Aktuelle Standards der (postneo-)adjuvanten systemischen Therapie und Möglichkeiten Response-adaptierter Therapien 2025

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Conflict of Interest

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Honoraries:

Lilly, Novartis, Roche, Pfizer, AstraZeneca, MSD, Abbvie, Gilead, Seagen, Daiichi;

Advisory role:

Lilly, Novartis, Roche, Pfizer, AstraZeneca, MSD, Gilead, Daiichi, Stemline

Travel expenses:

Roche, Daiichi, Gilead

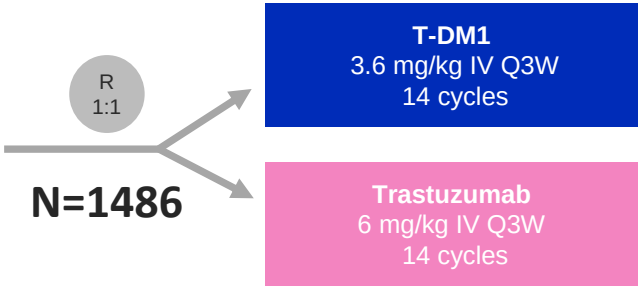
Neoadjuvant Therapie – hohe pCR-Raten mit dualer anti-HER2 Blockade

Study	Therapy -neoadj	pCR* all	pCR HR+	pCR HR-
Neo ALTTO	18 wks **Tra + Lap** 12 wks Paclitaxel **18 Wo**	**46 %**	41 %	61 %
Impassion50	12 wks **Tra + Per** 12 wks AC 12 wks Pac weekly	**63%**	55 %	71 %
GeparSepto	24 wks **Tra + Per** 12 wks NabPac → 12 wks EC **24 Wo**	**69 %**	64 %	81 %

Tra: Trastuzumab, Per: Pertuzumab, Lap: Lapatinib, Pac: Paclitaxel

Katherine Studie – Response getriggerte 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 of 6 cycles of chemotherapy**
    - Minimum of 9 weeks of taxane-based chemotherapy
    - Anthracyclines and alkylating agents permitted
    - All chemotherapy prior to surgery
  - **Minimum of 9 weeks of trastuzumab**
    - Second HER2-targeted agent allowed
- **Invasive residual disease in the breast or axillary lymph nodes**
- Randomization within 12 weeks of surgery



Radiation and endocrine therapy per protocol and local guidelines

Characteristics:

- HR pos
  72%
- Pre-treatment withTrastuzumab / Pertuzumab
  18%
- ypT1a, ypT1b or ypT1mic and ypN0
  21%

v Minckwitz G al. NEJM 2019
Loibl S et al SABCS 2023

Katherine Trial - Resultate

	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-Vortherapie
- Residual disease < 1cm and ypN0

!

v Minckwitz G al. NEJM 2019
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Postneoadjuvante Studien HER2-Positiv nach neoadjuvanter Therapie

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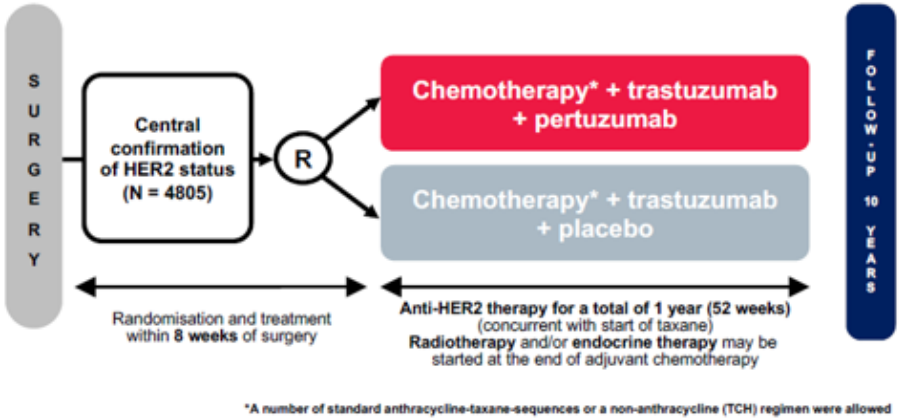
DESTINY-Breast05	T-DM1 vs T-DXd
Astefania trial	T-DM1 + Placebo vs T-DM1 + Atezolizumab
CompassHER2 RD Trial	T-DM1 vs T-DM1 + Tucatinib

Aphinity trial – Design

Key Inclusion criteria:

- HER2-positive
- Node-positive
  - any tumour size except T0
- Node-negative
  - Tumour size >1 cm
  - OR tumours >0.5 and ≤1 cm and at least 1 of:
    - grade 3 OR
    - HR-negative
    - age <35
- Baseline LVEF ≥55%

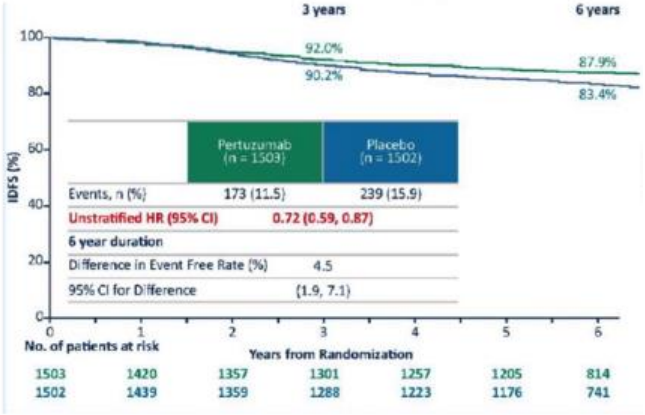


stratified according to nodal status, adjuvant chemotherapy regimen, hormone-receptor status, geographic region, and protocol version.

Piccart M al. J Clin Oncol 2021

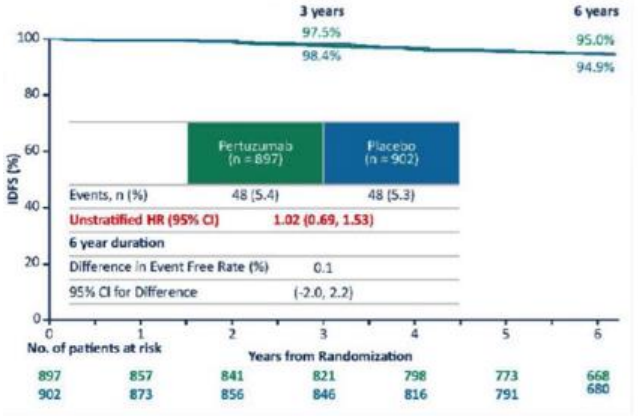
Aphinity trial – iDFS

Node positive



6 y Δ 4,5%

Node negative

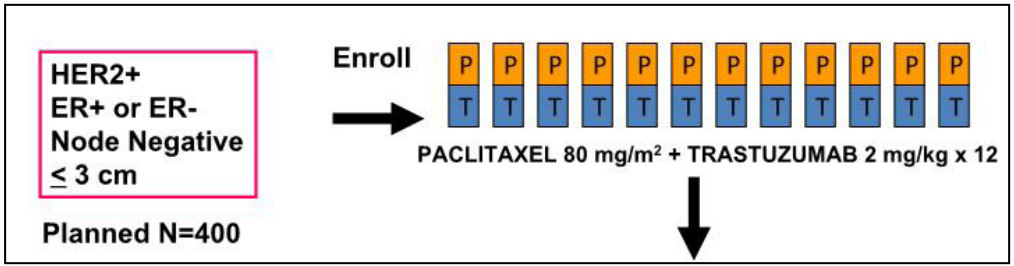


6 y Δ 0,1%

6 J OS 94,8% / 93,3%

Piccart M al. J Clin Oncol 2021

APT-trial Stadium 1 HER2+ BC



Primary tumor	
Size	
T1mic: ≤0.1 cm	9 (2.2)
T1a: >0.1 to ≤0.5 cm	68 (16.7)
T1b: >0.5 to ≤1.0 cm	124 (30.5)
T1c: >1.0 to ≤2.0 cm	169 (41.6)
T2: >2.0 to ≤3.0 cm	36 (8.9)

Tolaney S et al.: N Engl J Med. 2015 :134-41;
J Clin Oncol. 2019: 1868-1875; Lancet Oncol 2023. 273-285

APT-Trial – Results

	Point Est.	95% Conf. Interval	No. of Events
3-yr DFS	98.5%	97.2% to 99.7%	6
5-yr DFS	96.3%	94.4% to 98.2%	14
7-yr DFS	93.3%	90.4% to 96.2%	23
10-yDFS	**91.3%**		**31**

