A PHASE 1/1B DOSE ESCALATION AND COHORT EXPANSION STUDY OF MGC018 IN COMBINATION WITH LORIGERLIMAB IN PATIENTS WITH ADVANCED SOLID TUMORS (AST)

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Background The immune checkpoint molecule B7-homolog 3 (B7-H3) is highly expressed in multiple solid tumors with limited expression in normal tissue, may play an immune suppressive role, and favors cancer growth. MGC018 is an investigational anti-B7-H3 IgG1 antibody-drug conjugate with a duocarmycin-based DNA-alkylating payload that can damage DNA in both dividing and nondividing cells, causing cell death.1 As previously presented, Phase 1 testing of single-agent MGC018 (NCT03729596) demonstrated an acceptable safety profile with manageable toxicity in 115 patients and 25% objective response rate (ORR) among 32 evaluable patients in the NSCLC and mCRPC cohorts.2,3 Lorigerlimab is an investigational anti-B7-H3 antibody-drug conjugate (ADC), in patients with advanced solid tumors: preliminary results of phase I cohort expansion. Ann Oncol. 2021;32(suppl 5):S657–S658, Abstract #620P.

Methods This is a Phase 1/1b, open-label, multicenter, dose-escalation, and cohort-expansion study of MGC018+lorigerlimab in patients with relapsed/refractory, unresectable, locally advanced/metastatic solid tumors, including mCRPC, melanoma, pancreatic cancer, HCC, ovarian cancer, and RCC for whom there is no available therapy. Eligibility criteria include ECOG performance status ≤2 and having archival tumor or fresh biopsy specimens for B7-H3 and PD-L1 immunohistochemistry (IHC) analysis, although IHC results will not be used for patient selection. The primary objective is evaluation of safety/tolerability, dose-limiting toxicities, and the maximum-tolerated dose or maximum-administered dose for MGC018+lorigerlimab. Secondary objectives include assessment of pharmacokinetics, immunogenicity, and antitumor activity (ORR, DoR, progression-free survival, overall survival) of MGC018+lorigerlimab. MGC018 and lorigerlimab are administered as sequential infusions on Day 1 of each 28-day cycle, for up to 26 cycles. Dose escalation follows a 3+3 design with MGC018 escalating from 1.0-3.0 mg/kg and lorigerlimab fixed at 6 mg/kg. Cohort expansion of MGC018+lorigerlimab follows a Simon’s 2-stage design for each tumor-specific cohort. Safety assessments are based on AEs, graded by NCI CTCAE v5.0, occurring from the first dose until 30 days after the last dose or until starting another anticancer therapy. Tumor assessments are performed every 8 weeks for the first 6 months, then every 12 weeks until progressive disease. Response evaluation is determined using RECIST v1.1 or PCWG3 (for mCRPC). Enrollment ongoing.

Trial Registration Clinicaltrials.gov NCT05293496

REFERENCES

Ethics Approval Trial conduct was in accordance with Good Clinical Practice and Principles in the Declaration of Helsinki. An independent ethics committee approved the protocol at each participating site. All patients provided written informed consent.