GBG 88

Denosumab Added to 2 Different nab-Paclitaxel Regimens as Neoadjuvant Therapy in Patients with Primary Breast Cancer - Time to Event analysis from the GeparX 2 × 2 Randomized Clinical Trial

Sibylle Loibl, Mattea Reinisch, Marianne Just, Michael Untch, Oliver Stötzer, Andreas Schneeweiss, Peter A. Fasching, Pauline Wimberger, Sabine Seiler, Jens Huober, Marc Thill, Kerstin Rhiem, Christine Solbach, Claus Hanusch, Carsten Denkert, Knut Engels, Natalie Filmann, Johannes Holtschmidt, Jens-Uwe Blohmer, Theresa Link

-This is a joint study by GBG and AGO-B-

Disclosures

Prof. Dr. med. Sibylle Loibl

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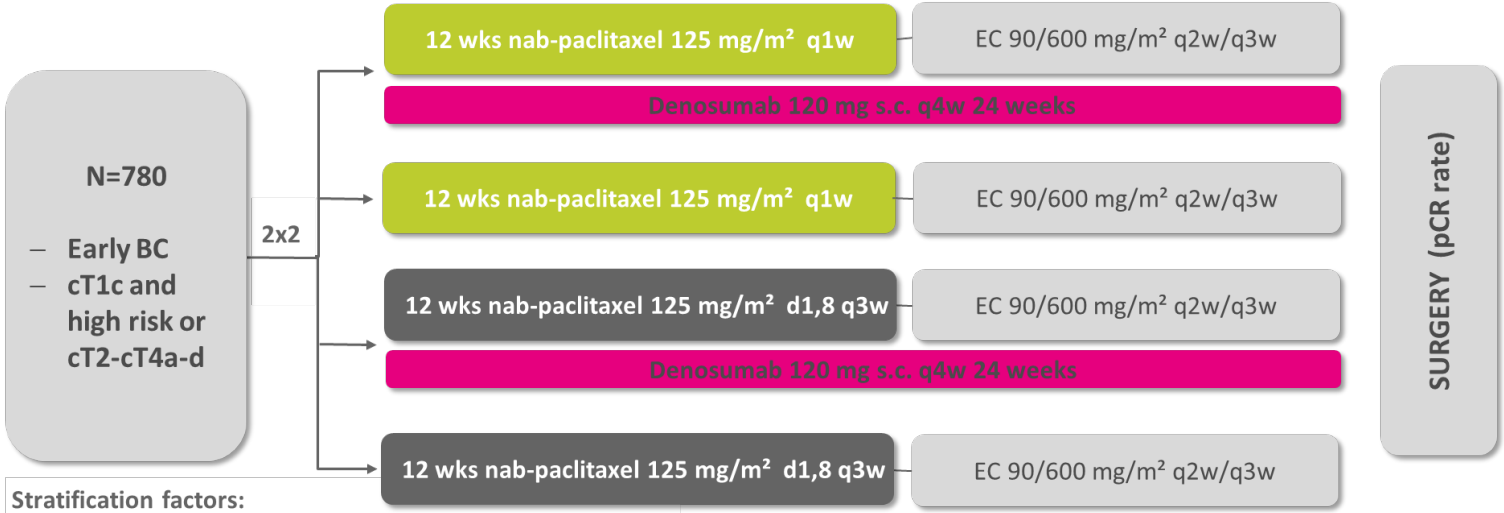
Introduction

- GeparX (GBG 88; NCT02682693) examined denosumab with anthracycline/taxane-based neoadjuvant chemotherapy (NACT) and two nab-paclitaxel schedules.



