

GBG

GERMAN  
BREAST  
GROUP



in person

**2.- 3. März 2023**

GBG Jahrestreffen

**20** YEARS  
ANNIVERSARY

# Neoadjuvante Therapie des Mammakarzinoms 2023

Dr. Theresa Link

Uniklinik Dresden

## Offenlegung potentieller Interessenkonflikte

### **1. Anstellungsverhältnis oder Führungsposition**

Keine

### **2. Beratungstätigkeit**

Keine

### **3. Aktienbesitz**

Keine

### **4. Honorare**

Vorträge: Amgen, Roche, Clovis, MSD, Novartis, Pfizer, Lilly, GSK, Gilead, Astra Zeneca, Daiichi Sankyo  
Advisory Board: Tesaro, MSD, Roche, Amgen, Pfizer, Lilly, Myriad, Esai, GSK, Gilead, Daiichi Sankyo, MSD, Novartis

### **5. Finanzierung wissenschaftlicher Untersuchungen**

Keine

### **6. Gutachtertätigkeit**

Keine

### **7. Andere finanzielle Beziehungen**

Kongress-/Vst-Teilnahme: MSD, Celgene, Clovis, Daiichi Sankyo, Pfizer, Astra Zeneca, Gilead, Daiichi Sankyo

# 2022/2023

Zulassungen

ASCO

ESMO

SABCS

03/22

03/23

05/22  
Pembro  
eBC

06/22  
Olaparib  
eBC

07/22  
T-Dxd  
2nd line

Neube-  
wertung  
HER2

01/23  
T-Dxd  
Her2low



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

Guidelines Breast  
Version 2022.1D

www.ago-online.de

FORSCHEN  
LEHREN  
HEILEN

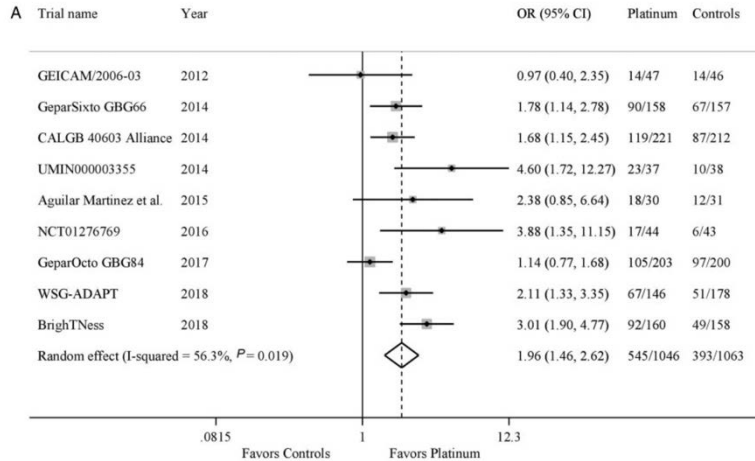
## Neoadjuvante systemische Chemotherapie Empfohlene Schemata

- Analog zu adjuvanten Standardschemata\*
- Taxan mono gefolgt von Anthrazyklin (umgekehrte Reihenfolge)
- Platinsalze beim TNBC (cT1 / cN0) (unabh. des BRCA-Status)
- Platinsalze beim TNBC (ab cT1 / cN+ o. cT2) (unabh. des BRCA-Status)
- Nab-Paclitaxel qw anstatt Paclitaxel q1w (bei TNBC)
- Pembrolizumab in Kombination mit Carbo / Paclitaxel → 4x EC q3w (TNBC\*\*)

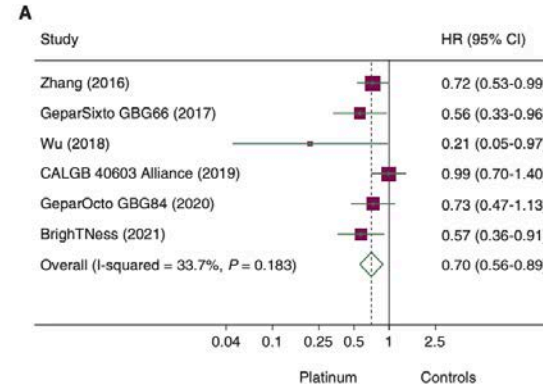
\* Siehe Kapitel adjuvante Chemotherapie  
\*\* ≥ 2 cm oder cN+, PD-L1 unabhängig

