The GeparSepto (NCT01583426), a phase 3 randomized neoadjuvant trial in patients with early breast cancer (BC), showed that nab-paclitaxel (nP) increased the pathological complete response (pCR) rate compared to paclitaxel (P) as part of a sequential taxane followed by anthracycline/docetaxel (EC) neoadjuvant chemotherapy (EC) in women aged 80 years or younger. nab-paclitaxel was significantly better than P in grade 3 sensory neuropathy (PSN) with nab-paclitaxel (150mg/m²) weekly compared to paclitaxel (80mg/m² weekly). Therefore the dose of nab-paclitaxel was reduced to 125mg/m² weekly (nP125) during the trial. The final safety results of GeparSepto showed that PSN grade 3 was significantly higher after nab-paclitaxel (10% vs. 3%, p<0.001). A sub-analysis showed that the risk-benefit ratio of nP125 was improved over nP150 with better drug adherence and relative dose intensity, lower frequency of PSN and comparable pCR.

We report follow-up (FU) data on PSN occurrence and resolution.

Objectives

Primary objectives:

- Rate of PSN grade 2-4 and 3-4 in patients treated with nP150, nP125 and P
- Percentage of patients treated with nP150, nP125 and P with PSN grade 2-4 and 3-4 resolved to grade 1 at the end of treatment (EOT), i.e. 30 days after the last chemotherapy administration
- Percentage of patients treated with nP150, nP125 and P with PSN grade 2-4 and 3-4 resolved to grade 1 during FU
- Time to resolution (tTR) of PSN grade 2-4 and 3-4 for P compared to nP150 and nP125 compared to nP150

Materials and Methods

Patients with untreated BC received paclitaxel 80mg/m² weekly or nab-paclitaxel 150/125mg/m² weekly followed by four cycles of epirubicin/paclitaxel (EC) every three weeks. In patients with HER2+ tumors trastuzumab 6mg/kg (loading dose 8mg/kg) and pertuzumab 420mg (LD 840 mg) were administered every three weeks (Figure 1). In case of PSN grade 2, nab-paclitaxel treatment was delayed by one week and subcutaneous epirubicin was administered at a lower dose (100mg/m² weekly). If symptoms did not resolve to grade 1 within 3 weeks, taxane treatment was stopped. In case of PSN grade 3-4 taxane treatment was discontinued. If PSN grade 2-4 was observed after the end of the study the protocol was amended in order to collect long-term data on PSN outcome as well as on treatment modalities. Since the data were retrospectively analyzed, time to PSN resolution could have been overestimated. PSN will be reported according treatment and dose received on day 1.

Results

- Overall 601 patients received P80, 220 patients nP150 and 385 patients nP125 on day 1. PSN grade 2-4 was observed in 19.0% of patients treated with P80 and in 41.8% with nP125 vs. 39.2% with nP125 (nP150 vs nP125: p=0.531). Grade 3-4 PSN was reported in 2.7% of patients in the P80 group, 14.5% in the nP150 group and 19.2% in nP125 (p=0.019). PSN grade 3-4 did not resolve at EOT in 29.8% of P 30.8% of nP150 and 29.8% of nP125. PSN grade 3-4 did not resolve at EOT in 14.4% of P, 35.8% of nP150 and 29.8% of nP125. PSN grade 3-4 did not resolve at EOT in 31.3%, 62.8% and 58.1% of the patients respectively (Figure 2).
- After a median FU of 162 weeks after EOT, the remaining PSN grade 2-4 was reduced to grade 1 in 61.8% of patients with P, 45.7% with nP150 and 51.1% with nP125, whereas PSN grade 3-4 resolved in 100.0%, 40.0% and 44.4% of patients respectively.
- The TTR of PSN grade 2-4 was significantly different between nP150 and nP125 (p<0.001); no significant difference was observed between P and nP125 (Figure 3A). Similarly, the TTR of PSN grade 3-4 was significantly different between nP150 and nP125 (p=0.043) but no significant difference was observed for P vs. nP125 (p=0.535) (Table 1; Figure 3B).

Conclusions

- nP125 is associated with a lower frequency of PSN compared to nP150 but higher frequency than P80. The PSN occurred after nP125 was associated with a more rapid resolution compared to nP150. Follow-up is continuing. Markers for selecting patients at risk are needed.

References

2. Zvon Michal G, Urdhuri M, Kemmler G, et al. Paclitaxel and nab-paclitaxel at a dose of 125 mg/m² weekly is more efficacious but less toxic than at 150 mg/m². Results from the randomized neoadjuvant randomized GeparSepto study (GBG 69). Presented at SABCS 2015.

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