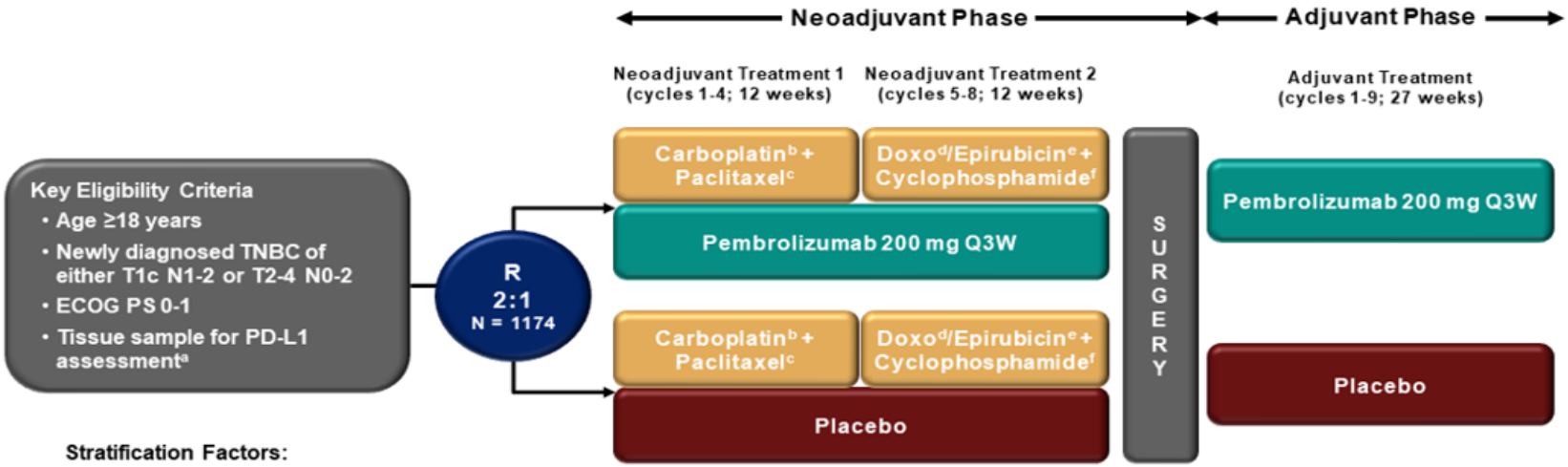
90.6% ER-
91.6% ER+

	Point Est.	95% Conf. Interval	No. of Events
3-yr OS	99.7%	99.2% to >99.9%	1
5-yr OS	98.7%	97.5% to 99.8%	5
7-yr OS	95.0%	92.4% to 97.7%	14
10-y OS	**94.3%**		**19**

BCSS 98.8%

Tolaney S et al.: N Engl J Med. 2015 :134-41; J Clin Oncol. 2019: 1868-1875; Lancet Oncol 2023. 273-285

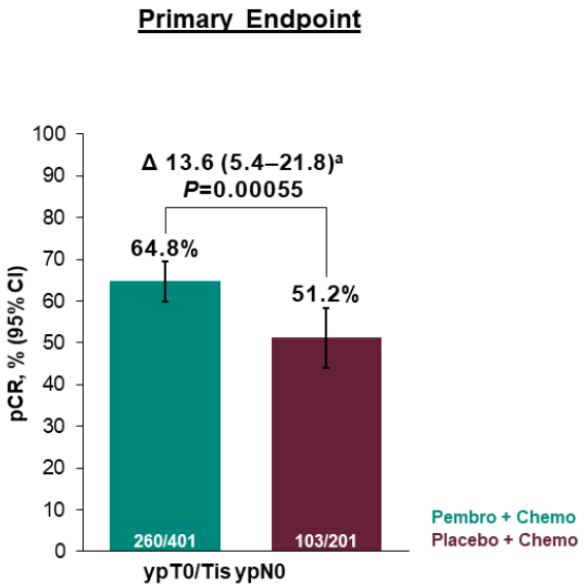
KEYNOTE-522 Study Design (NCT 03036488)



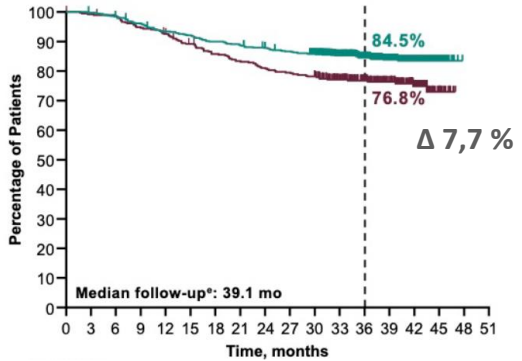
[a]Must consist of at least 2 separate tumor cores from the primary tumor. [b]Carboplatin dose was AUC 5 Q3W or AUC 1.5 QW. [c]Paclitaxel dose was 80 mg/m² QW. [d]Doxorubicin dose was 60 mg/m² Q3W. [e]Epirubicin dose was 90 mg/m² Q3W. [f]Cyclophosphamide dose was 600 mg/m² Q3W.

Keynote – 522 EFS nach 36 und 60 Mo

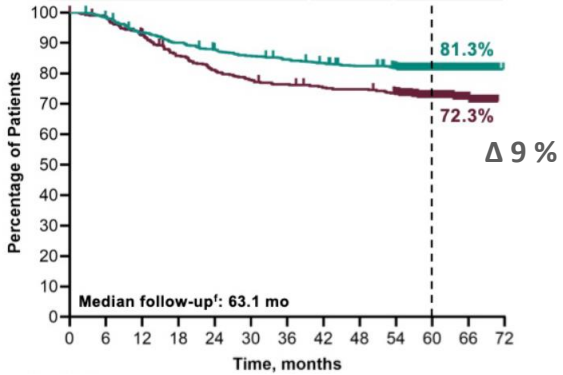
Events zwischen 36-60 Mo
+ 2.8% / + 3,5 %



IA4[a]	Events	HR (95% CI)	P value
Pembro + Chemo/Pembro	15.7%	0.63[c] (0.48–0.82)	0.00031[d]
Placebo + Chemo/Placebo	23.8%		

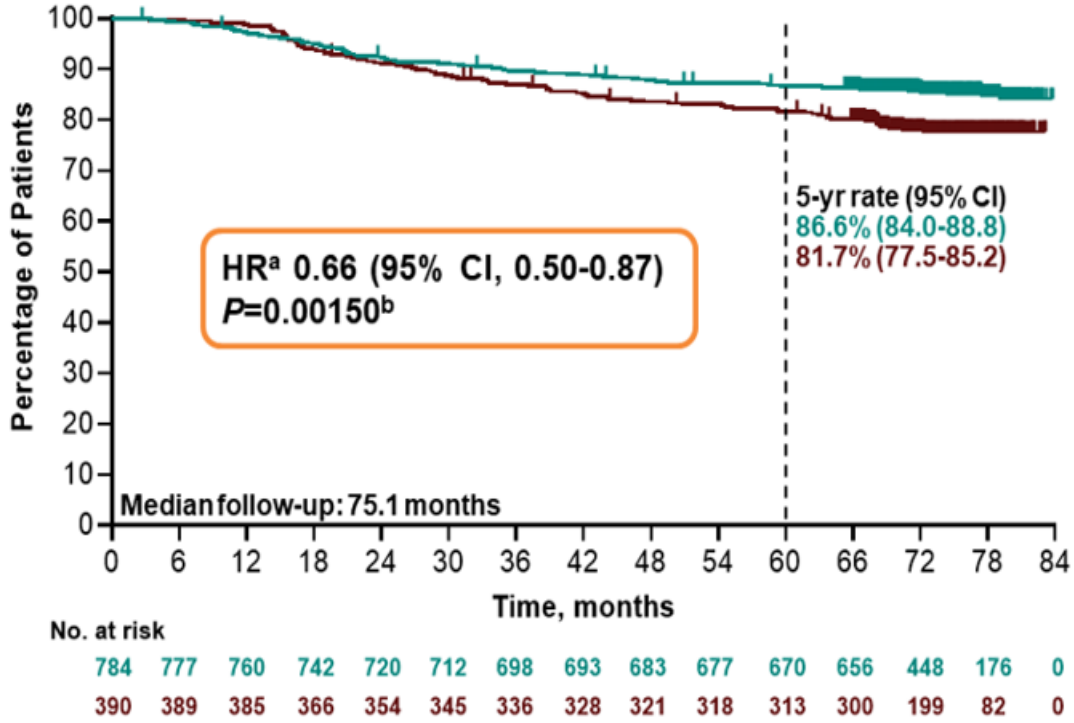


IA6[b]	Events	HR (95% CI)
Pembro + Chemo/Pembro	18.5%	0.63[c] (0.49–0.81)
Placebo + Chemo/Placebo	27.7%	



