

## EFFICACY AND SAFETY OF AK112, AN ANTI-PD-1/VEGF-A BISPECIFIC ANTIBODY, IN PATIENTS WITH PLATINUM-RESISTANT/REFRACTORY EPITHELIAL OVARIAN CANCER IN A PHASE 1 STUDY

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**Background** Platinum-resistant/refractory epithelial ovarian cancer (PROC) is a high unmet medical need with limited treatment options and a median survival of 12–15 months.<sup>1</sup> Single agent PD-(L)1 inhibitors have objective response rates (ORR) of less than 10%.<sup>2,3</sup> However, combination of nivolumab plus bevacizumab yields a higher ORR of 16.7% in platinum-resistant patients (pts), indicating synergistic activity between PD-1 inhibition and anti-angiogenic therapy in this disease.<sup>4</sup> Here, we present initial efficacy and safety data for AK112, a bispecific antibody targeting PD-1 and VEGF-A, in pts with PROC. **Methods** Pts with PROC were enrolled in an ongoing Phase 1a/1b study of AK112 (NCT04047290). Tumor assessments based on RECIST v1.1 were performed once every 8 weeks/2 cycles for the first 12 months, and every 12 weeks thereafter. **Results** As of 16 July 2021, 19 PROC pts, of which 6 had platinum-refractory disease, have received AK112 at doses ranging from 3 mg/kg to 30 mg/kg Q2W. Seventeen pts (89.5%) had  $\geq 2$  lines of prior therapy in the recurrent/metastatic setting and 7 pts (36.8%) had prior bevacizumab. Seventeen pts had at least 1 post-baseline tumor assessment. Median duration of follow-up was 4.5 months. ORR was 29.4% (5/17; 2 clear cell, 3 high-grade serous). Among the 5 responders, 3 pts received 20mg/kg Q2W AK112 and 1 pt each had 3mg/kg and 10mg/kg Q2W AK112. Median duration of response was not reached. One pt, who had clear cell PROC and received prior immune checkpoint inhibitor (ICI) therapy, had tumor shrinkage of 70% and continued treatment for more than 17 months. Another pt, who had high-grade serous ovarian cancer and prior treatment with bevacizumab, had tumour shrinkage of 65% and continued treatment for more than 4 months. Disease control rate (DCR) was 76.5% (13/17), with tumor shrinkage observed in 11 pts (64.7%). Twelve out of 19 (63.2%) pts experienced treatment-related adverse events (TRAEs). Three pts (15.8%) experienced Grade 3 TRAEs (hypertension and transaminitis in 1 pt; and hypertension and colitis). There were no Grade 4–5 TRAEs. Commonly reported TRAEs were hypertension (15.8%), arthralgia (15.8%), fatigue (15.8%), hypothyroidism (10.5%) and rash (10.5%).

**Conclusions** The initial results from Study AK112-101 demonstrate that AK112 garners an encouraging anti-tumor activity and a favorable safety profile in patients with platinum-resistant/refractory epithelial ovarian cancer. AK112 will be further evaluated for the treatment of platinum-resistant/refractory epithelial ovarian cancer in a Phase 2 study.

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**Trial Registration** ClinicalTrials.gov Identifier: NCT04047290

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**Ethics Approval** This study received ethics approval from Bellberry Human Research Ethics Committee (HREC) on 05 Nov 2019 (Application number 2019-05-459-AB). In accordance with ICH Good Clinical Practice Guidelines and the Declaration of Helsinki, study participants gave informed consent voluntarily before participating in this study.

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