Phase 1b study of WNT inhibitor vantictumab (VAN, human monoclonal antibody) with paclitaxel (P) in patients (pts) with 1st- to 3rd-line metastatic HER2-negative breast cancer (BC)

**BACKGROUND**

- Failure to effectively target cancer stem cells (CSCs) may be responsible for the limited success of targeted therapeutics in the breast, while CSCs are a driver of therapy resistance.
- Vantictumab (VAN) is a fully human IgG1 monoclonal antibody that binds to β-catenin, thereby inhibiting the Wnt signaling pathway.
- Nonclinical data show that VAN has broad anti-tumor activity in patient-derived breast cancer xenograft models, in particular when combined with taxanes.
- Phase 1a predictions (grey area, 10th, 50th, 90th percentiles).

**STUDY OVERVIEW**

- Established OMP-PE13 (upper panel) or OMP-B60 (lower panel) tumors were treated with vanitictumab (VAN) q4w; cohorts of ≥6 patients, 28 days assessment window for dose-limiting toxicities (DLTs)
- 3+3 dose escalation rules, 28-day assessment window for dose-limiting toxicities (DLTs)
- Cohorts of ≥6 patients with DLT (28 days)
- Nonclinical data:
  - Vantictumab (VAN) has broad anti-tumor activity in patient-derived breast cancer xenograft models, in particular when combined with taxanes.
  - Phase 1a predictions for VAN, 180%, 90%, 100% decrease or increase of tumor volume

**ONCOLOGICAL EFFICACY DATA**

- Activity of vantictumab in patient-derived breast cancer xenografts
- Exploratory Objectives
  - Neuropathy Peripheral
  - Hypophosphataemia
  - Anaemia
  - Alopecia
  - Constipation
- Additional AEs >10%, regardless of attribution: headache (8), muscle spasms (7), dyspnea (6), pyrexia (6), fatigue (5), anemia (5), neutropenia (5), infection (6), constipation (5)

**EXPLORATORY PREDICTIVE BIOMARKERS**

- Skin gene signature-only assay achieved best performance
- A more sensitive bone turnover marker was identified: cathepsin K increase of ≥50% and ≥50% decrease of procollagen type I C-terminal telopeptide
- Osteoblast markers were significantly related to tumor growth in both models. Osteoblast: 15% increase in procollagen type I C-terminal telopeptide, 15% decrease in procollagen type I C-terminal telopeptide

**SAFETY**

- Vantictumab-related Adverse Events (AEs) >5% and all AEs >10%:
  - Patients with elevated alanine aminotransferase: 80, 19 (61%)
  - Patients with a terminal half-life of 70%: 1, 2 (9.7%)

**BONE SAFETY**

- Bone-preservation therapy for more patients and target with specific bone safety plan
- Bone-safety profile in place
- Site report on safety of patients with DLT pathway genes

**CONCLUSIONS**

- Vontictumab is part of Oncogene's WNT pathway into the clinic
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