	Oxford		
	LoE	GR	AGO
	1a	A	++
	4	D	+/-
	1b	A	+
	1a	A	+
	1a	A	+
	1b	B	+

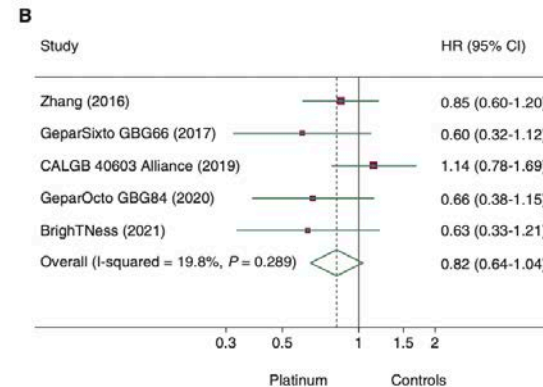
# Bedeutung von Platin



Verbesserung pCR

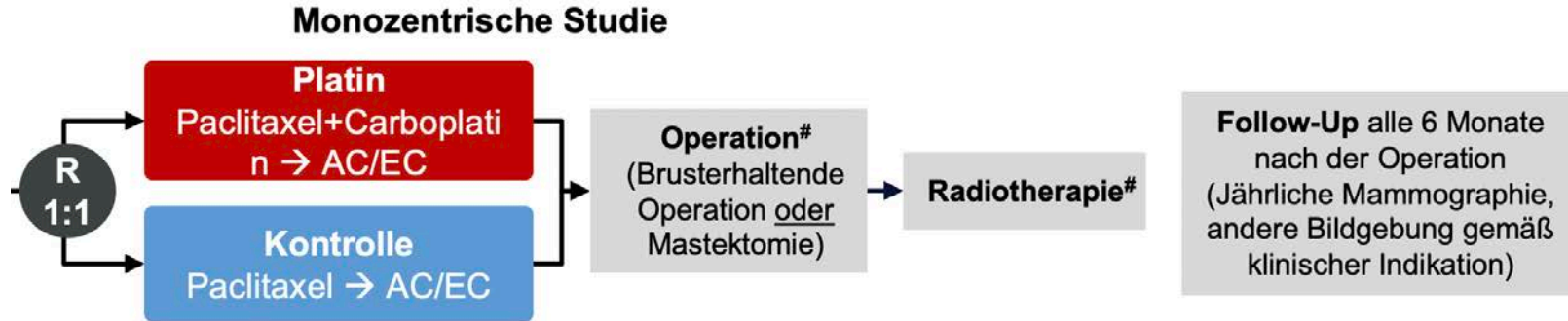


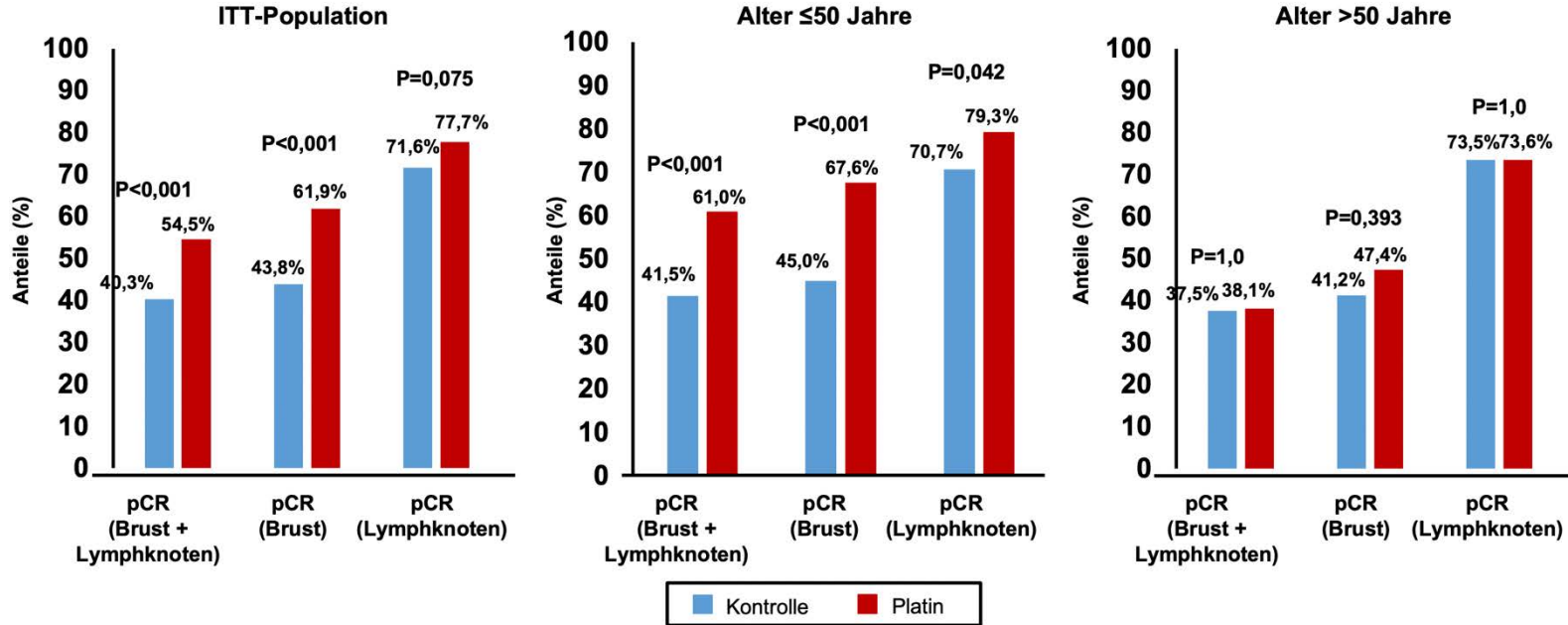
EFS



OS

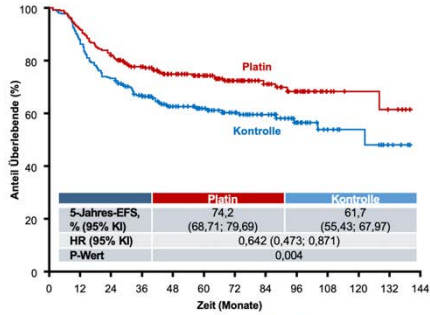
# Bedeutung von Platin





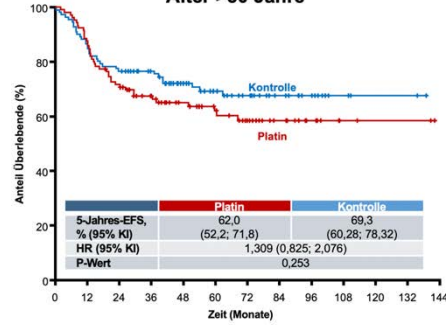
Multivariable (binäre logistische) Analyse für Faktoren, die die pCR beeinflussen: Behandlungsarm-Alter-Interaktion signifikant in einem Modell mit Behandlungsarm, Alter, cT-Größe, cN-Status, Familienanamnese.

Alter ≤50 Jahre



Kontrolle 245 213 179 149 115 98 69 49 32 14 9 4 0  
Platin 255 233 209 180 145 122 85 62 37 14 10 8 0

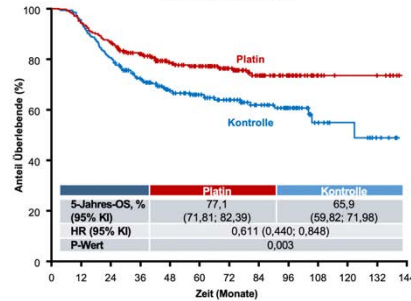
Alter >50 Jahre



Kontrolle 111 95 85 69 54 43 32 21 13 5 3 3 0  
Platin 106 93 75 59 45 37 27 17 10 3 2 2 0

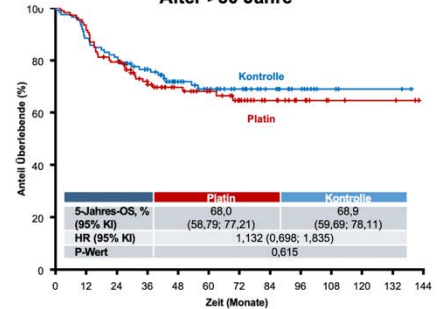
## OS

Alter ≤50 Jahre

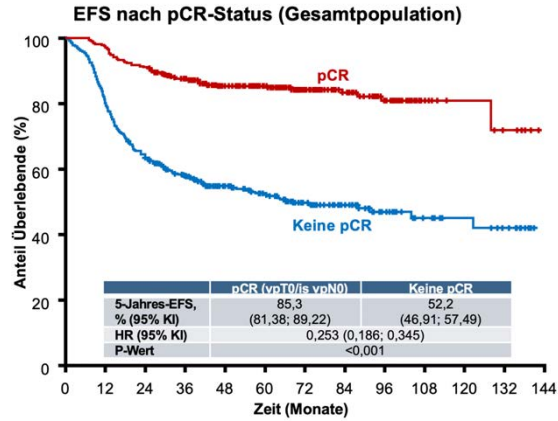


Kontrolle 245 232 197 160 125 104 74 53 35 15 9 4 0  
Platin 255 240 220 190 153 127 91 64 40 15 11 9 0

