GeparX - GBG 88
Investigating Denosumab as an add-on to neoadjuvant chemotherapy in RANK/L-positive or RANK/L-negative primary breast cancer and two different nab-paclitaxel schedules in a 2x2 factorial design

Jens-Uwe Blohmer, Theresa Link, Sherko Kümmel, Michael Untch, Marianne Just, Peter A. Fasching, Andreas Schneeweiss, Pauline Wimberger, Oliver Stötzer, Jens Huober, Marc Thill, Christian Jackisch, Kerstin Rhiem, Claus Hanusch, Carsten Denkert, Knut Engels, Valentina Nekljudova, Sibylle Loibl

-This is a joint study by GBG and AGO-B-
2x2 Study Design

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

N=780
- Early BC
- cT1c and high risk or cT2-cT4a-d

SURGERY + pCR Rate

12 wks nab-paclitaxel 125 mg/m² q1w → EC 90/600 mg/m² q2w/q3w
12 wks nab-paclitaxel 125 mg/m² q1w → EC 90/600 mg/m² q2w/q3w
12 wks nab-paclitaxel 125 mg/m² d1,8 q22 → EC 90/600 mg/m² q2w/q3w
12 wks nab-paclitaxel 125 mg/m² d1,8 q22 → EC 90/600 mg/m² q2w/q3w
Co-Primary Objectives and Endpoint

To compare the pCR (ypT0 ypN0) rate of:

- neoadjuvant treatment with or without denosumab in addition to neoadjuvant chemotherapy and

- of nab-Paclitaxel 125mg/m² weekly with nab-Paclitaxel 125mg/m² day 1,8 q22
Results pCR Rate (ypT0 ypN0)

• p-value stratified test; stratified by sTILs, Subtype, EC schedule and denosumab (only nab-paclitaxel regime)
Results pCR Rate in Subgroups for Nab-Paclitaxel Regimen

TNBC (N=317)

\[ \Delta \text{pCR 10.4 \%} \]
\[ p=0.056^* \]

\[ 60.4\% \]
\[ 50.0\% \]

HR+/HER2- (N=310)

\[ \Delta \text{pCR 1.3 \%} \]
\[ p=0.913^* \]

\[ 22.6\% \]
\[ 21.3\% \]

HER2+ (N=153)

\[ \Delta \text{pCR 6.0 \%} \]
\[ p=0.289^* \]

\[ 57.9\% \]
\[ 51.9\% \]

*p-value stratified test; stratified by sTILs, subtype, EC schedule and denosumab

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Summary and Conclusion

- In the GeparX study the addition of denosumab to NACT did not increase the pCR rate in early BC (41% with denosumab vs 43% without denosumab; p=0.582)
- Nab-paclitaxel 125mg/m² weekly resulted in a significantly higher pCR rate than given d1,8 q22 (45% vs 39%; p=0.062)
- Nab-paclitaxel 125mg/m² weekly resulted in a higher rate of SAEs and a higher rate of treatment discontinuations mainly due to adverse events compared to nab-paclitaxel 125mg/m² d1,8 q22
- In TNBC optimized NACT with nab-paclitaxel 125mg/m² weekly plus carboplatin followed by EC achieves a pCR rate of at least 60%
- Further translational research (e.g. RANK expression) is ongoing