Schmid P et al. N Engl J Med 2020, Schmid P et al. SABCS 2023

Keynote – 522 Update OS



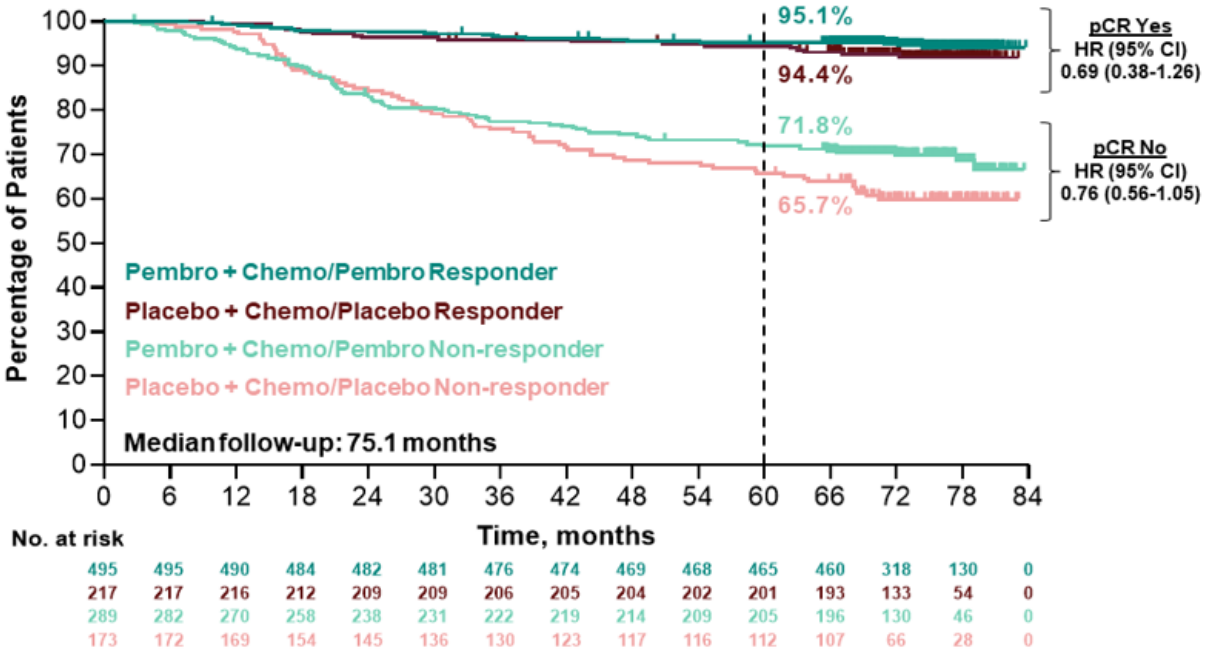
Δ 4.9%

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

J Schmid P et al. N Engl Med 2020, Schmid P et al. NEJM 2024

Keynote – 522 Update OS

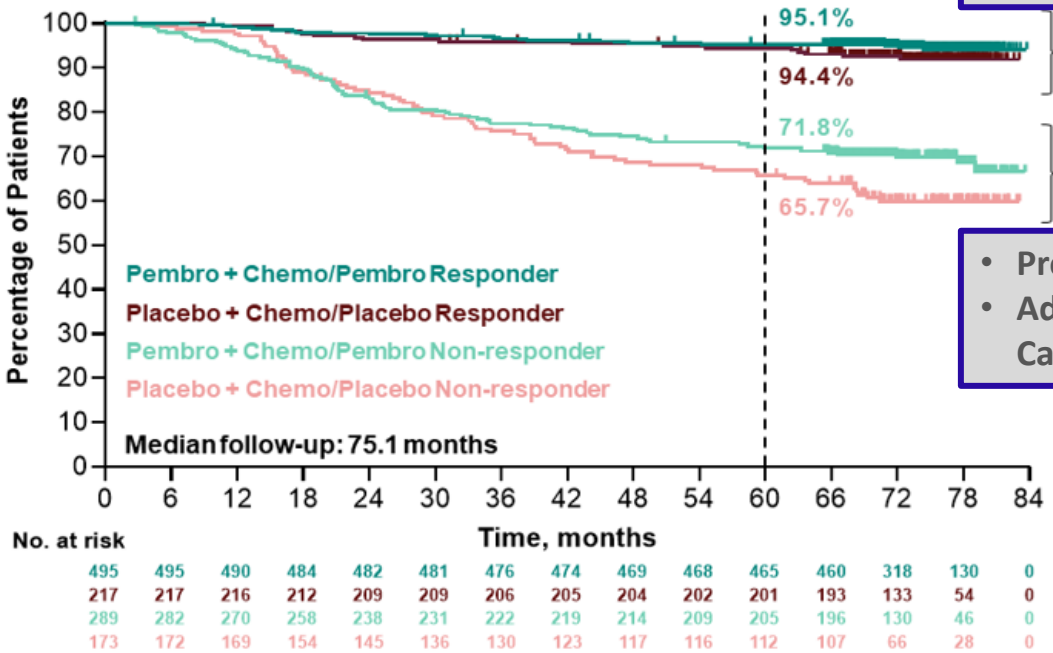
Overall Survival by Pathologic Complete Response (yp T0/Tis ypN0)



Schmid P et al. N Engl J Med 2020, Schmid P et al. NEJM 2024

Keynote – 522 Trial Update

Overall Survival by Pathologic Complete Response

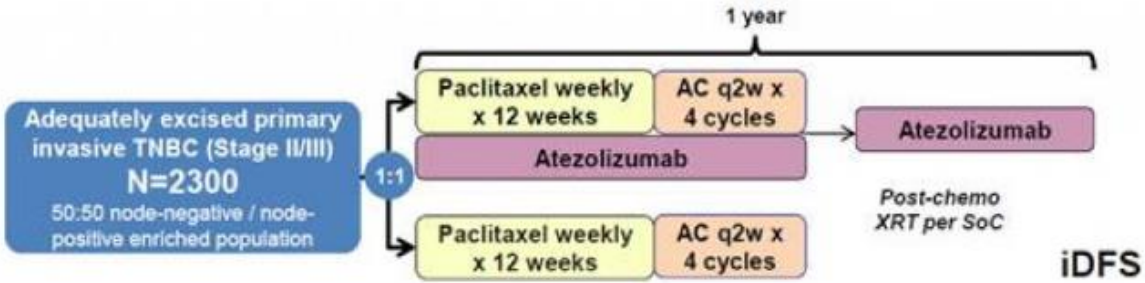


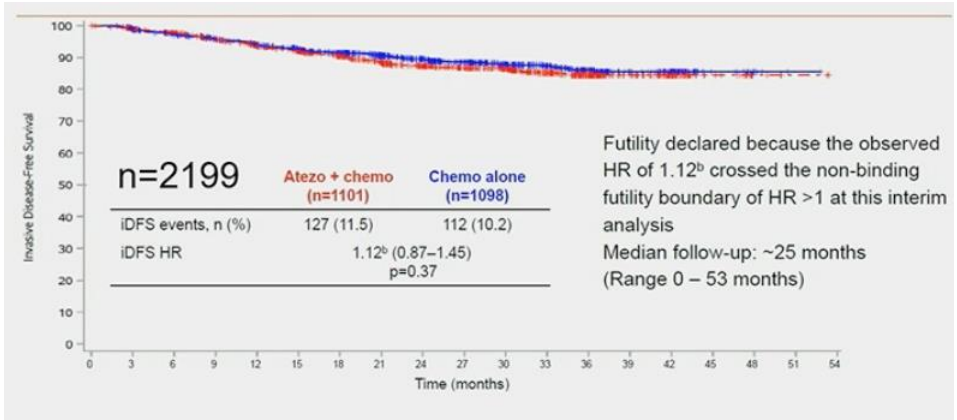
- OS Benefit gering
- Rolle Adjuvant Pembro?

- Prognose schlecht
- Add on Therapie, z.B. Cape, ADCs…..

Schmid P et al. N Engl J Med 2020, Schmid P et al. NEJM 2024

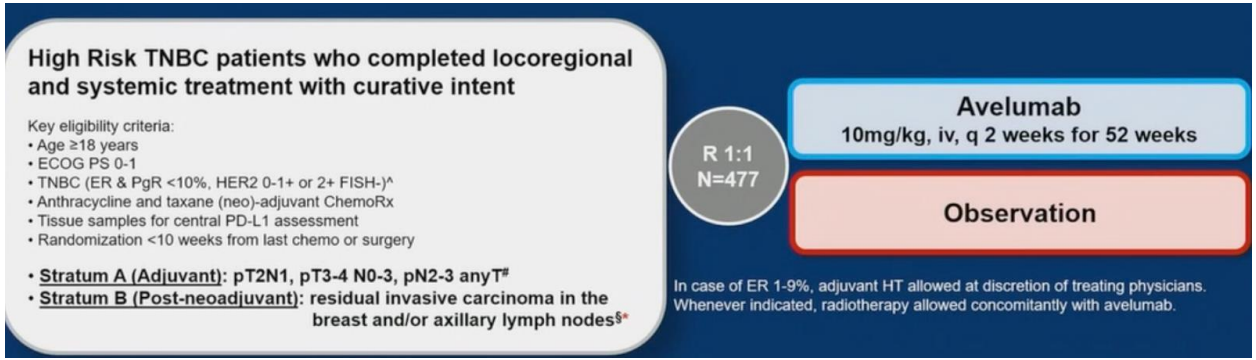
Immuntherapie Adjuvant beim TNBC – IMP30