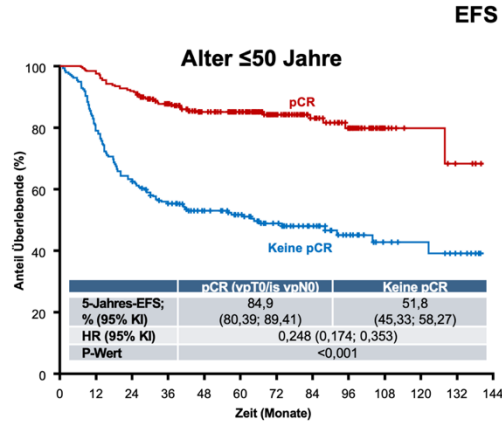
Alter >50 Jahre



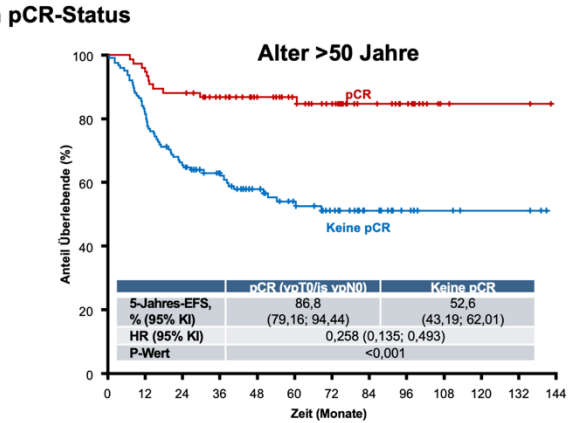
Kontrolle 111 98 90 69 54 43 32 21 13 5 3 3 0  
Platin 106 99 83 62 48 41 31 19 11 4 3 3 0



Keine pCR	359	288	227	189	141	116	84	58	34	20	15	11	0
pCR	324	315	295	256	209	178	124	84	55	16	9	6	0



Keine pCR	234	186	146	124	93	79	56	41	24	15	12	8	0
pCR	248	243	228	196	162	137	94	67	43	13	7	4	0



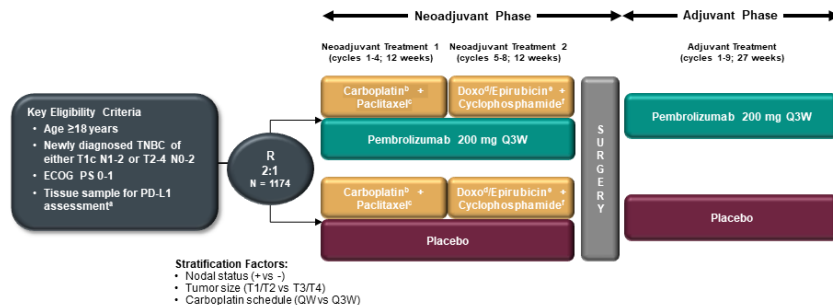
Keine pCR	125	102	81	62	48	37	28	17	10	5	3	3	0
pCR	76	72	67	60	47	41	30	20	12	3	2	2	0

# Bedeutung von Platin – ‚the end of the debate‘?

- Steigerung pCR
- Verbesserung EFS
- Unter 50 Jahren: Verbesserung OS
- Mehr Hämatotoxizität
- Checkpoint-Inhibition...

## KEYNOTE-522 Study Design (NCT03036488)

Schmid KN522 ESMO Virtual Plenary 2021



**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)

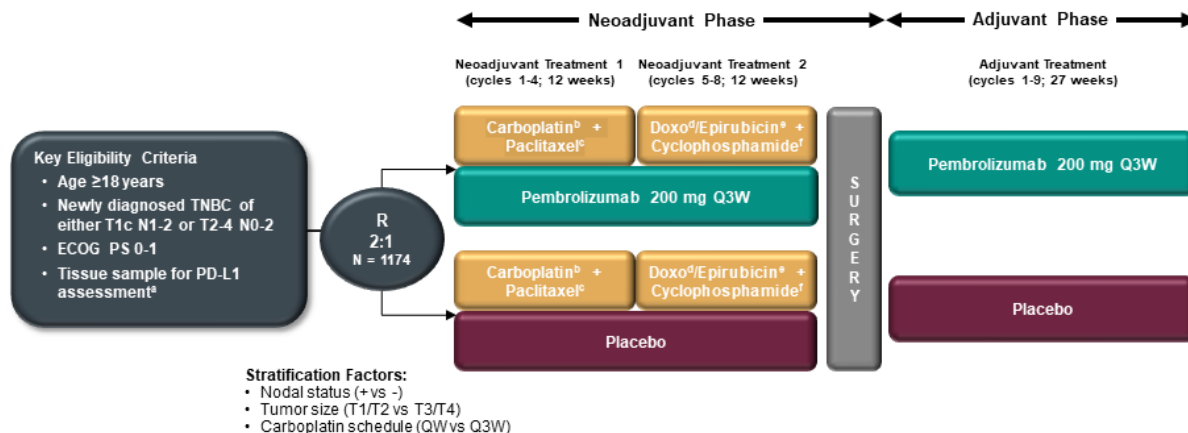
\*Must consist of at least 2 separate tumor cores from the primary tumor.  
<sup>b</sup>Carboplatin dose was AUC 5 Q3W or AUC 1.5 QW.  
<sup>c</sup>Paclitaxel dose was 80 mg/m<sup>2</sup> QW.

<sup>d</sup>Doxorubicin dose was 60 mg/m<sup>2</sup> Q3W.  
<sup>e</sup>Epirubicin dose was 80 mg/m<sup>2</sup> Q3W.  
<sup>f</sup>Cyclophosphamide dose was 600 mg/m<sup>2</sup> Q3W.