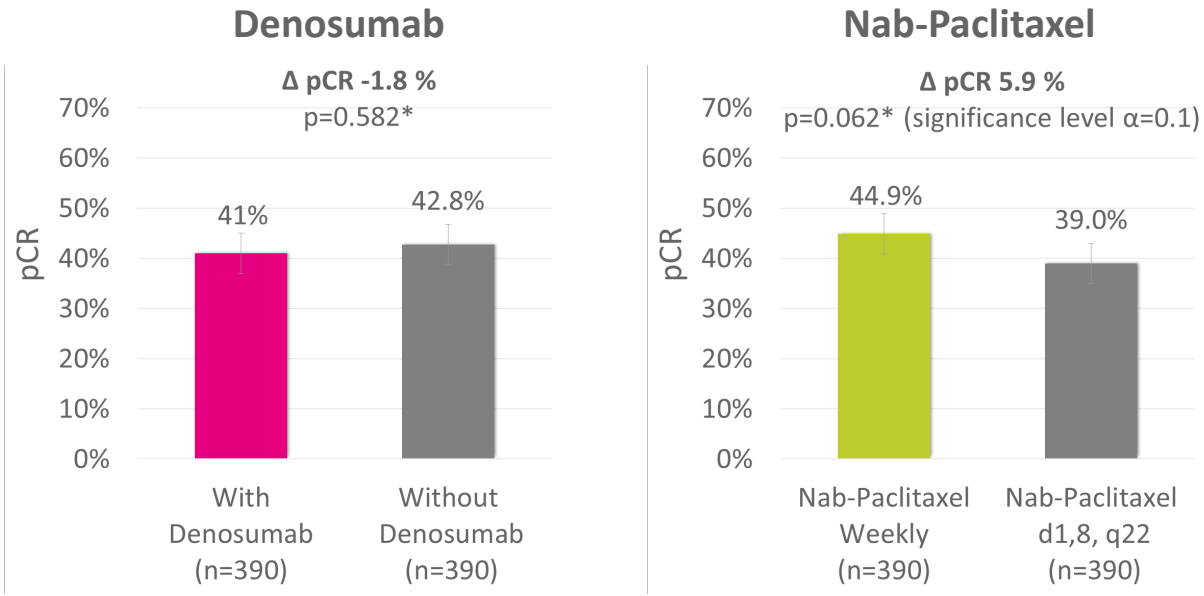
Stratification factors:
- sTILs
- Subtype
- EC schedule
- Denosumab (nab-paclitaxel randomization)

Treatment backbone:
HER2+: trastuzumab (ABP 980) + pertuzumab q3w
TNBC: carboplatin (AUC 2) q1w in addition to taxane

1. Blohmer et al. AMA Oncol. 2022

Introduction

- Weekly nab-paclitaxel demonstrated superior pathological complete response (pCR) rates, while the addition of denosumab did not significantly impact outcomes[1].



- p-value stratified test; stratified by sTILs, Subtype, EC schedule and denosumab (only nab-paclitaxel regime)

1. Blohmer et al. AMA Oncol. 2022

Objective and Patients

- Preplanned analysis of time-to-event endpoints (iDFS, DDFS, OS) based on the intention-to-treat (ITT) population

	With Denosumab N (%)*	Without Denosumab N (%)*	Nab-Pac weekly N (%)*	Nab-Pac d1,8 q22 N (%)*	Overall N (%) *
Age (years), median (range)	49.0 (23.0-78.0)	48.5 (22.0-80.0)	49.0 (23.0-78.0)	49.0 (22.0-80.0)	49.0 (22.0-80.0)
Pre-/perimenopausal	218 (55.9)	235 (60.3)	229 (58.7)	224 (57.4)	453 (58.1)
cT1/cT2	357 (92.5)	369 (95.6)	362 (94.3)	364 (93.8)	726 (94.0)
cT3/T4	29 (7.5)	17 (4.4)	22 (5.7)	24 (6.2)	46 (6.0)
cN+	155 (40.1)	154 (39.8)	152 (39.0)	157 (40.8)	309 (40.0)
HER2-/HR+	153 (39.2)	157 (40.3)	155 (39.7)	155 (39.7)	310 (39.7)
TNBC	160 (41.0)	157 (40.3)	159 (40.8)	158 (40.5)	317 (40.6)
HER2+	77 (19.7)	76 (19.5)	76 (19.5)	77 (19.7)	153 (19.6)
Ki-67 > 20%	317 (81.3)	331 (84.9)	327 (83.8)	321 (82.3)	648 (83.1)
sTILs >50%	31 (7.9)	31 (7.9)	31 (7.9)	31 (7.9)	62 (7.9)
EC q2w	206 (52.8)	208 (53.3)	207 (53.1)	207 (53.1)	414 (53.1)

