Phase 1b of WNT inhibitor ipafricept (IPA, decoy receptor for WNT ligands) with carboplatin (C) and paclitaxel (P) in patients (pts) with recurrent platinum-sensitive ovarian cancer (OC)

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**BACKGROUND**

Ipafricept (IPA) is a recombinant human carcinoma-derived secreted protein (CHA-1) with high-affinity binding to Wnt proteins that can inhibit downstream Wnt signaling. It is an fH cation-independent mannose 6-phosphate receptor that can bind to the Wnt/β-catenin signaling pathway.

**OBJECTIVES**

To assess safety, tolerability, and preliminary antitumor activity of ipafricept in combination with paclitaxel and carboplatin in patients (pts) with recurrent platinum-sensitive ovarian cancer.

**MATERIALS AND METHODS**

Pts with histologically confirmed recurrent platinum-sensitive ovarian cancer who had failed ≥ 2 prior therapies were enrolled in this Phase 1/2a multicenter, open-label, dose-escalation study. A total of 34 pts were treated in 4 dose levels: 0 mg/kg, 1 mg/kg, 5 mg/kg, and 10 mg/kg. The primary endpoint was the determination of optimal phase I dose (O-PID) (Dose level 1: 5 mg/kg Q3W; Dose level 2: 10 mg/kg Q3W). Secondary endpoints included antitumor activity, safety, PK/PD analyses, and exploration of mechanisms of action.

**RESULTS**

33 pts received treatment across the 4 dose levels: 8 0 mg/kg, 11 1 mg/kg, 10 5 mg/kg and 4 10 mg/kg (100%). Of these, 28 pts (85%) experienced ≥ 1 adverse event (AE), 23 pts (70%) ≥ 1 grade 3/4 AE, and 20 pts (61%) ≥ 1 emergent AE. The median number of cycles to treatment discontinuation was 2 (range 1-22). PFS results are pending. 5 pt deaths were observed across all dose levels: 1 dose level 0, 1 dose level 1, 2 dose level 5, and 1 dose level 10. 32 pts had best response data: 7 (21.9%) responders (PR, CR, SD), 19 (59.4%) stable disease (SD), 4 (12.5%) progressive disease (PD), and 2 (6.3%) unassessable. The median time to progression (TTP) was 7.5 months (range 22-120). The median overall survival (OS) was 12.5 months (range 3-45). No disease-related deaths were observed.

**CONCLUSIONS**

IPA was well tolerated in combination with carboplatin and paclitaxel in patients with recurrent platinum-sensitive ovarian cancer. No new safety signals were observed with the added regimen. Clinical activity was observed with IPA in combination with chemotherapy, and future studies of IPA are warranted.

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