# Zulassung Pembrolizumab eBC 05/2022

Schmid KN522 ESMO Virtual Plenary 2021

## KEYNOTE-522 Study Design (NCT03036488)



**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)

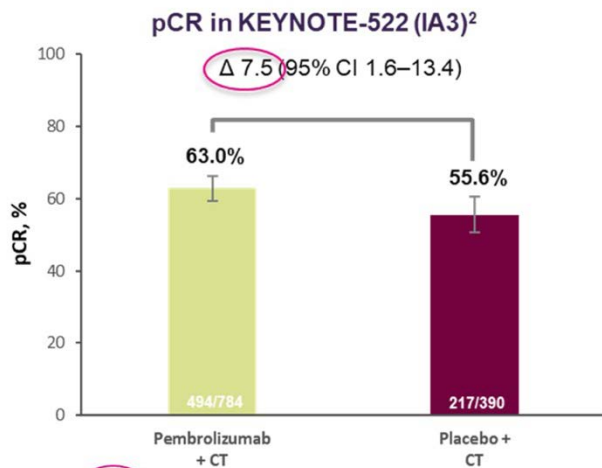
<sup>a</sup>Must consist of at least 2 separate tumor cores from the primary tumor.  
<sup>b</sup>Carboplatin dose was AUC 5 Q3W or AUC 1.5 QW.  
<sup>c</sup>Paclitaxel dose was 80 mg/m<sup>2</sup> QW.

<sup>d</sup>Doxorubicin dose was 60 mg/m<sup>2</sup> Q3W.  
<sup>e</sup>Epirubicin dose was 90 mg/m<sup>2</sup> Q3W.  
<sup>f</sup>Cyclophosphamide dose was 600 mg/m<sup>2</sup> Q3W.

# Keynote522

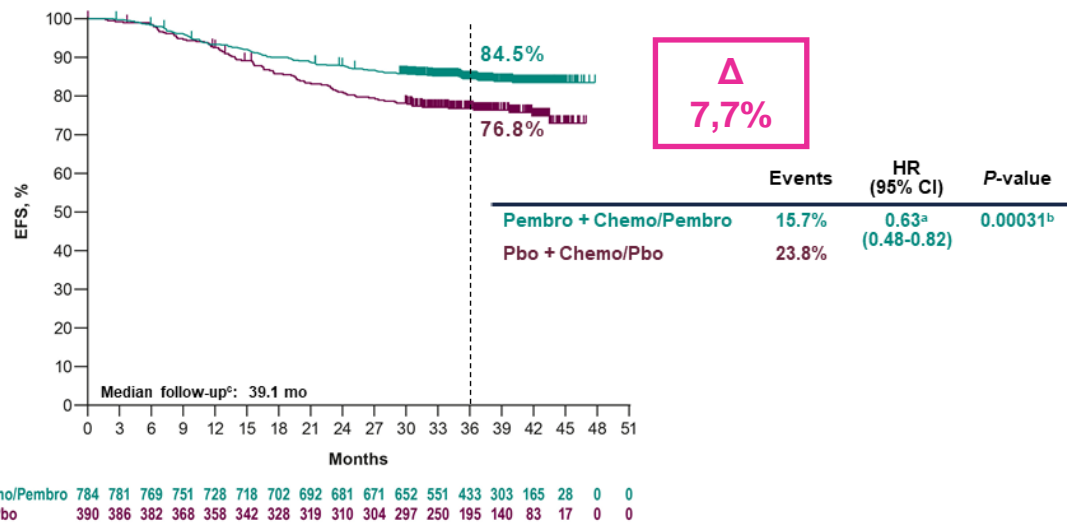
Schmid KN522 ESMO Virtual Plenary 2021

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



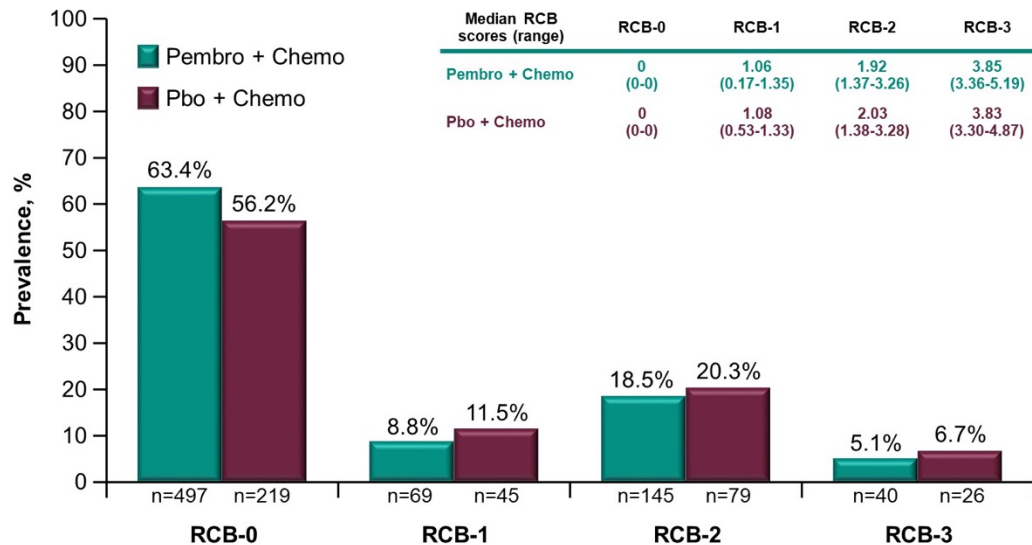
All 1174 participants in ITT  
(Data cut-off date 23 March 2020)

## Statistically Significant and Clinically Meaningful EFS at IA4



<sup>a</sup>Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. <sup>b</sup>Prespecified P-value boundary of 0.00517 reached at this analysis. <sup>c</sup>Defined as the time from randomization to the data cutoff date of March 23, 2021.

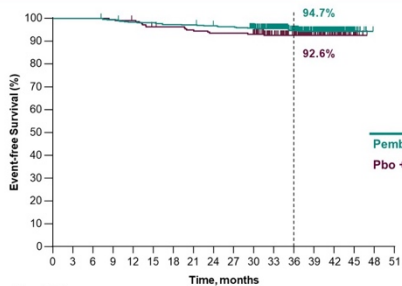
## Prevalence of RCB Categories in All Patients



Among all patients (n=1174), 54 patients (4.6%) had missing RCB categorical data: 33 (4.2%) in the pembro + chemo group and 21 (5.4%) in the pbo + chemo group. Data cutoff date: March 23, 2021.



### EFS in RCB-0



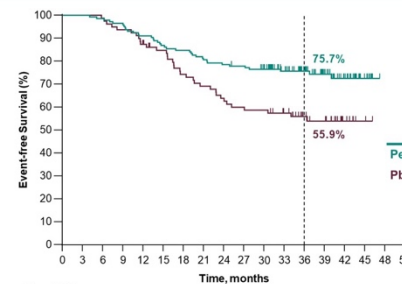
	n/N	Events	HR (95% CI)
Pembro + Chemo	26/497	5.2%	0.70 <sup>a</sup> (0.38-1.31)
Pbo + Chemo	16/219	7.3%	

No. at risk

497	497	493	487	486	482	481	476	474	463	390	310	223	124	18	0	0
219	219	218	216	209	208	205	202	202	199	167	132	89	58	10	0	0

<sup>a</sup>Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate. Data cutoff date: March 23, 2021.