* valid percent

1. Blohmer et al. AMA Oncol. 2022

Results

- After a median follow-up of 62.3 months 138 iDFS events were observed
- No new safety signals were identified

Denosumab

	With D	*Without D*	*Overall*
invasive locoregional relapse	21 (5.4)	15 (3.8)	36 (4.6)
invasive contralateral breast cancer	2 (0.5)	1 (0.3)	3 (0.4)
distant relapse	31 (7.9)	46 (11.8)	77 (9.9)
secondary malignancy	5 (1.3)	10 (2.6)	15 (1.9)
death	4 (1.0)	3 (0.8)	7 (0.9)
Overall iDFS events	63 (16.2)	75 (19.2)	138 (17.7)

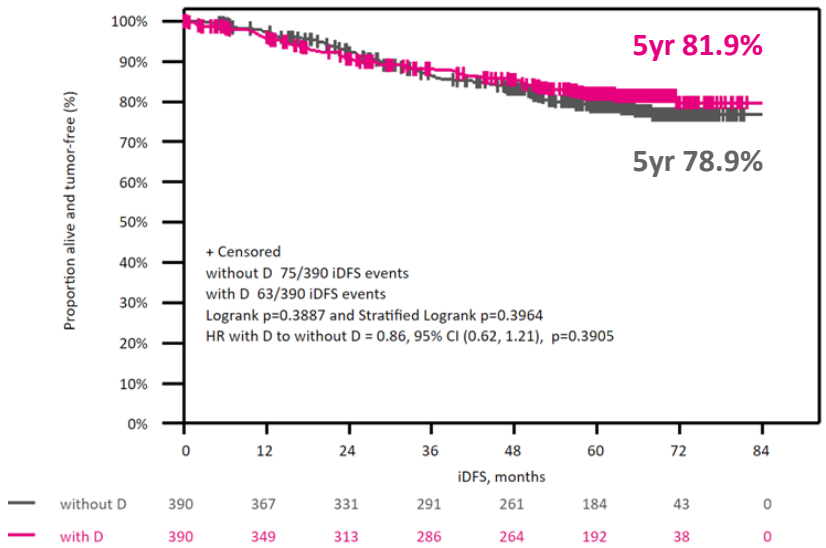
Nab-Paclitaxel

	nP weekly	*nP d1 d8*	*Overall*
invasive locoregional relapse	17 (4.4)	19 (4.9)	36 (4.6)
invasive contralateral breast cancer	1 (0.3)	2 (0.5)	3 (0.4)
distant relapse	39 (10.0)	38 (9.7)	77 (9.9)
secondary malignancy	7 (1.8)	8 (2.1)	15 (1.9)
death	2 (0.5)	5 (1.3)	7 (0.9)
Overall iDFS events	66 (16.9)	72 (18.5)	138 (17.7)

