GBG
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Denosumab as add-on to different regimen of nab-paclitaxel-anthracycline based neoadjuvant chemotherapy in early breast cancer: Subgroup analyses by RANK expression and HR status

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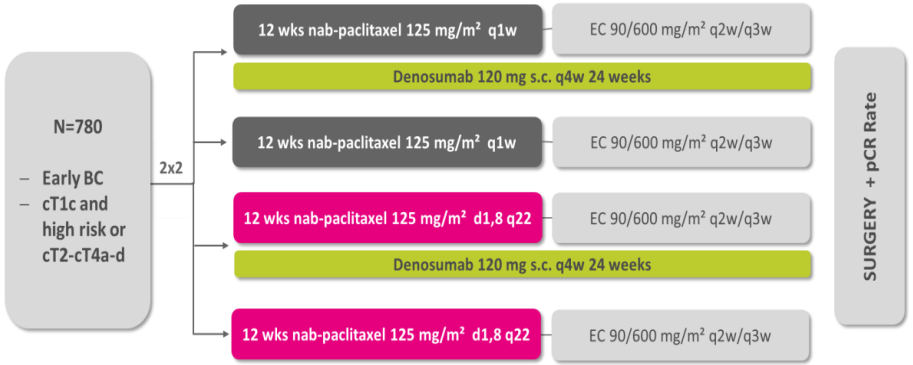
-This is a joint study by GBG and AGO-B-

AGO-B
BREAST STUDY GROUP

Disclosure Information

T. Link reports non-financial support from Pharma Mar, Daiichi Sankyo, Celgene; personal fees and non-financial support from MSD, Pfizer, Roche, Clovis; personal fees from Amgen, Novartis, Teva, Tesaro outside the submitted work. **J-U. Blohmer** reports personal fees from Amgen, AstraZeneca, Novartis, Pfizer, Roche, SonoScape outside the submitted work. **M. Untch** reports personal fees and non-financial support paid to the institution from Abbvie, Amgen, Astra Zeneca, Celgene, Daiji Sankyo, Eisai, Lilly, MSD Merck, Mundipharma, Myriad Genetics, Odonate, Pfizer, Roche, Sanofi Aventis Deutschland GmbH, TEVA, Novartis, Clovis Oncology; personal fees from BMS, Lilly, PUMA, Pierre Fabre, outside the submitted work. **P. A. Fasching** reports personal fees from Novartis during the conduct of the study; grants from BionTech, Cepheid, Novartis; personal fees from Roche, Pfizer, Celgene, Daiichi-Sankyo, Merck Sharp & Dohme, Macrogenics, Eisai, Puma, Lilly, AstraZeneca outside the submitted work. **A. Schneeweiss** reports grants from Celgene, Roche, AbbVie, Molecular Partner; expert testimony from Roche, AstraZeneca; travel expenses from Celgene, Roche, Pfizer; honoraria from Roche, Celgene, Pfizer, AstraZeneca, Novartis, MSD, Tesaro, Lilly outside the submitted work. **J. Huober** reports personal fees from Lilly, Celgene, MSD, Abbvie, EIsai,; personal fees and travel expenses from Pfizer, Roche, AstraZeneca; grants from Hexal, Celgene; grant and personal fees from Novartis; travel expenses from Daichii Sankyo outside the submitted work. **C. Jackisch** reports personal fees from AstraZeneca and Roche during the conduct of the study. **K. Rhiem** reports personal fees from AstraZeneca, Tesaro and Pfizer outside the submitted work. **C. Hanusch** reports personal fees from Roche, Novartis, Pfizer, Celgene, AstraZeneca, Lilly outside the submitted work. **W. Schmitt** reports grants from GBG during the conduct of the study; personal fees from AstraZeneca outside the submitted work. **P. Wimberger** reports personal fees from Amgen, AstraZeneca, MSD, Novartis, Pfizer, Roche, PharmaMar, Eisai, Teva, Clovis, Tesaro ousite the submitted work. **S. Seiler** reports personal fees for ad boards from Amgen, Hexal, Mundipharma; personal fee for presentations from Roche, travel expenses from Novartis outside the submitted work. **C. Denkert** reports personal fees from Novartis, Roche, MSD Oncology, Daiichi Sankyo, grants from Myriad Genetics, cofounder and shareholder from Sividon Diagnostics/Myriad outside the submitted work; patents EP18209672-cancer immunotherapy pending, EP20150702464-therapy response pending and a Software (VMscope digital pathology)-Ki67 evaluator pending. **S. Loibl** reports grant and honoraria for lectures and ad boards paid to institute from Amgen and Celgene during the conduct of the study; grants and honoraria for lectures and ad boards paid to institute from Roche, Teva, Abbvie, Astra Zeneca, Novartis, Pfizer, Daiichi-Sankyo; honoraria for lectures and ad boards paid to institute from Seattle Genetics, PriME/ Medscape, Lilly, Samsung, Eirgenix, BMS, Puma, MSD personal fees from Chugai, grants from Vifor, Immunomedics outside the submitted work; a patent EP14153692.0- immunsignature in TNBC pending. All remaining authors have declared no conflicts of interest.