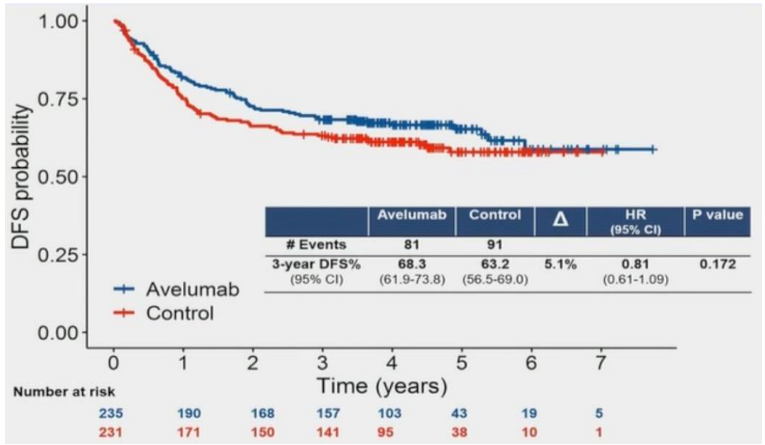


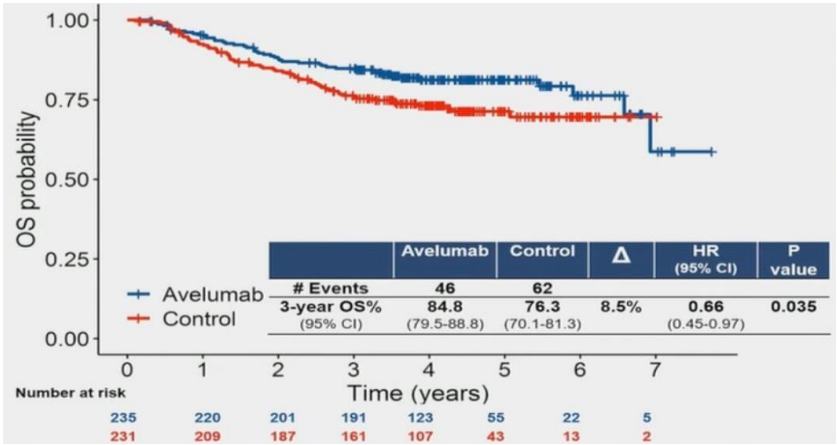
Ignatiadis M et al. SABCS 2023

Immuntherapie nur Adjuvant beim TNBC – Brave Studie



- 80% Stratum B
- 10% gBRCAmt
- Capecitabine 24% (CPI)
  18% (Control)

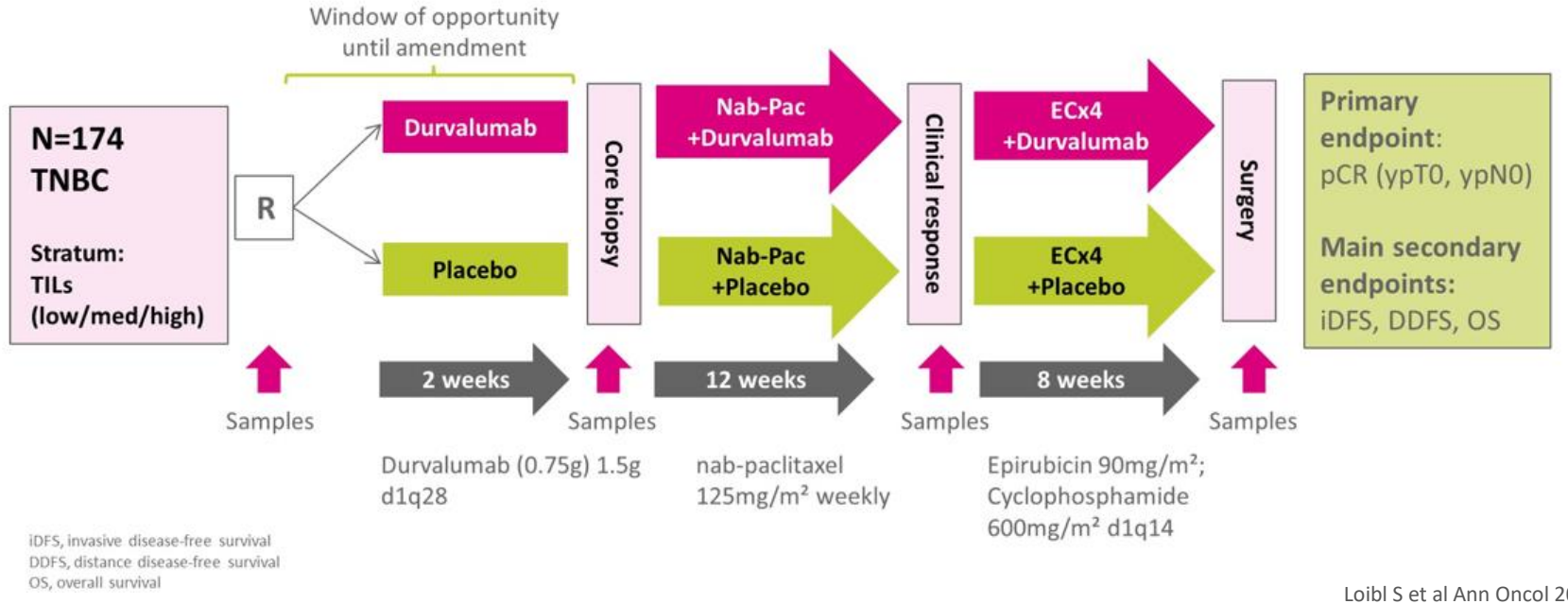




Conte P et al ASCO 2024

TNBC: GeparNuevo - Immuntherapie nur Neoadjuvant

Study Design



iDFS, invasive disease-free survival
DDFS, distance disease-free survival
OS, overall survival

Loibl S et al Ann Oncol 2022

TNBC: GeparNuevo - Immuntherapie nur Neoadjuvant

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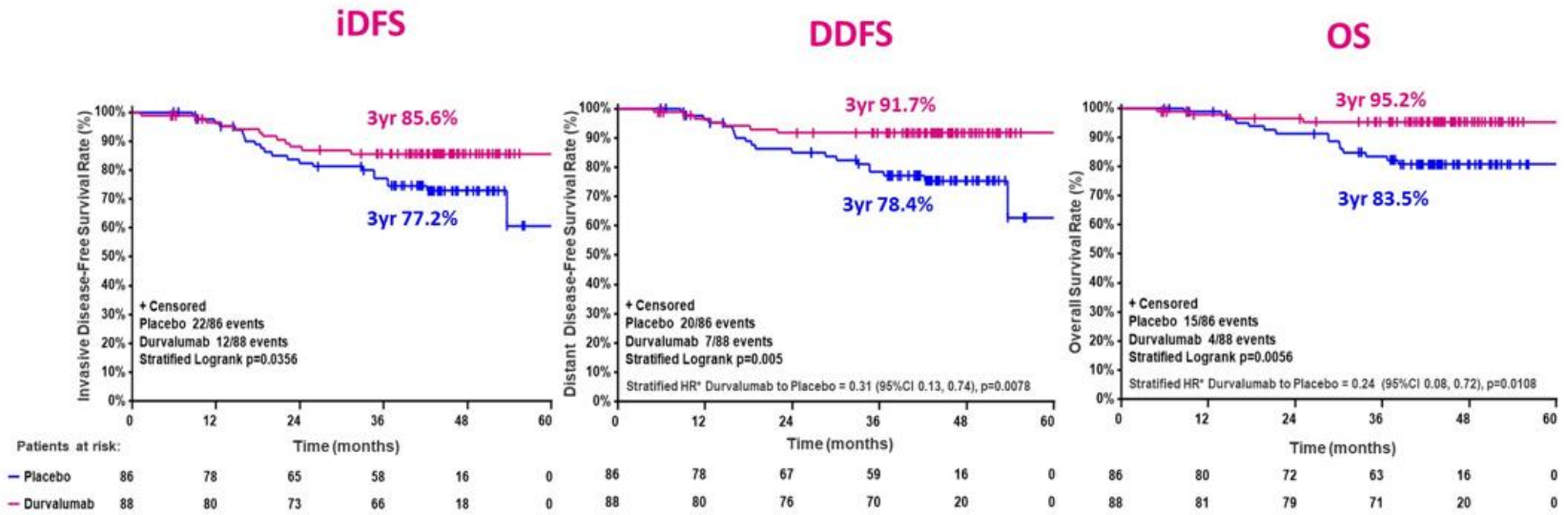
GBG GERMAN BREAST GROUP

