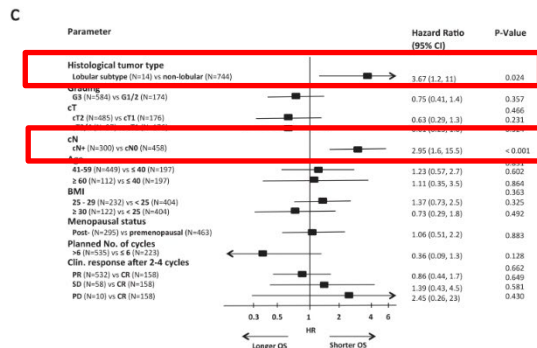


Fig. 2 Multivariate Cox regression models for disease-free survival (a), distant disease-free survival (b) and overall survival (c) in TNBC cohort. Error bars represent the 95%CI. HR hazard ratio, CI confidence interval, HER2 human epidermal growth factor receptor 2, TNBC triple-negative breast cancer.

ARTICLE OPEN

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

Jens Huober^{1,2,18}, Marion van Mackelenbergh^{3,18,52}, Andreas Schneeweiss⁴, Fenja Seither⁵, Jens-Uwe Blohmer⁶, Carsten Denkert⁷, Hans Tesch⁸, Claus Hanusch⁹, Christoph Salat¹⁰, Kerstin Rhiem¹¹, Christine Solbach¹², Peter A. Fasching¹³, Christian Jackisch¹⁴, Mattea Reinisch¹⁵, Bianca Lederer⁵, Keyur Mehta⁵, Theresa Link¹⁶, Valentina Nekjudova⁵, Sibylle Loibl^{5,52} and Michael Untch¹⁷

OS, Her2

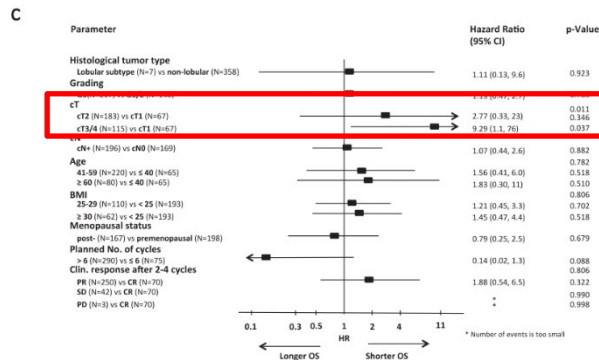


Fig. 3 Multivariate Cox regression models for disease-free survival (a), distant disease-free survival (b) and overall survival (c) in HER2+ / HR-cohort. Error bars represent the 95%CI. HR hazard ratio, CI confidence interval, HER2 human epidermal growth factor receptor 2, TNBC triple-negative breast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