GeparX Study: 2x2 Design

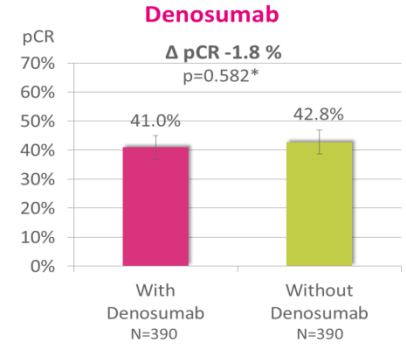


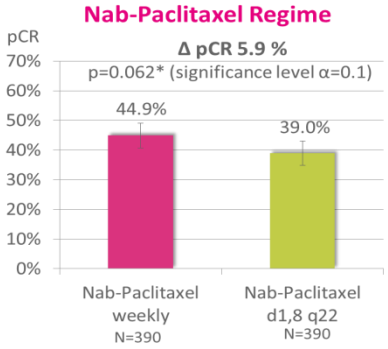
Stratification factors:
- sTILs
- Subtype
- EC schedule
- Denosumab

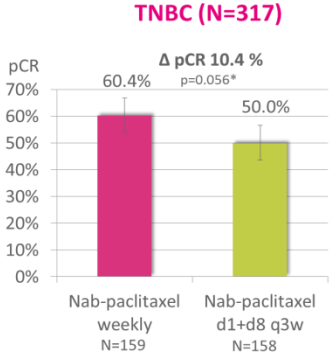
Treatment backbone:
- HER2+: Trastuzumab (ABP 980)+ Pertuzumab q3w
- TNBC: Carboplatin AUC2 q1w in addition to taxane

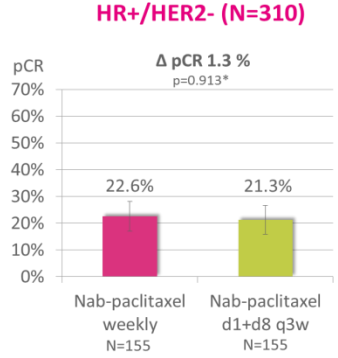
Co-primary objektives and endpoints:
- pCR (ypT0 ypN0) rate of:
  - with vs. without denosumab treatment
  - nab-paclitaxel 125mg/m² weekly vs. nab-paclitaxel 125mg/m² day 1,8 q22

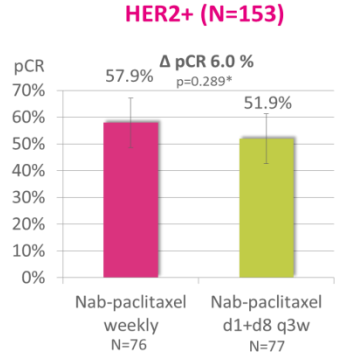
Co-primary efficacy endpoint analysis











*stratified by sTILs, Subtype, EC schedule and denosumab, as applicable

Blohmer et al. Cancer Res 2020; 80(4 Suppl): Abstract # GS3-01

Predefined Subgroups: pCR Rates

Subgroup	pCR rates Denosumab (%) with	without	p-value*	pCR rates nab-Paclitaxel (%) nP q1w	nP d1, 8 q22	p-value*
HR+/HER2-	21.6	22.3	0.961	22.6	21.3	0.913
TNBC	52.5	58.0	0.313	60.4	50.0	0.056
HER2+	55.8	53.9	0.821	57.9	51.9	0.289
EC q2w	40.3	43.3	0.609	46.9	36.7	0.038
EC q3w	41.8	42.3	0.794	42.6	41.5	0.597
>50% sTILs	71.0	61.3	0.528	71.0	61.3	0.135
≤50% sTILs	38.4	41.2	0.453	42.6	37.0	0.126
With Dmab	X	X	X	48.2	33.8	0.027
Without Dmab	X	X	X	41.5	44.1	0.665

