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IMM2510, an anti-PD-L1/VEGF bispecific antibody fusion protein, in patients with advanced solid tumors: A phase I dose-escalation study.

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Background: IMM2510 is a novel bispecific antibody fusion protein targeting PD-L1 and VEGF. The preclinical study demonstrated that IMM2510 induced significantly stronger anti-tumor activity than either monotherapy or combination of PD-L1 inhibitor and anti-VEGF antibody through blocking the PD-1/PD-L1 pathway and thus activate T cells and reducing VEGF-mediated tumor angiogenesis as well as an enhanced ADCC effect. We previously disclosed the preliminary clinical data of IMM2510, and here we further report safety and efficacy results of IMM2510 in the phase I dose escalation study. **Methods:** A phase I, multicenter, open-label, dose-escalation study, was designed to evaluate the safety, efficacy, recommended phase II dose (RP2D), and pharmacokinetics (PK) of IMM2510 in patients (pts) with advanced solid tumors. The study was designed with an accelerated titration followed by a standard 3+3 design. IMM2510 (0.007, 0.03, 0.1, 0.3, 1.0, 3.0, 6.0, 10.0, 20.0 mg/kg) was administered intravenously Q2W as monotherapy. **Results:** As of Dec 21, 2023, 33 pts had received IMM2510 at 9 dose levels (0.007-20.0 mg/kg), the median age was 57 years (range 36-74), the median prior line of therapy was 3 (range 1-13), and 27.3% pts received prior anti PD-1/PD-L1 inhibitor therapies. Treatment-related adverse events (TRAEs) occurred in 32 pts (97.0%). Most TRAEs were grade 1 or 2. The most common TRAEs (≥ 20%) of all grades were infusion related reaction (IRR) (72.7%), platelet count decreased (39.4%), anemia (33.3%) and diarrhea (21.2%). Grade ≥3 TRAEs occurred in 11 pts (33.3%). Grade ≥3 TRAEs (≥5%) were IRR (9.1%), platelet count decreased (6.1%), lymphocyte count decreased (6.1%) and diarrhea (6.1%). TRAEs leading to treatment discontinuation occurred in 3 pts (9.1%) which were IRR, hypersensitivity and pyrexia, respectively. No DLT occurred. In 25 response evaluable pts, 3 pts had confirmed PR: 1 pt with sq-NSCLC (onco-driver gene negative, previous IO treatment failure) at 3 mg/kg with tumor shrinkage 46% and still on the treatment with treatment duration over 20 months; 1 pt with sq-NSCLC at 10 mg/kg with tumor shrinkage about 32% along with treatment duration 9.4 months; 1 pt with thymus adeno-squamous carcinoma (PD-L1 CPS 80) at 20 mg/kg with tumor shrinkage over 53% and still remains on the treatment along with treatment duration 8.1 months. In addition, 7 pts with BOR SD and 4 of them had over 15% decreased tumor burden (1 cervical cancer at 3 mg/kg, 2 non-sq NSCLC at 10 and 20 mg/kg respectively, 1 ovarian cancer at 20 mg/kg). The half-life of IMM2510 in 20.0mg/kg dose group was around 6.8 days. The RP2D was determined to be 20.0 mg/kg. **Conclusions:** IMM2510 is well tolerated in general and preliminary anti-tumor activity in solid tumors is encouraging. The phase Ib/II is ongoing to enroll patients. Clinical trial information: NCT05972460. Research Sponsor: ImmuneOnco Biopharmaceuticals (Shanghai) Inc.