

A PHASE 1B/II CLINICAL STUDY OF AK112, A PD-1/VEGF BISPECIFIC ANTIBODY, IN COMBINATION WITH OLAPARIB IN BRCA GERMLINE WILD-TYPE PLATINUM SENSITIVE RECURRENT OVARIAN CANCER

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Background Ovarian cancer is the most lethal gynecologic malignancy. Most patients will experience disease recurrence after initial platinum-based chemotherapy. Although PRAP inhibitors showed clinical benefit in terms of progression free survival (PFS) as recurrence therapy in platinum-sensitive ovarian cancer with BRCA mutation, there is limited treatment options for patients who are BRCA wild-type. MEDIOLA study showed that the combination of PD-L1 inhibitor (durvalumab) plus PARP inhibitor (olaparib) and bevacizumab demonstrated higher ORR and PFS than reported for PD-1 and PARP inhibitor doublet or single-agent PARP or VEGF inhibitors in non-gBRCAm platinum-sensitive relapsed ovarian cancer.¹ Therefore, AK112, a bispecific antibody against PD-1 and VEGF, combined with PARP inhibitor may achieve a better anti-tumor effect in recurrent ovarian cancer.

Methods This multicenter, open-label, phase Ib/II study will evaluate the safety and efficacy of AK112 in combination with PARP inhibitor in BRCA1/2 germline wild-type (gBRAC1/2 WT) platinum-sensitive recurrent ovarian cancer patients. The dose-escalation phase will evaluate three dose levels of AK112 (10mg/kg, 20mg/kg, and 30mg/kg Q2W) in combination with fixed dose of olaparib (300 mg, BID) using a 3+3 study design to determine the recommended Phase 2 dose (RP2D). Phase II study will evaluate the efficacy and safety of AK112 at RP2D in combination with olaparib in subjects with BRCA1/2 germline wild-type (gBRAC1/2 WT) platinum-sensitive recurrent ovarian cancer. The primary efficacy endpoint is objective response rate (ORR) based on RECIST v1.1. Secondary endpoints include disease control rate (DCR), duration of response (DoR), time to response (TTR), progression free survival (PFS), overall survival (OS), pharmacokinetics, immunogenicity, the correlation between the antitumor activity and PD-L1 expression or the gBRCA1/2 mutation status in peripheral blood. Exploratory endpoints are the correlations between clinical activity and homologous recombination deficiency (HRD) as well as tumor infiltrating lymphocytes in tumor tissues. Subjects with gBRAC1/2 WT platinum-sensitive ovarian cancer who had received ≥ 2 lines of platinum-based chemotherapy will be enrolled. Subjects with active or prior autoimmune disease that may relapse, significant cardiovascular disease, prior exposure to PARP inhibitor, antiangiogenic therapy or immunotherapy will not be eligible.

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Trial Registration Clinical registration number: CTR20210713

REFERENCES

1. Annals of Oncology (2020) 31 (suppl_4): S551-S589. 10.1016/j.annonc.2020.07.016.

Ethics Approval This study received ethics approval from Ethics Committee of National Cancer Center/Cancer Hospital, Chinese Academy of medical sciences and Peking Union Medical College on 11 Mar 2021 (Approval number: 21/125-2796). 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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