### EFS in RCB-2



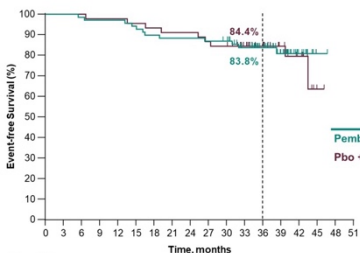
	n/N	Events	HR (95% CI)
Pembro + Chemo	37/145	25.5%	0.52 <sup>a</sup> (0.32-0.82)
Pbo + Chemo	35/79	44.3%	

No. at risk

145	145	143	140	132	126	123	117	114	112	107	90	70	46	26	9	0	0
79	79	78	74	69	65	57	53	49	46	45	40	29	24	7	2	0	0

<sup>a</sup>Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate. Data cutoff date: March 23, 2021.

### EFS in RCB-1



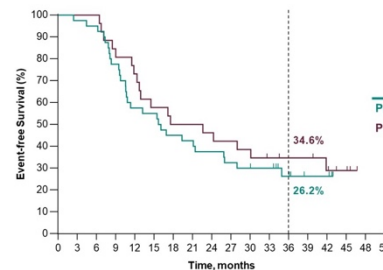
	n/N	Events	HR (95% CI)
Pembro + Chemo	12/69	17.4%	0.92 <sup>a</sup> (0.39-2.20)
Pbo + Chemo	9/45	20.0%	

No. at risk

69	69	68	67	67	65	62	61	61	60	59	50	38	24	9	1	0	0
45	45	44	44	43	42	41	41	39	38	32	25	18	11	1	0	0	0

<sup>a</sup>Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate. Data cutoff date: March 23, 2021.

### EFS in RCB-3



	n/N	Events	HR (95% CI)
Pembro + Chemo	29/40	72.5%	1.24 <sup>a</sup> (0.69-2.23)
Pbo + Chemo	18/26	69.2%	

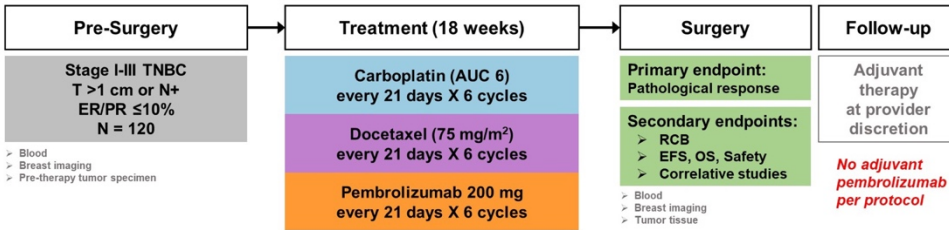
No. at risk

40	39	38	31	23	22	18	17	15	13	12	11	6	3	3	0	0	0
26	26	26	22	19	15	13	12	11	10	8	7	7	5	3	0	0	0

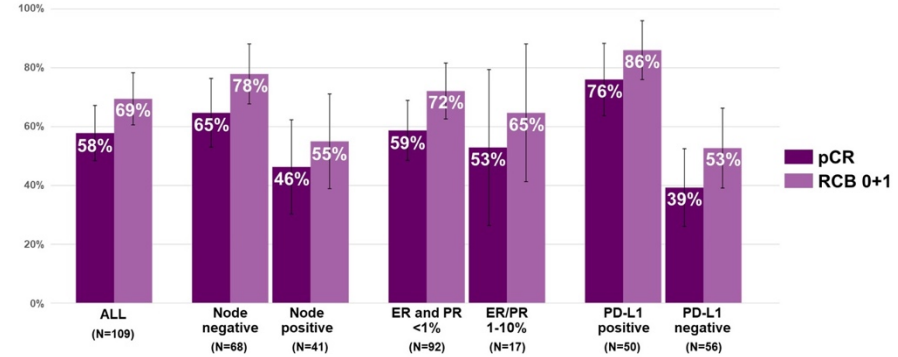
<sup>a</sup>Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate. Data cutoff date: March 23, 2021.

# Neopact

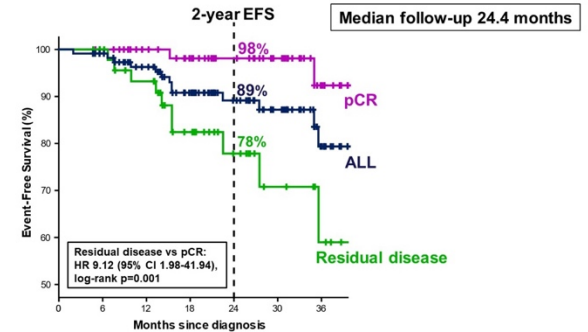
## Neoadjuvant Phase II Study of Pembrolizumab and Carboplatin plus Docetaxel in Triple Negative Breast Cancer (NeoPACT)



Sites: University of Kansas and Baylor University Medical Center



### Event-free survival



	Number at risk							
	113	108	95	75	54	37	18	
All								
pCR	63	62	55	48	38	28	13	
Residual disease	49	46	40	27	16	9	5	

Survival analysis includes all patients in the ITT population except for N=2 who are awaiting surgery

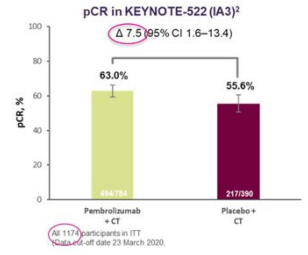
# Adjuvante Therapie?