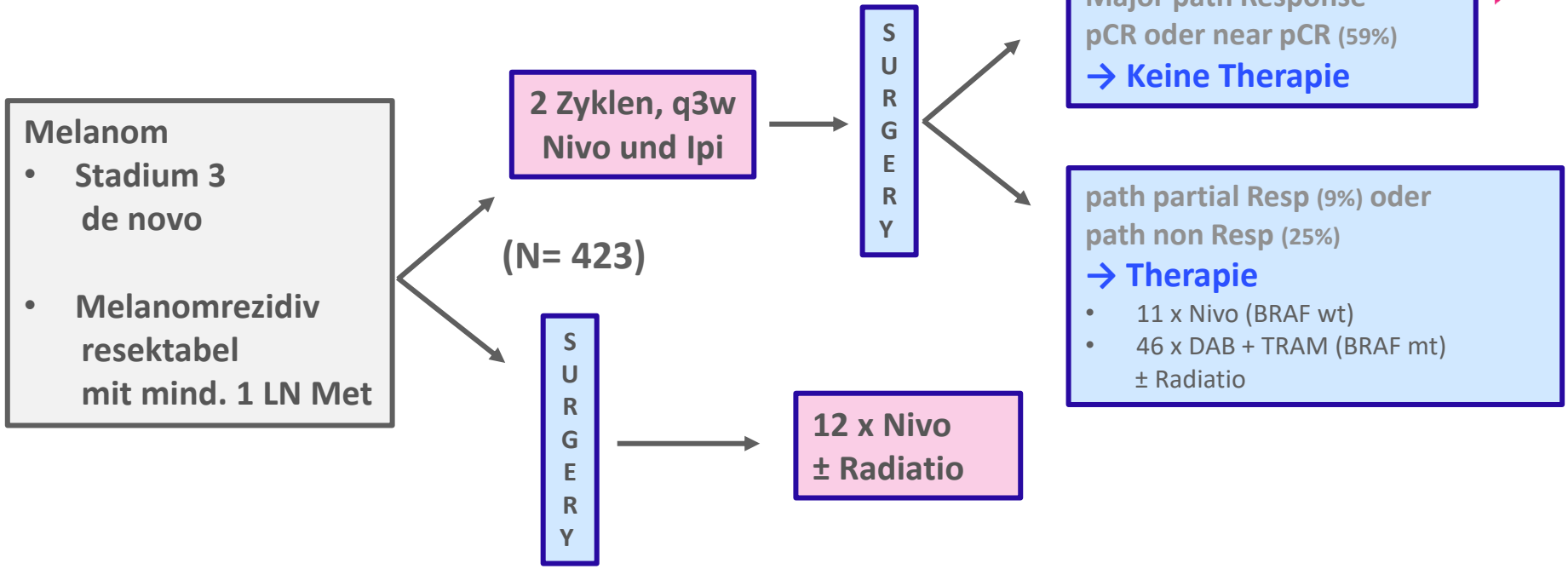
iDFS, DDFS and OS Between Treatment Arms

GeparNuevo



Loibl S et al Ann Oncol 2022

Nadine Studie

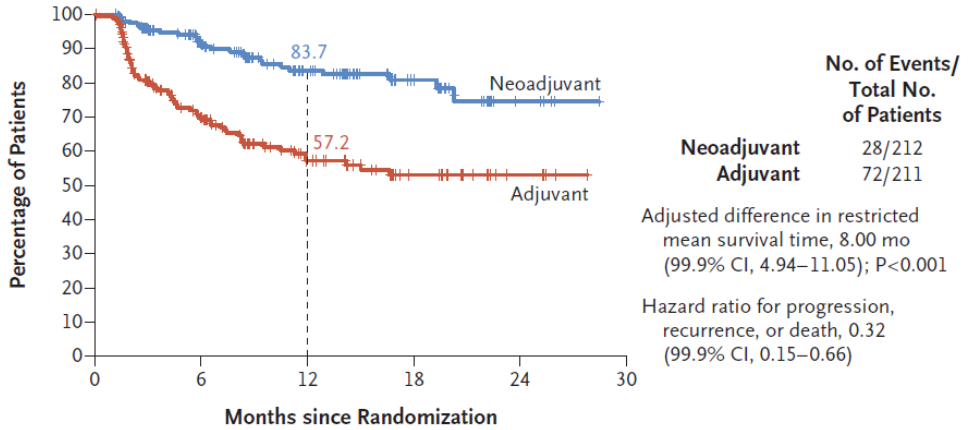


Near pCR: ≤ 10% vitale TuZellen, Nivo: Nivolumab, Ipi: Ipilimumab
DAB: Dabrafenib, TRAM: Trametinib

Blank CU et al NEJM 2024

Nadine Studie - EFS

ITT Population

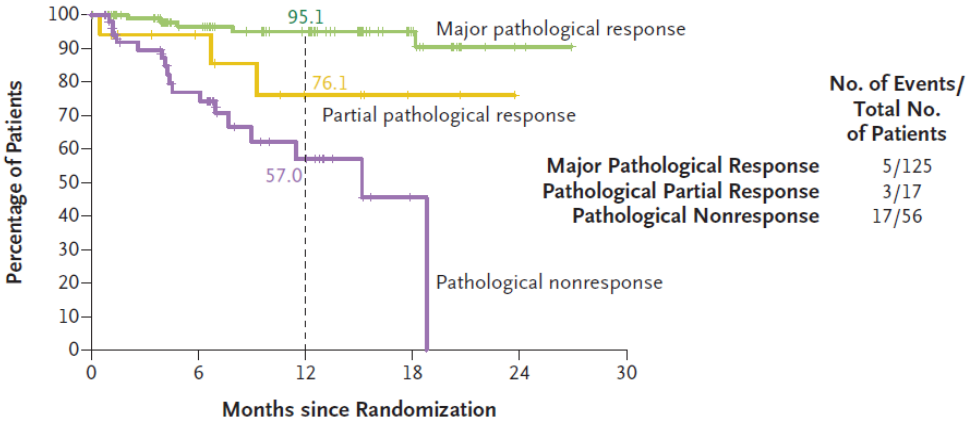


No. of Events/ Total No. of Patients	
Neoadjuvant	28/212
Adjuvant	72/211

Adjusted difference in restricted mean survival time, 8.00 mo (99.9% CI, 4.94–11.05); P<0.001

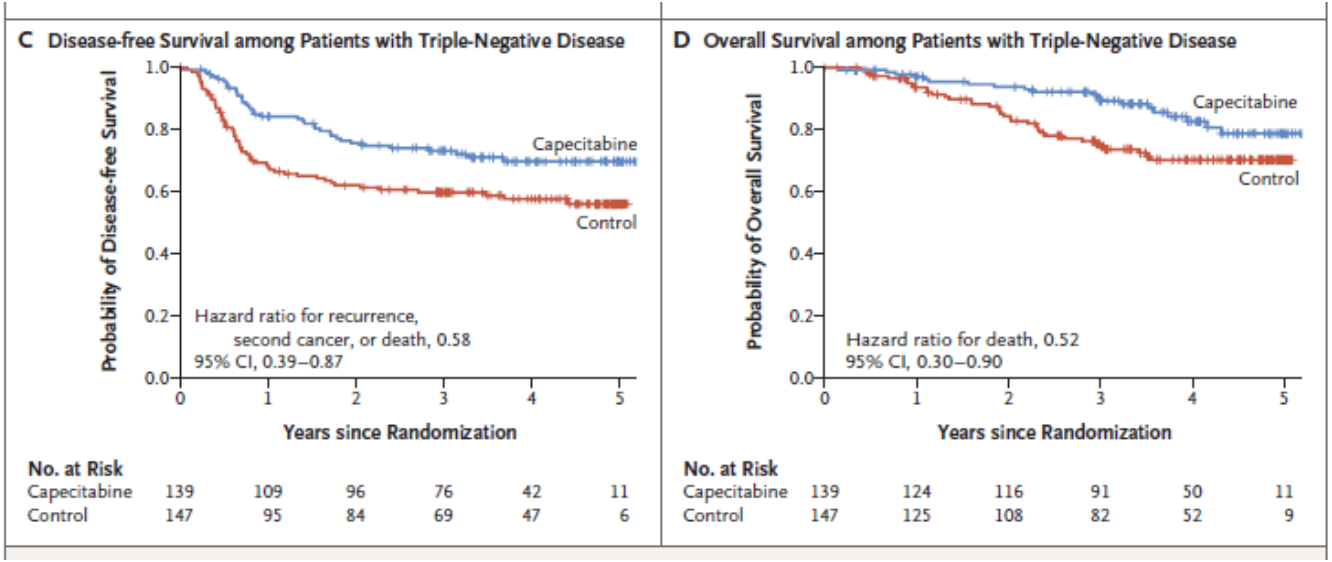
Hazard ratio for progression, recurrence, or death, 0.32 (99.9% CI, 0.15–0.66)

Neoadjuvante Population



No. of Events/ Total No. of Patients	
Major Pathological Response	5/125
Pathological Partial Response	3/17
Pathological Nonresponse	17/56

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%)

Masuda N et al, N Engl J Med 2017

TNBC – Neue Postneoadjuvante Studien

OptimICE-PCR
(N=1295)

OPT-PEMBRO
(N=2639)

