

VELOCITY-Lung

A Phase 2 Study Evaluating Safety and Efficacy of Sacituzumab Govitecan + Zimmerelimab + Etrumadenant in Patients With Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC) Progressing on or After Platinum-Based Chemotherapy and Checkpoint Inhibitors

Poster ID: CT049

Anjali Rohatgi,¹ James Chih-Hsin Yang,² Dong-Wan Kim,³ Molly Li,⁴ Joseph Park,⁵ Anna Seto,⁵ Jie Zhang,⁵ Nir Peled⁶

¹Washington University in St Louis, St Louis, MO, USA; ²National Taiwan University Hospital and National Taiwan University Cancer Center, Taipei City, Taiwan; ³Seoul National University Hospital, Seoul, Republic of Korea; ⁴Chinese University of Hong Kong, Hong Kong, China; ⁵Gilead Sciences, Inc, Foster City, CA, USA; ⁶Shaare Zedek Medical Center, Jerusalem, Israel

Background

- Lung cancer (of which non-small cell lung cancer [NSCLC] makes up 85%) is the leading cause of cancer-related deaths in the United States, with a 5-year survival rate of 6% for patients diagnosed with distant metastases^{1,2}
- Single-agent chemotherapy is the standard of care for patients with metastatic NSCLC progressing on or after platinum-based chemotherapy and checkpoint inhibitors (CPI) but is associated with poor outcomes^{2,3}
- Sacituzumab govitecan is an antibody-drug conjugate (**Figure 1**) approved by the US Food and Drug Administration (FDA) for patients with metastatic triple-negative breast cancer who received ≥2 prior chemotherapies (≥1 in the metastatic setting) and has FDA-accelerated approval for patients with locally advanced or metastatic urothelial cancer who have previously received a platinum-containing chemotherapy and either programmed cell death receptor-1 (anti-PD-1) or programmed cell death-ligand 1 (anti-PDL-1) inhibitor⁴
- Sacituzumab govitecan monotherapy demonstrated an objective response rate of 17%, with a manageable safety profile in 54 patients with metastatic NSCLC who had multiple prior therapies,⁵ and a phase 3 study is currently ongoing in this population (NCT05089734)
- Zimmerelimab (anti-PD-1) and etrumadenant (dual adenosine receptor antagonist) (**Figure 2**) are under clinical investigation for antitumor activity⁶; combination treatment including zimberelimab + etrumadenant has been well tolerated, with a manageable safety profile⁷
- Here, we describe the design of substudy-02 of the VELOCITY-Lung phase 2 platform study (NCT05633667), which will evaluate efficacy and safety of novel treatment combinations, including sacituzumab govitecan + zimberelimab + etrumadenant, in patients with advanced or metastatic NSCLC progressing on or after platinum-based chemotherapy and CPI

Figure 1. Sacituzumab Govitecan: A Novel⁶ Antibody-Drug Conjugate⁸⁻¹¹

SN-38 payload

- SN-38 is more potent than parent compound, irinotecan (TOPO I inhibitor)
- SN-38 was chosen for its moderate cytotoxicity (with IC₅₀ in the nanomolar range), permitting delivery in high quantity to the tumor

Humanized anti-Trop-2 antibody

- Directed toward Trop-2, an epithelial antigen expressed on many solid cancers

Linker for SN-38

- pH-sensitive, hydrolyzable linker for SN-38 release in targeted tumor cells and tumor microenvironment, allowing bystander effect
- High drug-to-antibody ratio (7.6:1)

Adapted from Rugo HS, et al. TROPICS-02: A Phase III study investigating sacituzumab govitecan in the treatment of HR+/HER2- metastatic breast cancer. *Future Oncol.* 2020;16:705-715.
Complete licensing info can be found here: <http://creativecommons.org/licenses/by-nc-nd/4.0/>.
IC₅₀, half maximal inhibitory concentration; TOPO I, topoisomerase I; Trop-2, trophoblast cell surface antigen 2.

Figure 2. Combined Inhibition of PD-1, and the Adenosine (ADO) Axis May Enhance Anti-Cancer Immune Responses

Zimmerelimab
anti-PD-1 mAb

- Demonstrated activity across multiple advanced tumor types, including NSCLC^{7,12,13}
- Approved in China for classical Hodgkin Lymphoma^{a,14}

Etrumadenant
A2R antagonist

- Dual A_{2(a/b)}R antagonist: designed to block ADO-mediated effects on both lymphoid and myeloid cells
- Full engagement of target across dosing interval (≥90% RO at trough)

^aGloria Biosciences secured approval in China for zimberelimab and conducts its activities independently of Arcus.
ADO, adenosine; A2R, adenosine 2a and 2b receptor; mAb, monoclonal antibody; NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein 1; RO, receptor occupancy.