## KN522

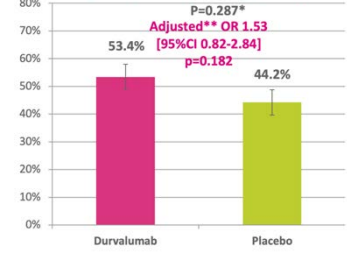
## GeparNuevo

## NeoPACT

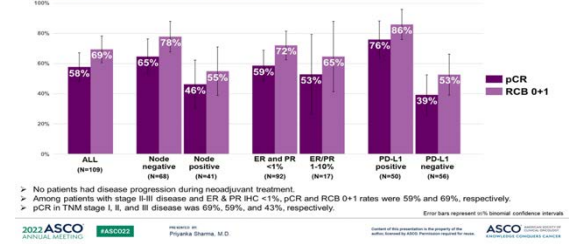
KEYNOTE-522 (IA3)<sup>2</sup>  
Pembrolizumab + CT vs placebo + CT in early TNBC



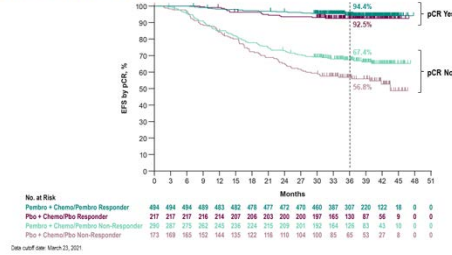
Primary endpoint: pCR – ypT0, ypN0



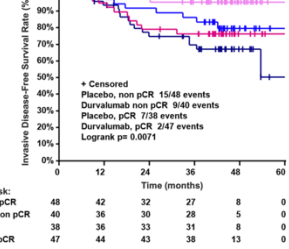
RESULTS: Pathologic response



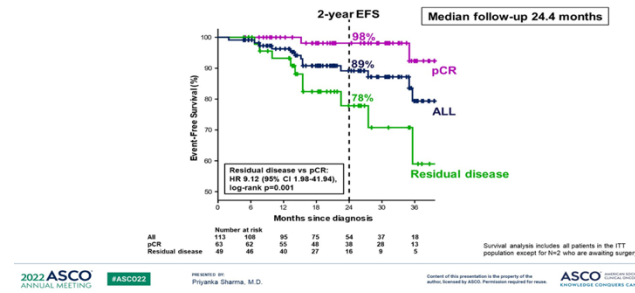
EFS by pCR (ypT0/Tis ypN0)



iDFS



Event-free survival

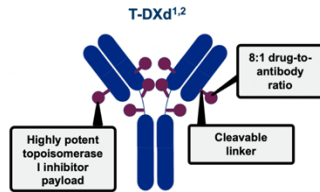




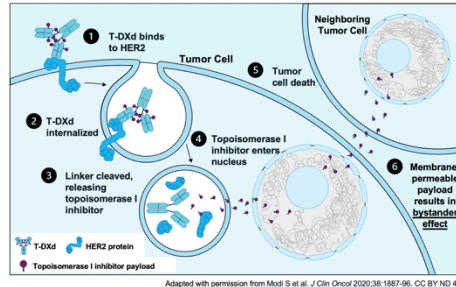


Check E, Nature 2007;446:964–66.

## Trastuzumab-Deruxtecan



Internalization of T-DXd leads to release of the DXd payload and subsequent cell death in the target tumor cell and neighboring tumor cells through the bystander effect<sup>1,2</sup>

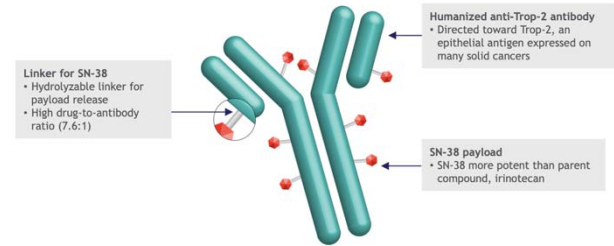


Adapted with permission from Modi S et al. J Clin Oncol 2020;38:1887-96. CC BY ND 4.0.

## Sacituzumab-Govitecan

### Background (cont.)

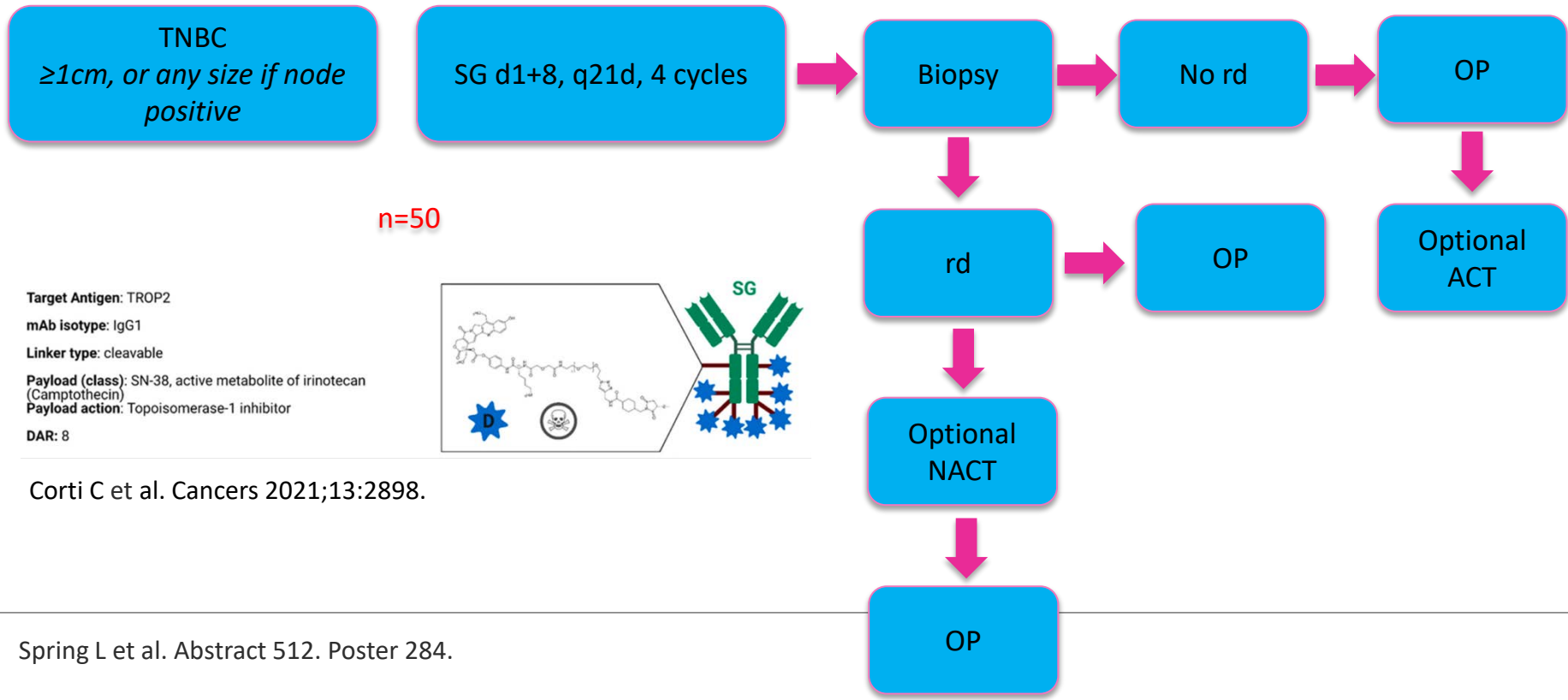
Figure 1. Sacituzumab Govitecan Antibody-Drug Conjugate