pCR
nach
CHT-Pembro

SURGERY

- **Pembro**
- **OBSERVATION**

Ascent 05

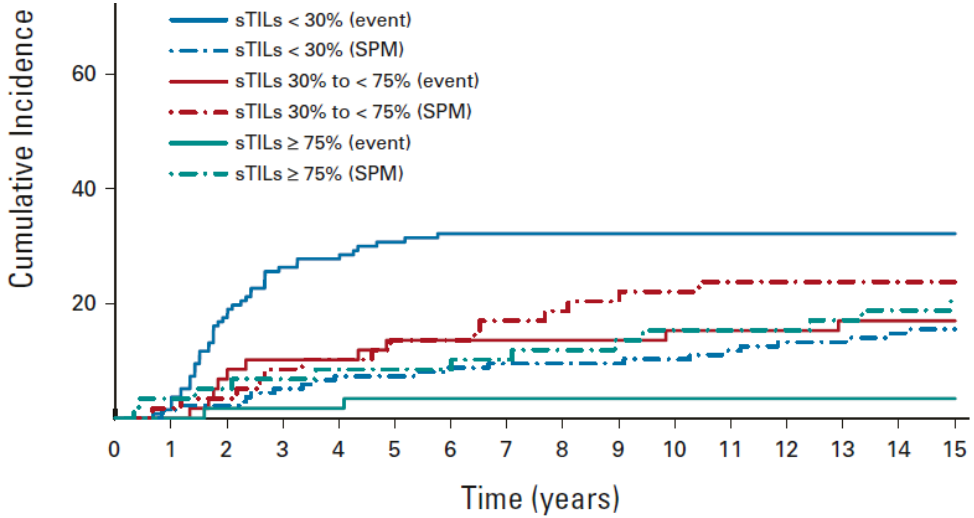
Keine pCR
nach
CHT-± Immuntherapie

SURGERY

- **SG x 8 +- Pembro**
- **PC / Cap x 8 + Pembro**

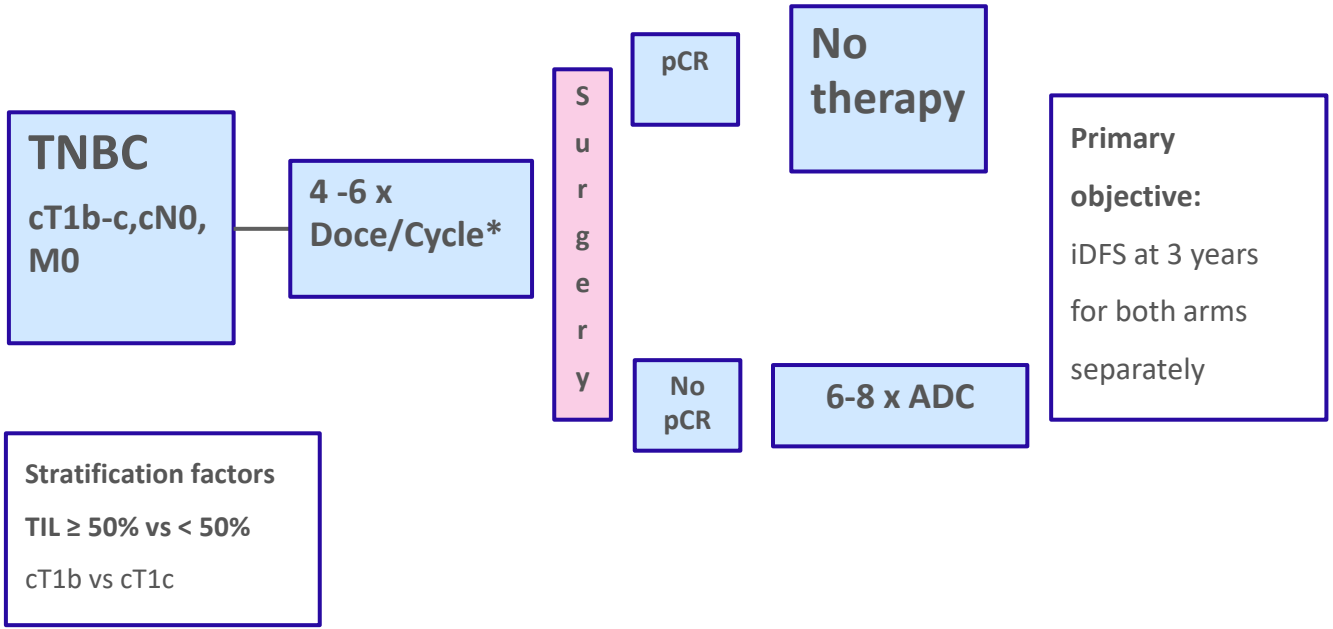
TNBC und keine adjuvant CHT – Observations-Studie

sTILs Level	No.	Distant Metastasis or Death at 3 Years (95% CI)	Second Primary Malignancy at 3 Years (95% CI)	Distant Metastasis or Death at 10 Years (95% CI)	Second Primary Malignancy at 10 Years (95% CI)
< 30%	136	26.7 (19.3 to 34.1)	4.4 (1.0 to 7.9)	32.6 (24.5 to 40.6)	9.7 (4.6 to 14.8)
30% to < 75%	57	10.5 (2.5 to 18.5)	8.8 (1.4 to 14.2)	15.8 (6.2 to 25.4)	22.8 (11.8 to 33.8)
≥ 75%	59	1.7 (0 to 5.0)	6.8 (0.3 to 13.3)	3.4 (0 to 8.1)	15.3 (6.1 to 24.5)



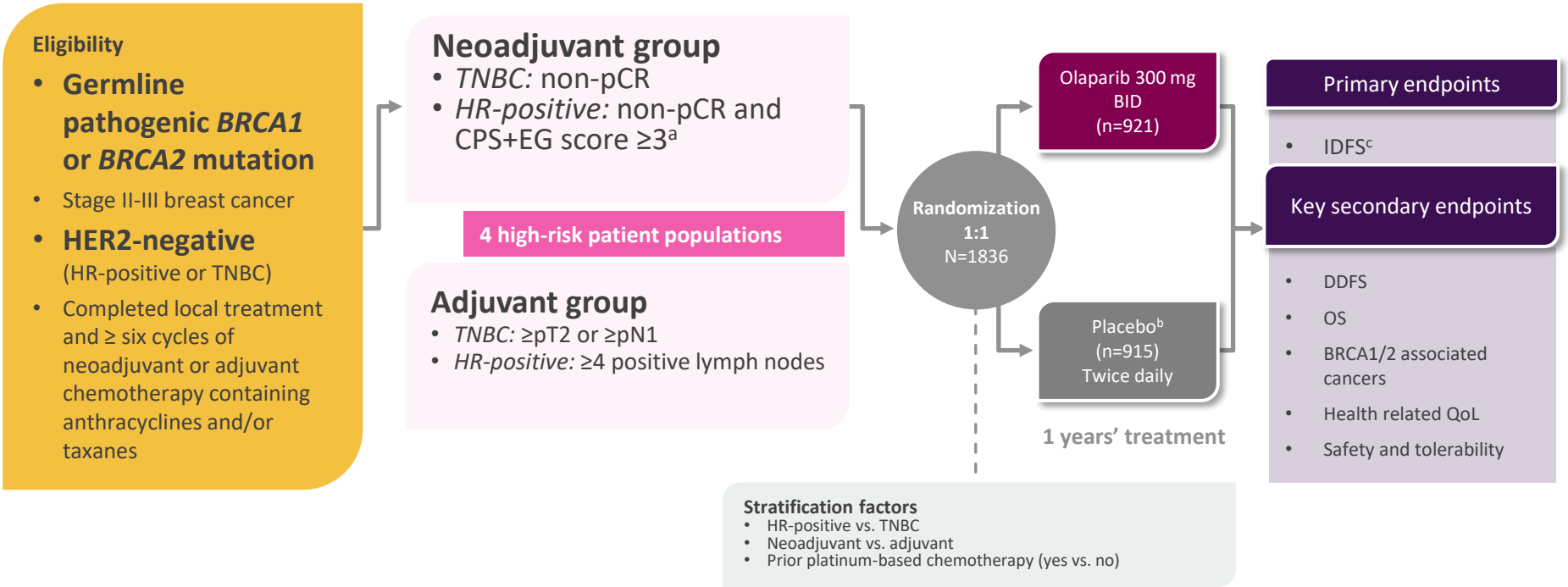
Characteristic	Overall N = 441 (100%)
Age, years, median (IQR)	35 (32-38)
sTILs, median % (IQR)	20 (5-70)
T stage, No. (%)[a]	
1[b]	4 (0.9)
1a	2 (0.5)
1b	32 (7.2)
1c	218 (49.4)
2	175 (39.7)
3	10 (2.3)
Tumor grade, No. (%)[c]	
1	3 (0.7)
2	59 (13.4)
3	379 (85.9)

