A PHASE I/II STUDY OF REGN7075 (EGFRxCD28 COSTIMULATORY BISPECIFIC ANTIBODY) IN COMBINATION WITH CEMIPIMAB (ANTI-PD-1) IN PATIENTS WITH ADVANCED SOLID TUMORS

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Background T-cell redirecting bispecific antibodies (bsAbs) are therapeutics that recognize two distinct antigens: a tumor-associated antigen on tumor cells to promote recruitment of T-cells to the tumor, and a receptor on T-cells to potentiate anti-tumor activity. REGN7075 is a human immunoglobulin G4-based costimulatory bsAb designed to bridge epidermal growth factor receptor (EGFR) positive tumor cells with CD28 positive T-cells and to provide amplified T-cell receptor-CD3 complex-mediated T-cell activation within the tumor, through the activation of CD28 co-stimulation. In genetically humanized immunocompetent mouse models, REGN7075 in combination with anti-PD-1 (antibody directed against programmed cell death-1 receptor) improved anti-tumor activity compared with either single agent alone.¹

Methods This is an open label, Phase I/II, first-in-human study evaluating the safety, tolerability, pharmacokinetics, and preliminary anti-tumor activity of REGN7075 (EGFRxCD28) alone and in combination with cemiplimab in patients with advanced solid tumors (NCT04626635). Patients must have a protocol-defined advanced solid tumor, be ≥18 years of age (≥20 years in Japan), have an Eastern Cooperative Oncology Group performance status of 0 or 1, and be naïve to anti-PD-1/anti-PD-ligand(L)1. This study includes dose escalation (a 4+3 design modified from 3+3; Part 1) and expansion phases (Part 2). In Part 1, patients will receive a lead-in of REGN7075 monotherapy for 3 weeks followed by combination therapy with cemiplimab 350 mg every 3 weeks. Study therapies are administered until disease progression, intolerable adverse events, withdrawal of consent, or other stopping criterion is met. Once a recommended Phase 2 dose is determined in Part 1, four tumor-specific expansion cohorts will be opened: non-small cell lung cancer (PD-L1 ≥50%), triple-negative breast cancer, colorectal cancer (microsatellite stable), and cutaneous squamous cell carcinoma. Primary endpoints are safety and tolerability of REGN7075 alone or in combination with cemiplimab for Part 1, and objective response rate per Response Evaluation Criteria in Solid Tumors version 1.1 for Part 2. This study is currently open to enrollment.

Trial Registration ClinicalTrials.gov identifier NCT04626635.

REFERENCES

1. Waite JC, Wang B, Haber L, et al. Tumor-targeted CD28 bispecific antibodies enhance the antitumor efficacy of PD-1 immunotherapy. *Sci Transl Med* 2020;**12**:2325.

Ethics Approval This study was conducted in accordance with the principles of the Declaration of Helsinki and the International Conference on Harmonization Good Clinical Practice guidelines. The study protocol and all amendments were approved by the institutional review board/ethics committee at each participating study site.

Consent All patients provided written informed consent.

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