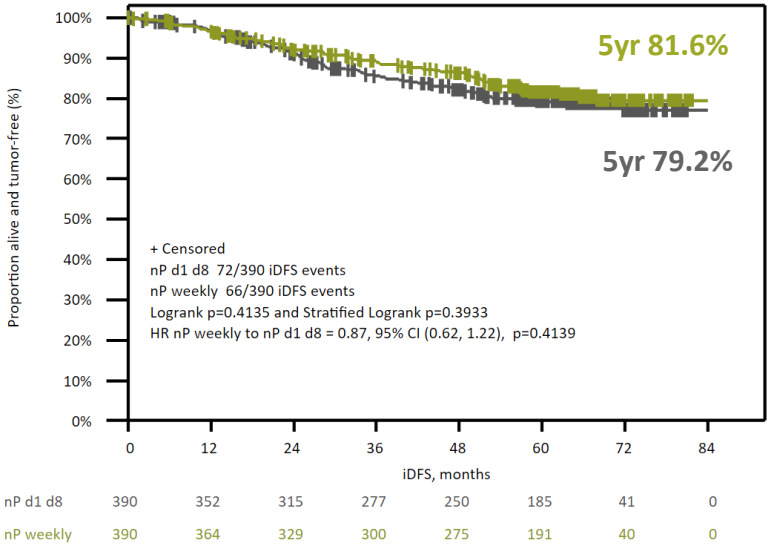
1. Loibl S et al. The Oncologist 2017; 2. Cui SABCS 2021

Results: Invasive disease free survival (iDFS)

Denosumab

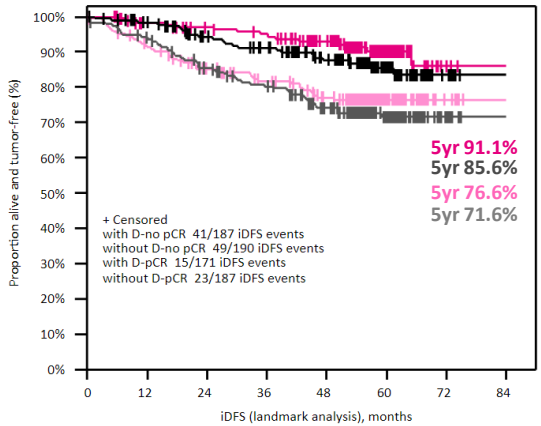


Nab-Paclitaxel



Results: stratified by pCR (Denosumab)

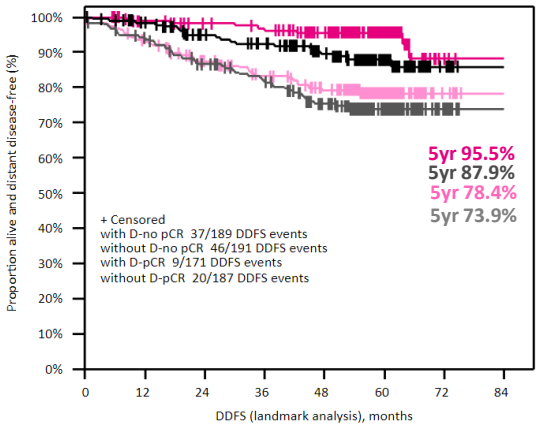
iDFS



with D-no pCR	187	167	146	133	113	52	6	0
without D-no pCR	190	175	152	138	111	55	6	0
with D-pCR	171	158	150	144	125	56	5	0
without D-pCR	187	175	153	142	118	53	6	0

	Hazard Ratio (95% CI) with D : without D	p-value	p-value for Interaction
No-pCR	0.857 (0.566, 1.30)	0.467	0.551
pCR	0.670 (0.350, 1.28)	0.228	

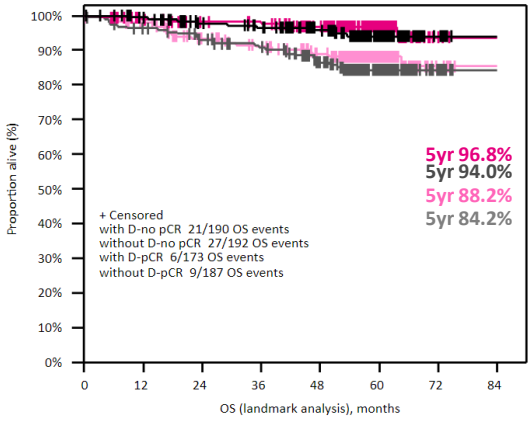
DDFS



with D-no pCR	189	170	149	135	116	53	6	0
without D-no pCR	191	176	155	141	114	58	7	0
with D-pCR	171	159	151	145	128	58	5	0
without D-pCR	187	175	154	144	120	55	6	0