* stratified by sTILs, Subtype, EC schedule and denosumab, as applicable

Subgroup Analysis by RANK

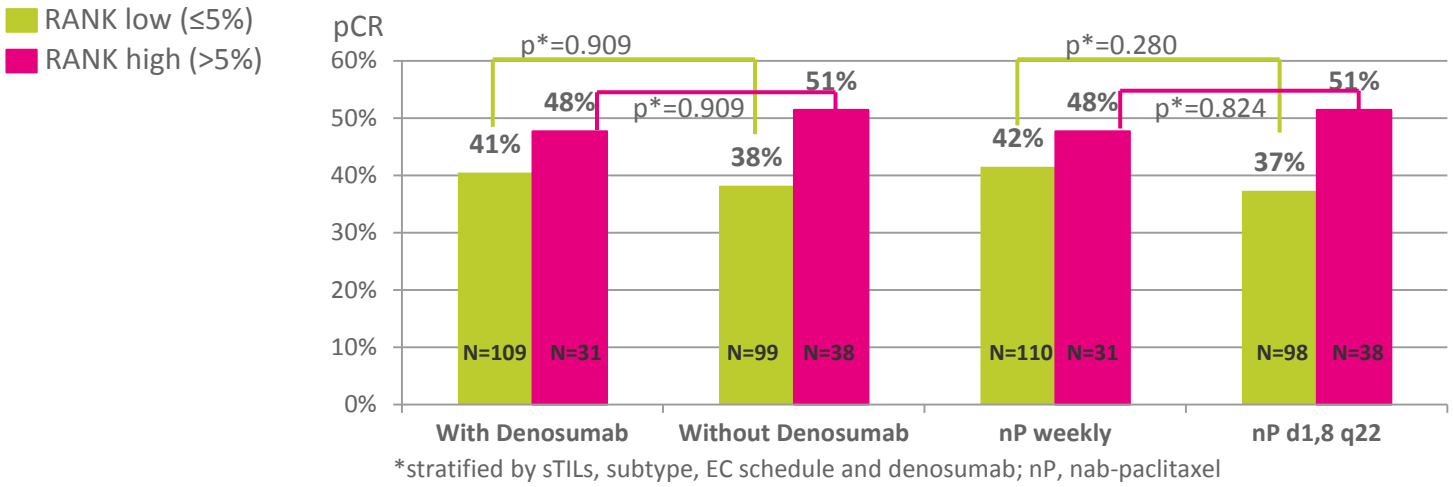
Association of RANK expression with baseline patient and tumor characteristics

Parameter	Category	RANK low (≤5%), N (%)	RANK high (>5%), N (%)	p-value
Age (years)	<40	82 (15.5)	45 (32.4)	<0.001
BC subtype	HR+/HER2-	233 (44.1)	33 (23.7)	<0.001
	TNBC	182 (34.5)	87 (62.6)	
	HER2+	113 (21.4)	19 (13.7)	
Tumor grade	G3	336 (63.6)	104 (74.8)	0.033
Ki-67	>20%	426 (80.7)	127 (91.4)	0.002
sTILs	median (range)	10.0 (0.0-90.0)	20.0 (2.0-90.0)	0.002

- Of the 780 patients included in GeparX study, 667 had evaluable RANK protein values.
- RANK expression was categorized at 75th percentile (Q3) into low (≤5%) or high (>5%).
- A high RANK expression was detected in 139/667 (20.8%) of the patients.

Pfitzner B et al.
Breast Cancer Res Treat. 2014.

