Survival analysis of the prospectively randomized phase III GeparSepto trial comparing neoadjuvant chemotherapy with weekly nab-paclitaxel with solvent-based paclitaxel followed by anthracycline/cyclophosphamide for patients with early breast cancer – GBG69


Introduction
The GeparSepto study showed that the substitution of paclitaxel (P) with nab-paclitaxel (nP) followed by epirubicin/cyclophosphamide (EC) as neoadjuvant chemotherapy increased the rate of pathological complete response (pCR) from 29% to 38% (p<0.001). A pronounced improvement of pCR from 26% to 48% (OR: p<0.001) was achieved in patients with triple-negative BC (TNBC) (Untch et al. Lancet Oncology 2016). It has not yet been shown whether these effects on pCR will be translated into a survival benefit. We here report the survival analysis of the GeparSepto trial.

Patients and Methods
In the GeparSepto trial (NCT01583426) patients were randomized in a 1:1 ratio to receive either nP 125mg/m² or P 80 mg/m² q1w for 12 weeks followed by 4 cycles of conventionally dosed EC (E: 90mg/m²; C: 600 mg/m²) q3w (Furlanetto et al. Annals Oncol 2016). Patients with HER2+ tumors received trastuzumab 6(8)mg/kg q3w and pertuzumab 420(840)mg q3w concomitantly to all chemotherapy cycles (Loibl et al. Annals Oncol 2016). Patients with untreated, histologically confirmed uni- or bilateral, cT2- cT4d breast carcinoma, and no clinically relevant cardiovascular and other co-morbidities were included. Primary objective was pCR rate (ypT0 ypN0). Secondary objectives were invasive disease-free survival (IDFS), and overall survival (OS) overall and according to stratified subpopulations, amongst other time to event endpoints, quality of life focusing on peripheral sensory neuropathy (PNP), treatment of PNP, and cardiac toxicity, detection of circulating tumor (ct) DNA at the time of surgery and during follow up and correlation with pCR and early relapses. The IDFS analysis is planned after 248 events have occurred. The log-rank test will have 80% power to detect an improvement of the 5 year IDFS from 75% to 81.8% (HR=0.70) at a 2-sided significance level of α=0.05.

Results
In 69 German centers, 1229 patients were randomly assigned (07/2012 – 12/2013) to receive either nP (606) or P (600). nP was given for the majority of cycles at a dose of 150mg/m² to 179 patients and at a dose of 125mg/m² to 426 patients. Follow-up is still ongoing. The expected number of events will be awaited for October 2017.
**Conclusion**
Neoadjuvant GeparSepto study demonstrated a significantly higher pCR rate when patients receivednP instead of P as part of an anthracycline/taxane based sequential chemotherapy. The expected long-term results will help to assess the overall benefit of nP in BC and the surrogate value of pCR for survival endpoints.