	Hazard Ratio (95% CI) with D : without D	p-value	p-value for Interaction
No-pCR	0.821 (0.532, 1.27)	0.372	0.216
pCR	0.462 (0.210, 1.01)	0.054	

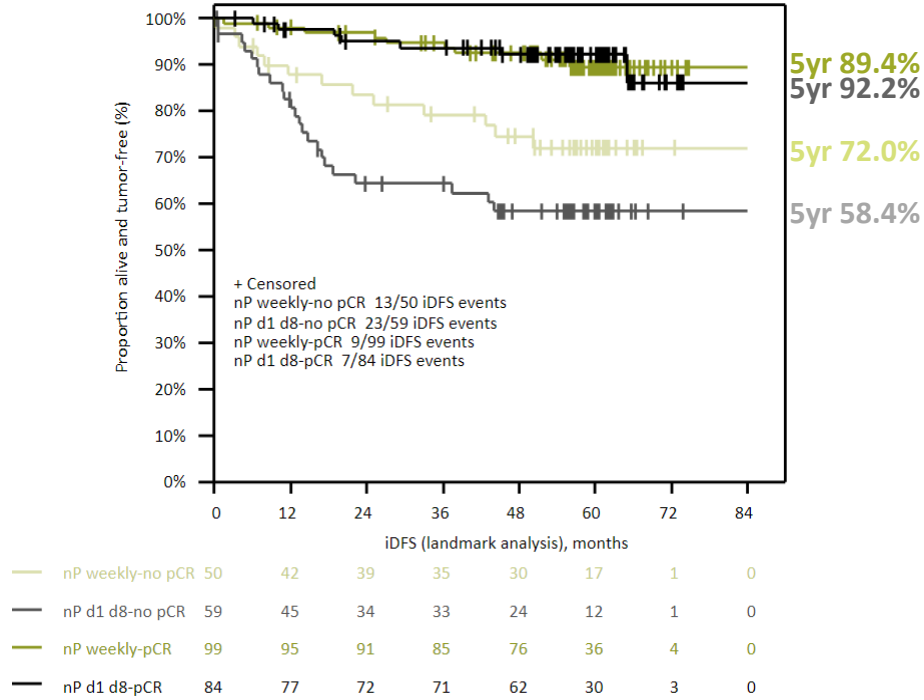
OS



with D-no pCR	190	179	157	146	126	59	7	0
without D-no pCR	192	181	168	158	131	64	8	0
with D-pCR	173	161	152	147	130	59	5	0
without D-pCR	187	177	159	151	130	58	6	0

	Hazard Ratio (95% CI) with D : without D	p-value	p-value for Interaction
No-pCR	0.807 (0.456, 1.43)	0.460	0.826
pCR	0.708 (0.252, 1.99)	0.513	

Results: iDFS by pCR in TNBC (nabPaclitaxel)



	Hazard Ratio (95% CI) nP weekly : nP d1 d8	p-value	p-value for Interaction
No-pCR	0.582 (0.294, 1.15)	0.119	0.302
pCR	1.060 (0.393, 2.83)	0.915	

1. Loibl S et al. The Oncologist 2017; 2. Cui SABCS 2021

Summary and Conclusions

- GeparX is the first randomized trial assessing the long-term effects of adding denosumab to anthracycline/taxane-based neoadjuvant therapy
- While there were fewer distant relapses observed with denosumab, the difference lacked statistical significance
- Weekly nabPaclitaxel increased the pCR rate in TNBC which translated to an increase in iDFS in non-pCR patients

1. Loibl S et al. The Oncologist 2017; 2. Cui SABCS 2021

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GBG

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