Background Vudalimab (XmAb20717) is a humanized bispecific monoclonal antibody that simultaneously targets PD-1 and CTLA-4 and binds preferentially to PD-1/CTLA-4 dual-positive cells. In a Phase 1 study, vudalimab was generally well-tolerated and associated with complete and partial responses in various solid tumor types, including ovarian cancer and metastatic castration-resistant prostate cancer (mCRPC). These tumor types typically are not responsive to single-agent immune checkpoint inhibitor (ICI) therapy but have shown better outcomes in studies in which anti-PD-1 and CTLA-4 therapies have been combined. This Phase 2 study is designed to evaluate the safety and antitumor activity of vudalimab in selected gynecological oncologic indications and high-risk mCRPC.

Methods This is a multicenter, two-stage, open-label study being conducted in the United States. Patients with histologically confirmed platinum-resistant high-grade serous ovarian cancer; chemotherapy relapsed or refractory clear cell ovarian, endometrial, or peritoneal cancer; ICI-refractory microsatellite stable (MSS) endometrial cancer (EC); previously treated recurrent or metastatic cervical cancer; or high-risk mCRPC will be enrolled into parallel cohorts. Patients must have measurable disease by response evaluation criteria in solid tumors (RECIST) 1.1. Prior treatment with anti-PD-1 and PDL-1/PDL-2 therapy is excluded, except for patients with MSS EC and cervical cancer; prior anti-CTLA-4 treatment is excluded for all patients. Vudalimab will be administered intravenously every 3 weeks at a fixed dose of 1000 mg (1200 mg for patients ≥ 80 kg). Antitumor effects will be evaluated using RECIST 1.1; additionally, disease assessment via bone scans and PSA will be performed in patients with mCRPC. Safety and tolerability will be assessed based on treatment-emergent adverse events. Pharmacodynamic effects in peripheral blood and tumor, and potential biomarkers associated with clinical response will be explored. In Stage 1 (n = 10/cohort), a primary endpoint of objective response rate (ORR) ≥ 20% at 12 weeks (based on investigator review) will determine which cohorts advance into Stage 2 (n = 20/cohort), where primary and secondary endpoints of ORR (based on independent central review) and duration of response, respectively, will be determined for the combined number of patients enrolled into Stages 1 and 2 (n = 30). Enrollment has been initiated.

Trial Registration NCT05032040

REFERENCE

Ethics Approval The study was approved by each institution’s IRB.

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