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)

¹Diwakar Davar*, ²Vincent Ribrag, ²Clementine Sarkozy, ³Elena Garralda, ³Honey Kumar Oberoi, ⁴Amitkumar Mehta, ⁵Giuseppe Curigliano, ⁶Carmen Belli, ⁷Jasmine Zain, ⁷Alex Herrera, ⁸Rachel Sanborn, ⁹Ecaterina Dumbrava, ¹⁰Andres Forero-Torres, ¹¹Stephen Ansell. ¹UPMC Hillman Cancer Center, Pittsburgh, PA, USA; ²Gustave-Roussy Institute, Villejuif, France; ³Vall d'Hebron University Hospital, Barcelona, Spain; ⁴Birmingham Comprehensive Cancer Center, Birmingham, AL, USA; ⁵University of Milano and European Institute of Oncology, IRCCS, Milan, Italy; ⁶European Institute of Oncology, IRCCS, Milan, Italy; ⁷City of Hope Medical Center, Duarte, CA, USA; ⁸Providence Cancer Institute, Portland, OR, USA; ⁹MD Anderson Cancer Center, Houston, TX, USA; ¹⁰Seagen Inc, Seattle, WA, USA; ¹¹Mayo Clinic, Rochester, MN, USA

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

REFERENCES

1. Blake SJ, Dougall WC, Miles JJ, et al. Molecular pathways: Targeting CD96 and TIGIT for cancer immunotherapy. *Clin Cancer Res* 2016;**22**(21):5183–5188.
2. Chauvin JM, Zarour HM. TIGIT in cancer immunotherapy. *J Immunother Cancer* 2020;**8**:e000957.
3. Johnston RJ, Comps-Agrar L, Hackney J, et al. The immunoreceptor TIGIT regulates antitumor and antiviral CD8+ T cell effector function. *Cancer Cell* 2014;**26**(6):923–937.
4. Chauvin JM, Pagliano O, Fourcade J, et al. TIGIT and PD-1 impair tumor antigen-specific CD8+ T cells in melanoma patients. *J Clin Invest* 2015;**125**(5):2046–2058.
5. Rodriguez-Abreu D, Johnson ML, Hussein MA, et al. Primary analysis of a randomized, double-blind, phase 2 study of the anti-TIGIT antibody tiragolumab (tira) plus atezolizumab (atezo) versus placebo plus atezo as first-line (1L) treatment in patients with PD-L1-selected NSCLC (CITYSCAPE). *J Clin Oncol* 2020;**38**(15 suppl):9503.
6. Smith A, Zeng W, Lucas S, et al. Poster 1583. SEA-TGT is an empowered anti-TIGIT antibody that displays superior combinatorial activity with several therapeutic agents. Presented at: American Association for Cancer Research Annual Meeting; April 9–14, 2021; Virtual Meeting.

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.

<http://dx.doi.org/10.1136/jitc-2021-SITC2021.474>