SAKK Studienideie: TNBC cT1b, cN0

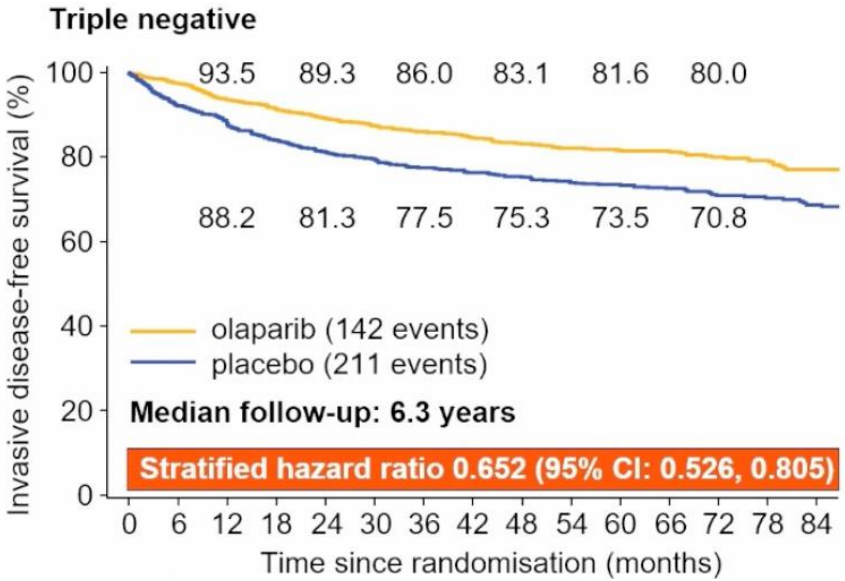


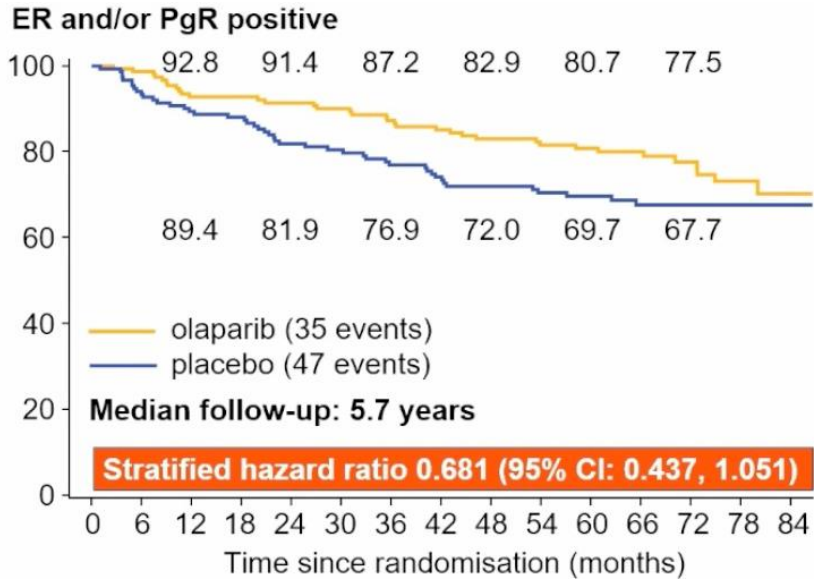
- * based on MRI response after 4 cycles Doce/Cyclo: if cCR surgery, if non cCR 2 more cycles
- Definition of TNBC: ER/PgR < 10% (tbd)
- TILs are centrally tested

OlympiA: Olaparib versus Placebo



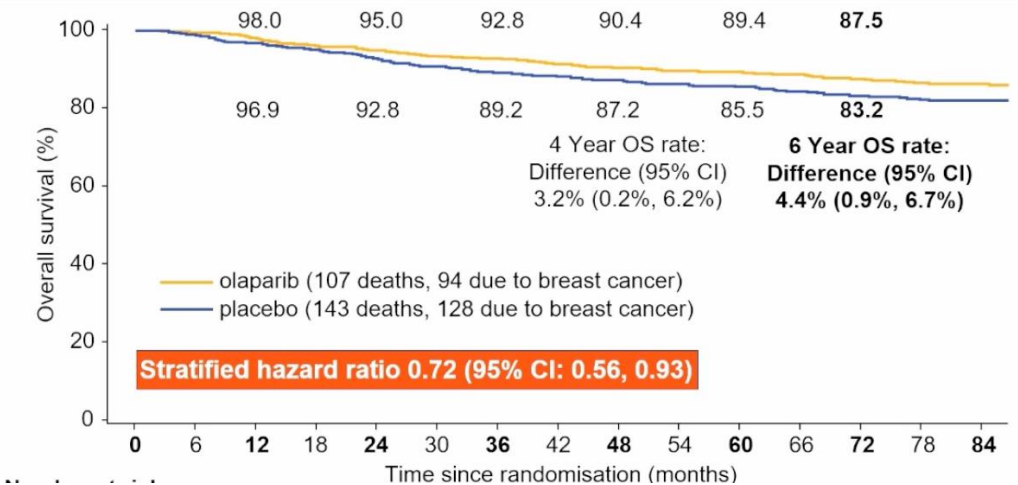
OlympiA: Olaparib versus Placebo iDFS – Update

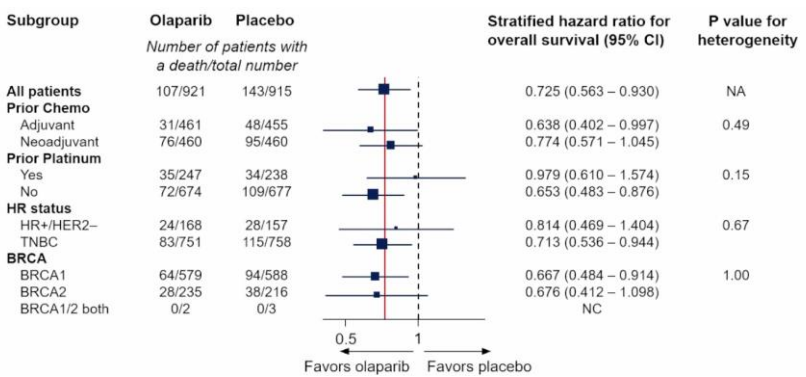




Garber J et al SABCS 2024

OlympiA: Olaparib versus Placebo OS – Update





Garber J et al SABCS 2024

TBCRC 048 (Olaparib Expanded) Expansion cohorts: Phase II study of olaparib monotherapy in metastatic breast cancer (MBC) patients with germline (g) mutations in *PALB2* or somatic (s) mutations in *BRCA1* or *BRCA2*

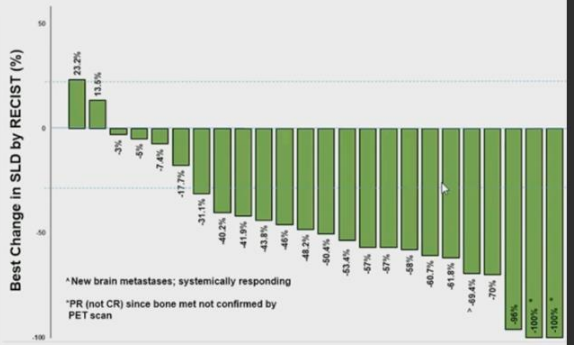
g*PALB2*
N=24

Best Response	Responses (rate, %)
Complete Response (CR)	1 (4%)
Partial Response (PR)	17 (71%)
Stable Disease (SD)	5 (21%)
Progressive Disease (PD)	1 (4%)

ORR = 75% (18/24, 80%-CI: 60%-86%)

CBR (18 wks) = 83% (20/24, 90%-CI: 66%-94%)

Datacut May 3, 2024



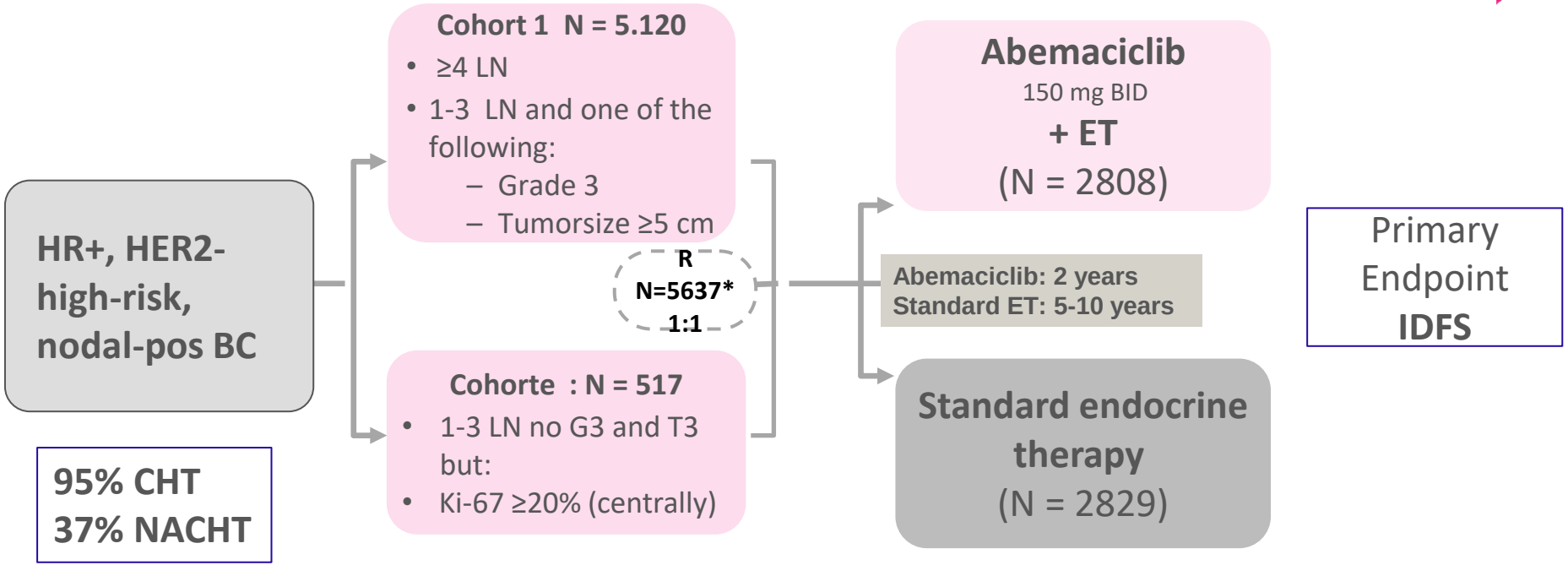
Tumor subtype	Responses
TNBC	2/2
ER+/HER2-neg	13/19
HER2+	3/3

