DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20892

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Announcement of Availability to Investigators of Sacituzumab Govitecan (NSC 820016)

For Clinical Study Proposals

The Cancer Therapy Evaluation Program (CTEP) is accepting Letters of Intent (LOIs) to conduct clinical studies using sacituzumab govitecan (SG), a trophoblast antigen 2 (TROP2)-targeted antibody-drug conjugate (ADC), which is being researched by CTEP as an anticancer agent in collaboration with Gilead Sciences, Inc. CTEP may consider requests to support nonclinical, correlative-focused studies with SG on a case-by-case basis. All clinical and nonclinical, correlative-focused researchers interested in working with the agent are welcome to apply. Proposals for clinical trials should be supported by a strong rationale and robust preclinical data (see "Components of a Competitive Letter of Intent" at http://ctep.cancer.gov/protocolDevelopment/lois_concepts.htm). ***All proposals approved by CTEP will be sent to the industry collaborator for a commitment to supply drug for the study.***

TROP2, or trophoblast cell surface antigen 2, is a transmembrane calcium signal transducer glycoprotein involved in myriad signaling pathways and cell processes like proliferation, survival, and invasion (Shvartsur *et al*., 2015). TROP2 has differential expression in normal tissues but is highly expressed in many cancers, most notably in solid gynecologic, genitourinary (GU), and head and neck tumors (Shvartsur *et al*., 2015). SG takes advantage of TROP2 expression in cancer to facilitate cytotoxicity through ADC biology. By linking an anticancer agent to a monoclonal antibody, the ADC more specifically binds to the surface of TROP2-expressing cancer cells, thus facilitating rapid internalization and efficient release of payload in those cancer cells and the surrounding tumor microenvironment. This enables efficient tumor killing while potentially minimizing the effect on healthy tissues. SG is a TROP2-directed ADC featuring an anti-TROP2 humanized monoclonal antibody linked to SN-38, the active metabolite of the topoisomerase I (TOPO I) inhibitor irinotecan (Goldenberg and Sharkey, 2019). SN-38, a synthetic camptothecin, inhibits TOPO I activity, ultimately inducing double strand DNA breaks and apoptosis (Goldenberg and Sharkey, 2019; Maurya *et al*., 2011). Preclinical studies with SG have shown its efficacy as anticancer agent in a number of solid tumor models and is also active in preclinical models with mosaic TROP2 expression (Goldenberg and Sharkey, 2019; Perrone *et al*., 2020). Treatment with SG has been shown to inhibit tumor growth and promote tumor regression in gynecologic, lung, and breast cancer (BC) cells and xenografts (Goldenberg and Sharkey, 2019; Lopez *et al*., 2020; Perrone *et al*., 2020).

SG has been examined in several clinical studies to date, the first of which was a Phase I/II basket trial (NCT01631552). In 54 non-small cell lung cancer (NSCLC) patients, SG treatment led to an objective response rate (ORR) of 16.7%, a median duration of response (mDoR) of 6.0 months, a median progression free survival (mPFS) of 4.4 months, and a median overall survival (mOS) of 7.3 months (Bardia *et al*., 2021). In 62 small cell lung cancer (SCLC) patients, SG treatment led to an ORR of 17.7%, mDoR of 5.7 months, mPFS of 3.7 months, and a mOS of 7.1 months (Bardia *et al*., 2021). In 18 endometrial cancer patients, SG treatment led to an ORR of 22.2%, mPFS of 3.2 months, and a mOS of 11.9 months (Bardia *et al*., 2021). Among all cohorts, the most common treatment-related adverse events (TRAEs) were nausea (62.6%), diarrhea (56.2%), fatigue (48.3%), alopecia (40.4%), and neutropenia (57.8%), with the most common serious TRAEs being febrile neutropenia (4.0%) and diarrhea (2.8%) (Bardia *et al*., 2021). In a Phase II basket study (NCT03964727) in patients with advanced/metastatic endometrial cancer who had progressed on a median of three prior therapies, SG monotherapy led to an ORR of 25%, mPFS of 5.6 months, and stable disease (SD) in

40% of patients (Santin *et al*., 2023). In the Phase II open-label trial in advanced/metastatic urothelial cancer (UC) (NCT03547973), 113 patients who progressed on prior platinum-based or checkpoint inhibitor therapy received SG therapy, and reported ORR was 27%, mDoR was 7.2 months, mPFS was 5.4 months, and OS was 10.9 months. Key TRAEs included neutropenia (35%), leukopenia (18%), anemia (14%), diarrhea (10%), and febrile neutropenia (10%) (Tagawa et al., 2021).

Following safety and efficacy results from ASCENT (NCT02574455) and TROPiCS-02 (NCT03901339), SG received FDA approval for patients with BC: it was approved for patients with unresectable locally advanced or metastatic triple-negative BC and for patients with unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative BC. See the table below for ongoing studies assessing the efficacy of SG in metastatic BC, NSCLC, and endometrial carcinoma.

Study Title	Trial Information	Clinical Trials ID
ASCENT-04	Phase III - SG + Pembro vs Physician's Choice + Pembro as 1L in mTNBC	NCT05382286
ASCENT-05	Phase III - SG + Pembro vs Physician's Choice as adjuvant in TNBC	NCT05633654
ASCENT-07	Phase III - SG vs Physician's Choice in HR+/HER2- chemo-naïve mBC	NCT05840211
EVOKE-02	Phase II – SG + Pembro ± chemo as 1L in mNSCLC	NCT05186974
EVOKE-03	Phase III – Pembro vs SG + Pembro as 1L in mNSCLC	NCT05609968
VELOCITY-Lung	Phase II – novel combinations in NSCLC, including SG	NCT05633667
ASCENT-GYN-01	Phase III - SG vs Physician's Choice in endometrial cancer after chemo and immunotherapy	NCT06486441
TROPiCS-03	Phase II – SG in solid tumors (basket trial)	NCT03964727
Pembro = pembrolizumab; 1L = first line		

Clinical Studies of Interest to CTEP for Sacituzumab Govitecan

CTEP is interested in exploring SG as monotherapy or in rational combinations with novel therapies including and beyond the current FDA indications (*e.g.,* breast, thoracic, gynecologic, and other cancers).

Correlative Studies of Interest to CTEP for Sacituzumab Govitecan

CTEP would be interested in any correlative studies that would potentially identify predictive biomarkers for SG, as well as any studies that would advance the development of SG. Correlative studies of interest will be reviewed and approved by CTEP and the pharmaceutical collaborator on a case-by-case basis.

Obtaining Forms and Contact Information

For clinical study proposals, the LOI Submission Form may be downloaded from the CTEP website at http://ctep.cancer.gov/protocolDevelopment/lois_concepts.htm.

If you are interested in obtaining the agent for nonclinical studies, whether alone or in association with a proposed clinical study, please complete the DCTD Nonclinical Request Form, which may be downloaded from the CTEP website at http://ctep.cancer.gov/industryCollaborations2/agreements_agents.htm.

Further instructions for completing and submitting the forms may be found within the respective documents.

Questions may be addressed to Lorraine Pelosof, MD, PhD, Medical Officer, Investigational Drug Branch, CTEP, DCTD, NCI (phone: 240-276-6281; fax: 240-276-7894; e-mail: lorraine.pelosof@nih.gov).

A complete list of agents available for distribution by CTEP may also be found on the CTEP website at http://ctep.cancer.gov/industryCollaborations2/agreements_agents.htm.

References

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