Inhibition of tumor angiogenesis has proven to be a successful approach to treating cancer and two ligands responsible for tumor angiogenesis are vascular endothelial growth factor (VEGF) and Delta-like ligand 4 (DLL4) which is one of the 5 ligands in the Notch pathway. In addition, inhibition of DLL4 reduces the homing of a tumor in xenograft models by reducing the number of tumor cells homing to the tumor that is directed against both human DLL4 and VEGF. Navicixizumab was developed specifically to block the anti-DLL4 and anti-VEGF vascular homing and angiogenic efficacy for their respective ligands. Navicixizumab was efficacious in all of the human tumor xenograft models tested which included breast, colon, gastric, glioblastoma, non-small cell lung cancer, pancreatic, ovarian and renal cell carcinoma. Finally, navicixizumab had a response rate of 85%/10% of heavily pretreated ovarian cancer pts who were treated in an earlier single agent Phase 1 trial.

**Background**

- **Patient Demographics (n=34)**
  - Navicixizumab Dose Level: 2 mg/kg, 3 mg/kg, Total
  - NAVICIXIZUMAB Dose: 100 mg/kg, 150 mg/kg, Total
  - NAVICIXIZUMAB Total: 200 mg/kg, 300 mg/kg, Total

**Preclinical Xenograft Data**

- **Efficacy in ovarian xenograft models as a single agent and in combination with paclitaxel**
- **Reduces tumor growth and homogeneity**

**Methods**

This is an ongoing Phase 1b trial of navicixizumab in platinum resistant ovarian cancer pts who have failed >2 prior therapies &/or bevacizumab. Paclitaxel 210 mg/m² was given on Days 1, 8 and 15. A navicixizumab was given on Days 1, 8 and 15 of every 28-day cycle. This study was designed as a dose escalation trial testing navicixizumab doses of 2 or 3 mg/kg followed by an expansion cohort of 3 or 4 mg/kg in 30–34 pts. The expansion cohort was undertaken with 3 mg/kg as higher doses did not show increased activity, so it resulted in more severe toxicity. The study was designed to evaluate navicixizumab for hypertension being employed. Thirty-four patients have been enrolled of the study at 7 centers. Subjects were assessed for safety, immunogenicity, PK, biomarkers, and efficacy. Patients enrolled in the dose escalation cohort were treated for 2 cycles from the time of the first dose through Day 28. The maximum tolerated dose (MTD) was defined as the highest dose level at which ≤1 of 6 patients experienced a≥CTC 3.1, 6 patients will ultimately be treated at the MTD dose level. Three subjects were enrolled in cohort 1 and dosed at 3 mg/kg and 2 patients were enrolled in cohort 2 and dosed at 4 mg/kg. While there were no CTC 3.1, 16 patients were enrolled at navicixizumab 3 mg/kg on the ongoing single-agent Phase 1 trial, which suggested that maximal efficacy was achieved at the 3 mg/kg navicixizumab dose in the expansion portion of the study. Data entered in the database through August 12, 2016 are presented. This study is sponsored by OncoMed Pharmaceuticals Inc.

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