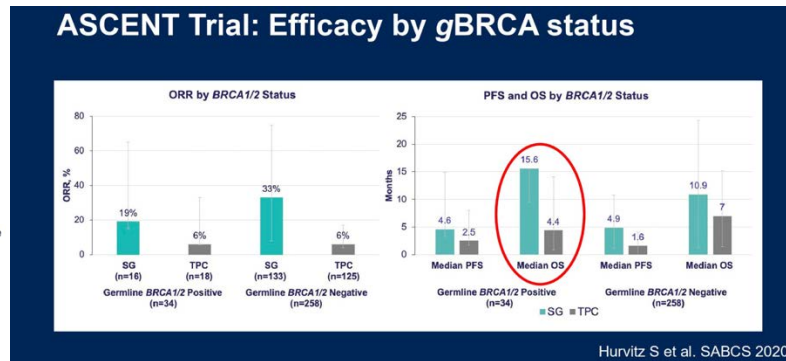
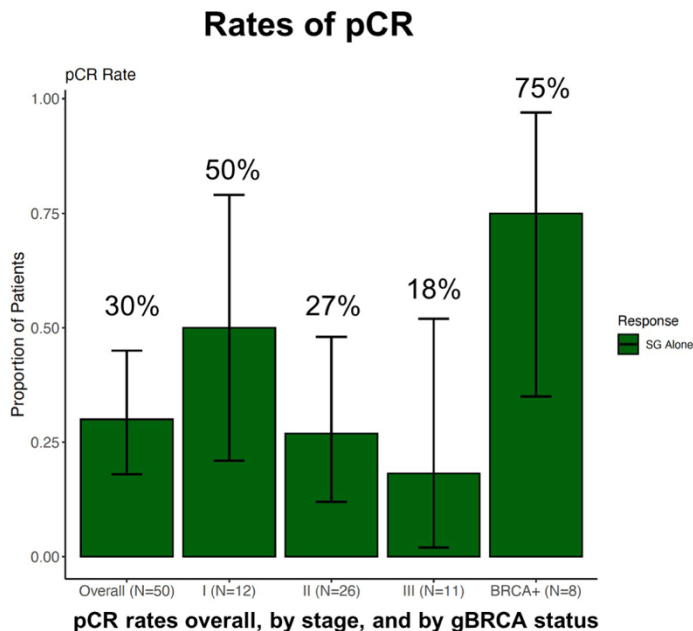
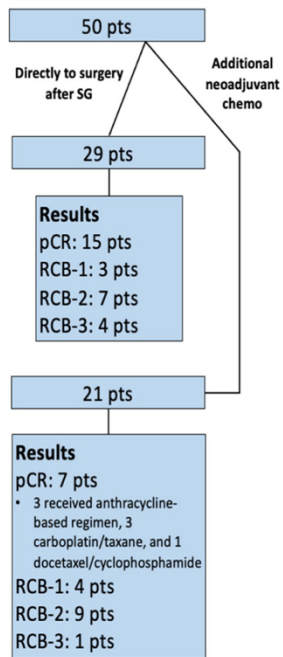
Mod. Bardia A et al. ESMO 2020, Proffered Paper Session 1 – Breast cancer, metastatic, Abstract No. LBA17

# NeoSTAR

## Phase 2 study of response-guided neoadjuvant sacituzumab govitecan (IMMU-132) in patients with localized triple-negative breast cancer



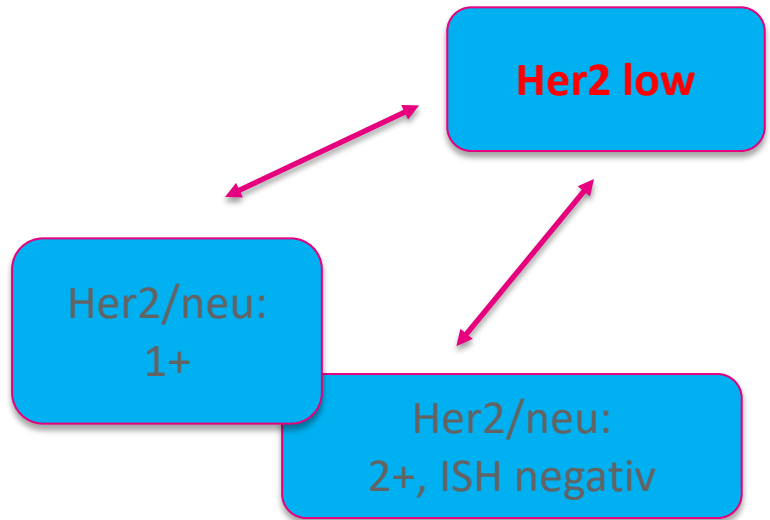
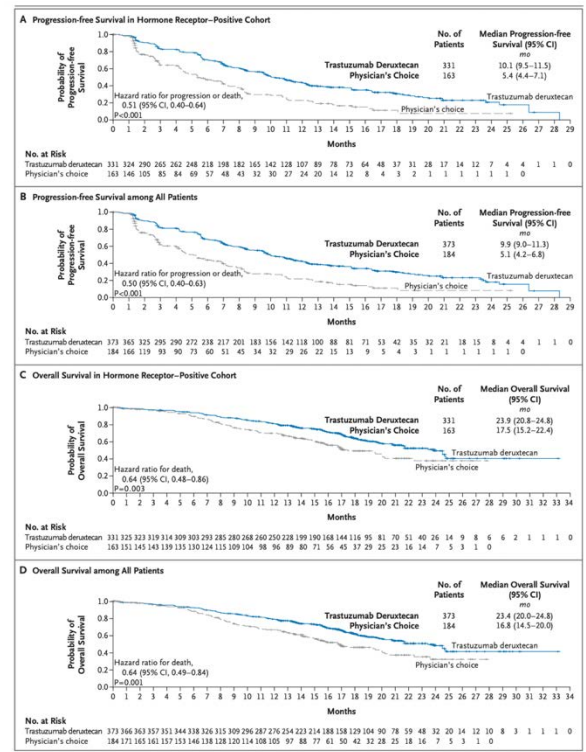
## Results (2)





