474 PHASE 1 STUDY OF SEA-TGT, A HUMAN, NONFUCOSYLATED ANTI-TIGIT MONOCLONAL ANTIBODY WITH ENHANCED IMMUNE-EFFECTOR FUNCTION, IN PATIENTS WITH ADVANCED MALIGNANCIES (SGNTGT-001, TRIAL IN PROGRESS)

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Background T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory domains (TIGIT), and costimulatory receptor CD226 competitively bind 2 ligands, CD155 and CD112, which are expressed by tumor cells and antigen-presenting cells in the tumor microenvironment.[1 2] Dual TIGIT/programmed cell death protein-1 (PD-1) blockade increased tumor antigen-specific CD8+ T-cell expansion and function in vitro and promoted potent antitumor response in vivo.[3 4] TIGIT/PD-1 dual blockade using a TIGIT monoclonal antibody (mAb) with intact Fc produced clinical responses in advanced cancer.[5] SEA-TGT is an investigational, human, nonfucosylated mAb directed against TIGIT. SEA-TGT binds to TIGIT, blocking inhibitory checkpoint signals directed at T cells. SEA-TGT enhances binding to activating FcγRIIIa and decreases binding to inhibitory FcγRIIb; this depletes immunosuppressive regulatory T cells and amplifies naive and memory T cells, potentially augmenting PD-1 inhibition effects. Preclinically, at suboptimal doses, SEA-TGT plus anti-PD-1 mAbs had superior antitumor activity than either agent alone.[6]

Methods Safety and antitumor activity of SEA TGT in ~377 adults (≥18 years) will be evaluated in this phase 1, multicenter, open-label, dose-escalation/expansion study. Part A will assess the safety/tolerability of SEA TGT to determine maximum tolerated and recommended doses. Part B will assess the safety and antitumor activity of the recommended dose in disease-specific expansion cohorts. Part C will assess SEA-TGT plus sasanlimab in dose-expansion cohorts after an initial safety run-in. Patients with histologically/cytologically confirmed relapsed/refractory/progressive metastatic solid tumors including non-small cell lung cancer (NSCLC), head and neck squamous cell carcinoma (HNSCC), gastric/gastroesophageal junction carcinoma, cutaneous melanoma, bladder, cervical, ovarian or triple-negative breast cancer, or selected lymphomas will be eligible for Parts A and B. Part C will enroll patients with histologically confirmed advanced NSCLC (high [tumor proportion score (TPS) ≥50%] and low [TPS=1–49%] PD ligand 1 [PD-L1] expression), cutaneous melanoma, and HNSCC without previous anti–PD-1/PD-L1 therapy exposure. SEA TGT will be administered on Day 1 of 21-day cycles.Laboratory abnormalities, adverse events, dose-limiting toxicities, and dose-level safety and activity are primary endpoints. Secondary endpoints are objective response (OR) and complete response (CR) rates, duration of OR/CR, progression-free survival, overall survival, pharmacokinetics (PK), and antidrug antibodies. Exploratory analysis will include pharmacodynamics (PD), PK/PD relationships, biomarkers, and resistance to SEA-TGT. This trial is recruiting in Europe and North America.

Trial Registration NCT04254107

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Ethics Approval Institutional review boards or independent ethics committees of participating sites approved the trial, which will be conducted in compliance with the Declaration of Helsinki and International Conference on Harmonisation Guidelines for Good Clinical Practice. All patients will provide written informed consent.

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