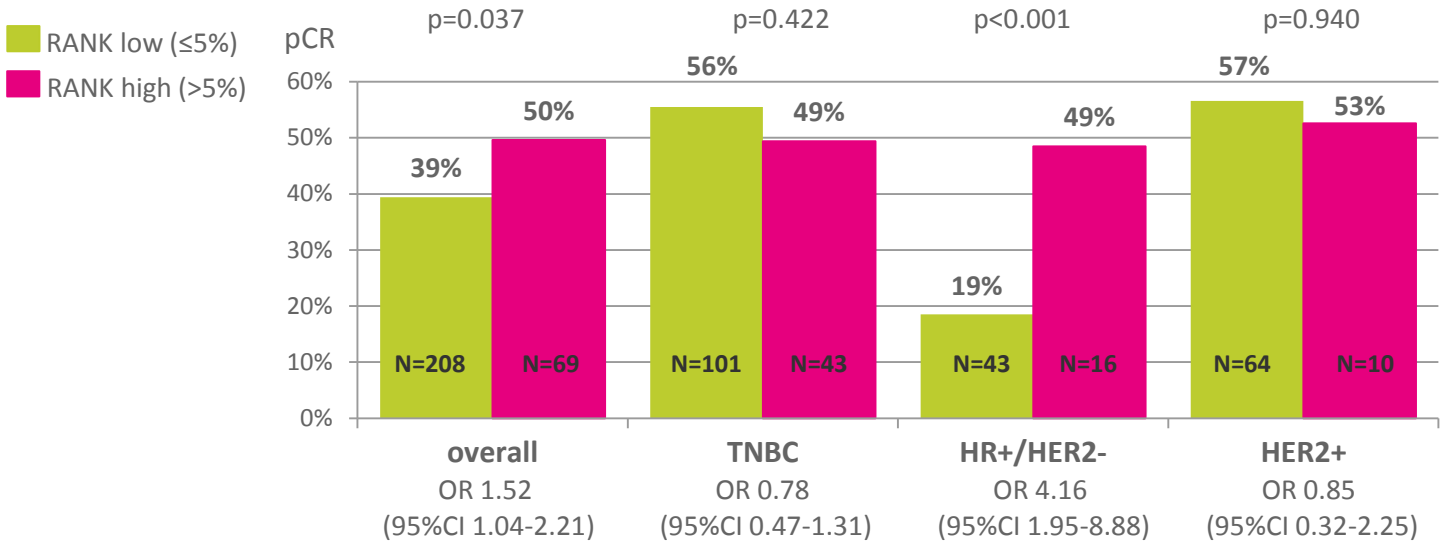
pCR Rates by RANK and Treatment



*stratified by sTILs, subtype, EC schedule and denosumab; nP, nab-paclitaxel

Parameter	Denosumab			Nab-paclitaxel (nP) regime		
	OR (with vs. without) [95% CI]	p-value	interaction p-value	OR (nP weekly vs. nP d1,8 q22) [95% CI]	p-value	interaction p-value
RANK low	1.10 [0.78-1.56]	0.589	0.528	1.19 [0.84-1.69]	0.318	0.833
RANK high	0.86 [0.44-1.68]	0.667		1.30 [0.67-2.52]	0.447	

pCR Rates by RANK and Subtype



Interaction Test RANK*subtype
(%, high vs low) p=0.0012

- Overall, RANK expression did not add additional predictive value (OR=1.05 [95%CI 0.69-1.60], p=0.823) when adjusted for BC subtype and the continuous variables age, Ki-67 and sTILs in multivariate model.
- In HR+/HER2- RANK expression was an independent significant predictor of pCR (OR=2.98 [95%CI 1.30-6.79], p=0.010) when adjusted for the continuous variables age, Ki-67 and sTILs.

Summary and Conclusion

- A high RANK expression was detected in 20.8% of the patients.
- A high RANK expression was associated with significantly higher pCR rates (49.6% vs. 39.4%; p=0.037).
- This effect was driven by patients with HR+/HER2- BC.
- However, a clinical benefit of denosumab in relation to RANK expression could not be shown. Further explorative analyses are still ongoing.

Acknowledgement

- All patients and their families
- All participating sites
- Slides are available on the webpage of GBG: www.gbg.de

Cooperating partners

Central Pathology:
Carsten Denkert
Wolfgang Schmitt
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Britta Beyer

Financial and Drug Support

RANK Immunohistochemistry

Cryostorage Biomaterial

Patient Self-Registry

GBG

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