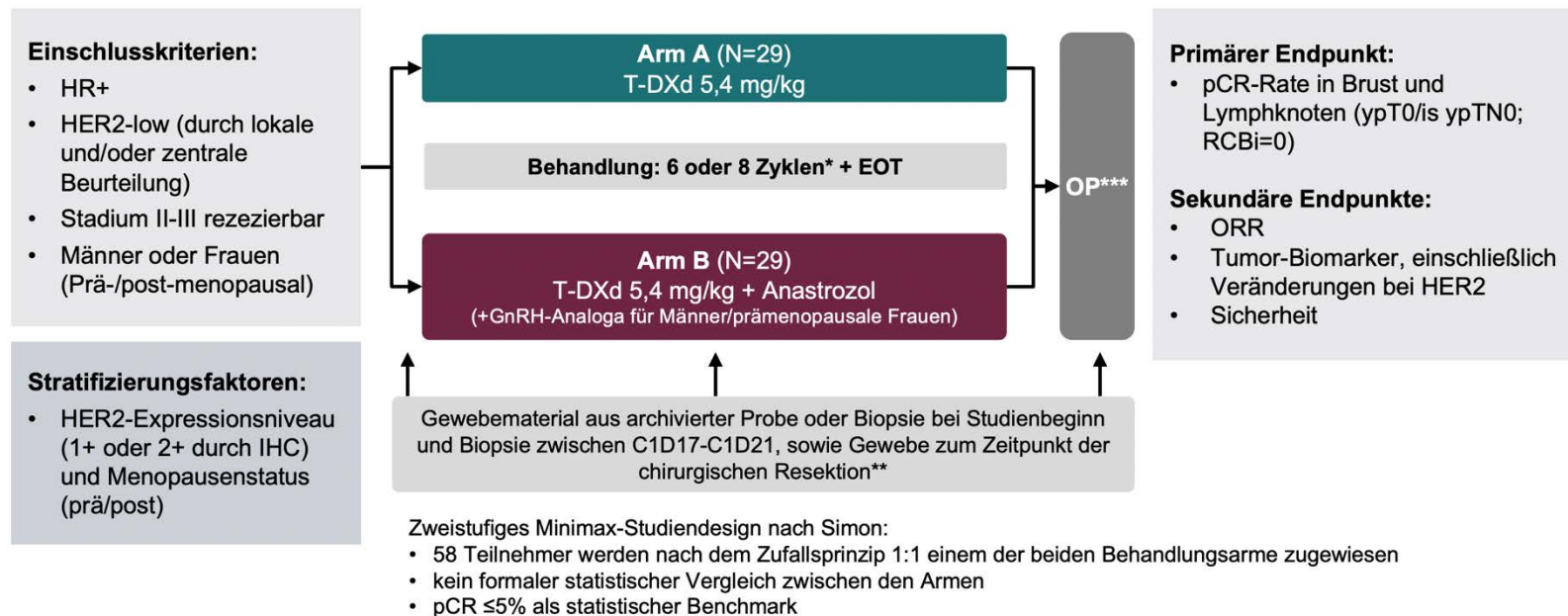
# HER2 low

## DESTINY-Breast04





# TRIO-US B-12 TALENT

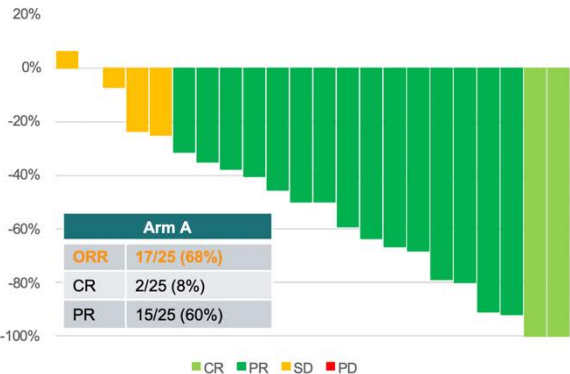


\*Ursprünglich wurden 6 Behandlungszyklen durchgeführt, im Jahr 02/2022 wurde die Anzahl der Behandlungszyklen durch eine Protokollanpassung von 6 auf 8 erhöht;

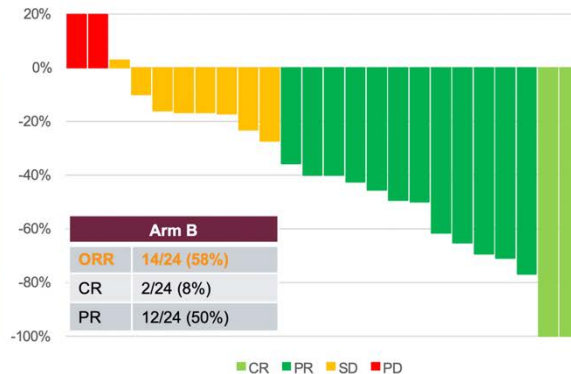
\*\*Alle für die Studie entnommenen Gewebe: zentrale pathologische Untersuchung; \*\*\* Nach der Operation, adjuvante Therapie nach Ermessen des behandelnden Arztes.  
T-DXd, Trastuzumab-Deruxtecan; RCBi, Index der Resttumorlast.

# TRIO-US B-12 TALENT

Arm A (T-DXd)  
N=25\*



Arm B (T-DXd + Anastrozol)  
N=24\*\*



Waterfall Plot, der die Veränderung der Tumorgöße nach der Behandlung mit T-DXd im Vergleich zum Ausgangswert gemäß RECIST v1.1 darstellt. Die zu behandelnde Population für die ORR umfasst alle Patienten, die mindestens einen Zyklus der Therapie laut Protokoll erhalten haben, Data Cut-Off 25.11.2022; \*4 Patienten, die noch in Behandlung sind; 3 Patienten hatten eine Bildgebung (die Behandlung wurde vorzeitig abgebrochen); \*\*5 Patienten, die noch in Behandlung sind, aber für die ORR-Analyse der Intention-to-Treat (ITT) gemäß Protokoll aufgenommen wurden

## HER2-IHC-Veränderung vom Ausgangswert bis OP mit T-DXd (zentrale Bewertung)\*



Grün: Abnehmende HER2-IHC-Färbung vom Ausgangswert bis zur OP  
Grau: Gleichbleibende HER2-IHC-Färbung vom Ausgangswert bis zur OP



# Vielen Dank für Ihre Aufmerksamkeit!

One day Alice came to a fork in the road and saw a Cheshire cat in a tree. „Which road do I take?“ she asked. „Where do you want to go?“ was his response. „I don't know“, Alice answered. „Then“, said the cat, “it doesn't matter which way you go“.



GBG

GERMAN  
BREAST  
GROUP



in Kooperation mit

**2.- 3. März 2023**  
GBG Jahrestreffen

**20** YEARS  
ANNIVERSARY

[www.gbg.de](http://www.gbg.de)