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.3 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 FcRIIa and decreases binding to inhibitory FcRIib; 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.5

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.