2024 ASCO ANNUAL MEETING #ASCO24 PRESENTED BY: Nadine Tung MD

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

See you in Vienna

Monarch E Study



S. Johnston,….Huober J et al Lancet Oncol 2023

Monarch E Study – Cohort 1 median FU 54 months

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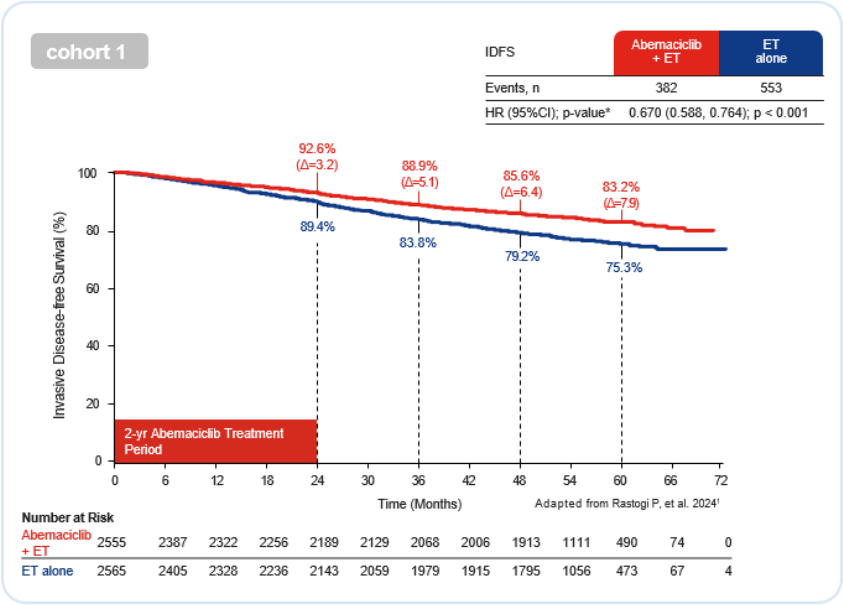
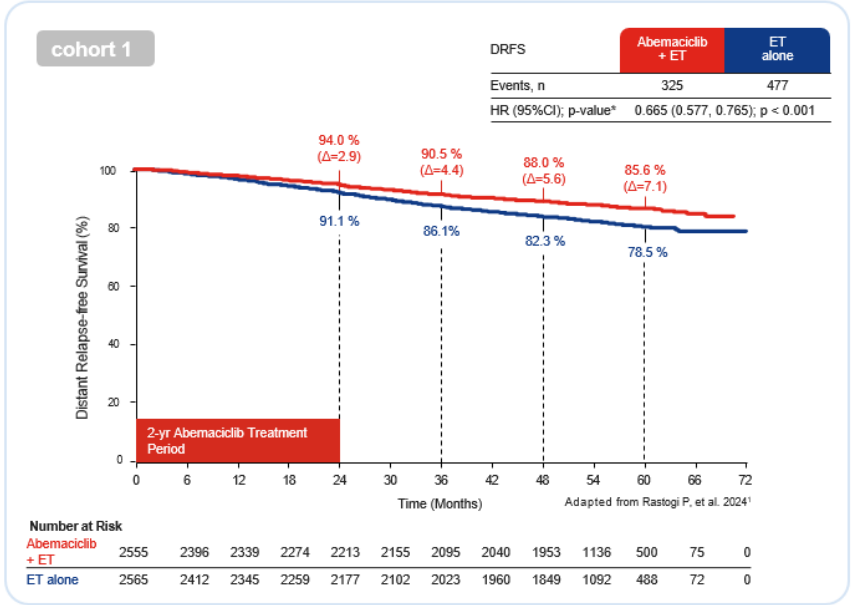
IDFS – Cohort 1 Δ 3.2 - 5.1 - **6.4 – 7.9**

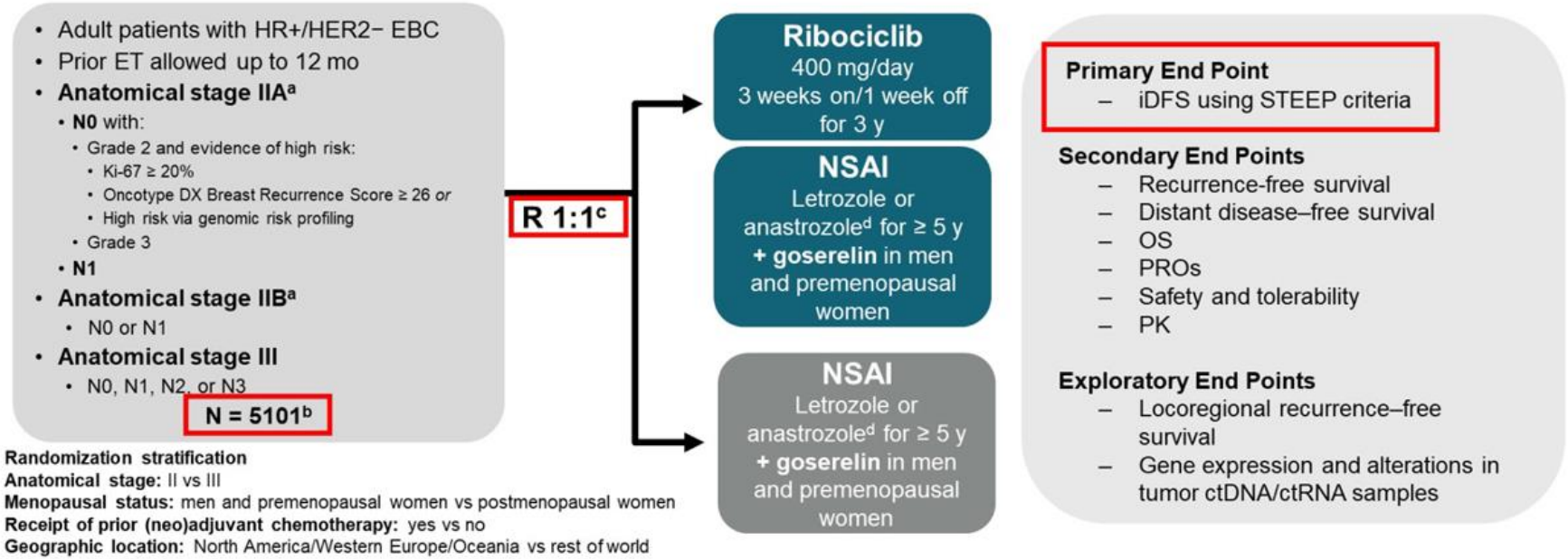
DRFS – Cohort 1 Δ 2.9 - 4.4 - **5.6 - 7.1**





Rastogi P, ...Huober J et al JCO 2024

Natalee Study



Differences to MonarchE

Includes some N0 pts and Ribociclib is given for 3 years

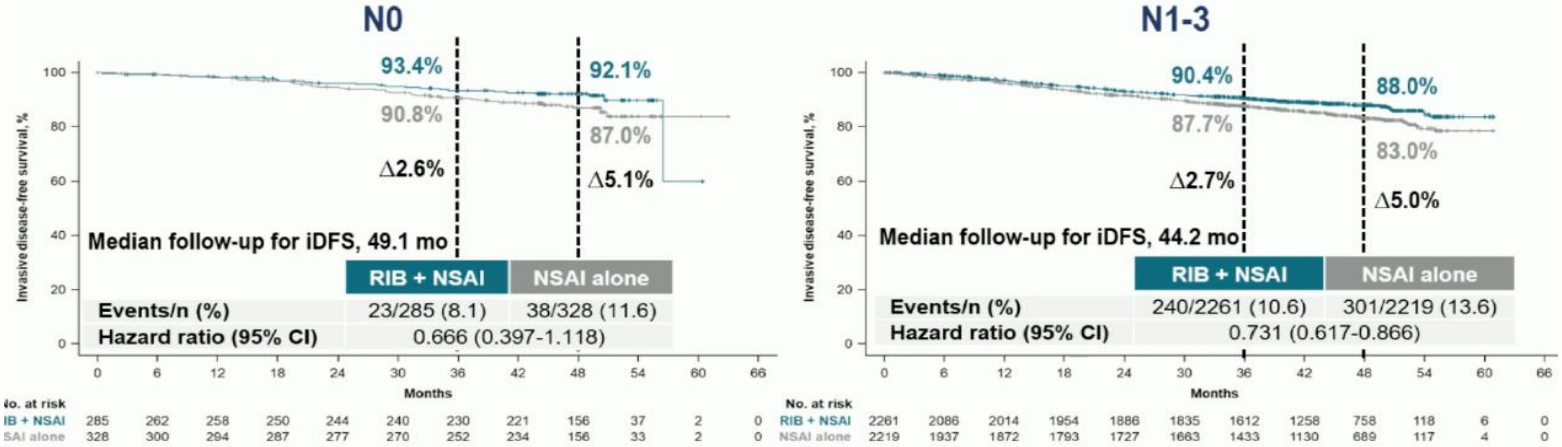
G Hortobagyi et al. SABCS 2023

iDFS by Nodal Status

iDFS by Nodal Status

BARCELONA 2024 ESMO congress

RIB + NSAI showed an increasing magnitude of iDFS benefit over time for patients with N0 or N1-3 disease



iDFS, invasive disease–free survival; N, node; NSAI, nonsteroidal aromatase inhibitor; RIB, ribociclib

Peter A. Fasching

Heilung durch Innovation, Kompetenz und Partnerschaft – führend in der Brustkrebs-Forschung

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22. Annual Scientific Meeting 06. – 07. März 2025