Methods

Figure 3: VELOCITY-Lung: An Open-Label, Multicenter, Randomized, Phase 2 Platform Study of Novel Treatment Combinations in Patients With Advanced or Metastatic NSCLC Progressing on or After PT-Based Chemotherapy and CPI (NCT05633667)^a

Substudy-02 (N=~23-133)

Preliminary Phase

Expansion Phase

Study Population

- Age ≥18 years
- Stage IV NSCLC
- Measurable disease by RECIST version 1.1
- ECOG PS 0-1
- Any PDL-1 status

Sacituzumab Govitecan
(10 mg/kg D1 & D8 of 21-D cycle) + **Zimmerelimab**
(360 mg D1 of 21-D cycle) + **Etrumadenant** (150 mg QD on D1 through D21) (N=~23)

Novel treatment combinations to be added in the future

Sacituzumab Govitecan
(10 mg/kg D1 & D8 of 21-D cycle) + **Zimmerelimab**
(360 mg D1 of 21-D cycle) + **Etrumadenant** (150 mg QD on D1 through D21) (N=~55)

Comparator arm:
Docetaxel (75 mg/m² D1 of 21-D cycle) or **Sacituzumab Govitecan** (10 mg/kg D1 & D8 of 21-D cycle)

Continue treatment until PD, death, unacceptable toxicity, initiation of subsequent anticancer therapy, or protocol specified discontinuation criteria are met

Primary endpoint

- ORR per RECIST v1.1

Secondary endpoints

- PFS and DOR per RECIST v1.1
- OS
- Safety

Stratification by:

- Histology (squamous vs nonsquamous)
- Received prior targeted therapy for actionable genomic alterations (yes vs no)

^aSubstudy-01 evaluates novel treatment combinations in treatment-naïve mNSCLC. ^bSubjects will be recruited and randomized to the expansion phase treatment and comparator arms only if the treatment passes preliminary stage.
^cThe randomization ratio will be determined by the sponsor depending on the number of experimental arms initiated in the expansion stage, the comparator arm, and any newly added preliminary stage treatment arms.
CPI, checkpoint inhibitor; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PDL-1, programmed cell death ligand 1; PFS, progression-free survival; PT, platinum; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors.

Key Eligibility Criteria (Substudy-02)

Inclusion

- Patients with nonsquamous histology must have *EGFR* and *ALK* alterations evaluated
- Patients with actionable gene mutations must have received 1 previous approved targeted therapy appropriate to the genomic alteration
- Progression or recurrence after PT-based chemotherapy and CPI given either in combination or sequentially

Exclusion

- Mixed SCLC and NSCLC histology
- Previous topo-1 inhibitor (including as ADC), Trop-2 targeting agent, docetaxel
- Known active CNS metastases and/or carcinomatous meningitis^a
- Active autoimmune disease or secondary malignancy

^aPatients with previously treated brain metastases with stable CNS disease for at least 4 weeks are permitted.
ADC, antibody-drug conjugate; ALK, anaplastic lymphoma kinase; CNS, central nervous system; CPI, checkpoint inhibitor; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; PT, platinum; RECIST, Response Evaluation Criteria in Solid Tumors; SCLC, small-cell lung cancer; TOPO-I, topoisomerase type 1; Trop-2, trophoblast cell surface antigen 2.

References

- Siegel RL, et al. *CA Cancer J Clin.* 2022;72:7-33.
- Duma N, et al. *Mayo Clin Proc.* 2019;94:1623-1640.
- Horvath L, et al. *Mol Cancer.* 2020;19:141.
- TRODELVY (sacituzumab govitecan-hziy). [Prescribing information]. Foster City, CA: Gilead Sciences, Inc.; 2023.
- Heist RS, et al. *J Clin Oncol.* 2017;35:2790-2797.
- <https://clinicaltrials.gov/ct2/show/NCT04791839>.
- Johnson ML, et al. *J Clin Oncol.* 2022;40(suppl. 36):397600-397600.

- Goldenberg DM, et al. *Oncotarget.* 2015;6: 22496-22512.
- Avellini C, et al. *Oncotarget.* 2017;8:58642-58653.
- Rugo HS, et al. *Future Oncol.* 2020;16:705-715.
- Cardillo TM, et al. *Bioconjugate Chem.* 2015;26: 919-931.
- Shen L, et al. *Ann Onc.* 2018;29(suppl 10):X22-X23.
- Lin S, et al. *J Clin Oncol.* 2019;37(suppl. 4):125-125.
- Lin N, et al. *Eur J Cancer.* 2022;164:117-126.

Acknowledgments

- We thank the patients and their caregivers for helping us realize the possibilities of this research
- We thank the dedicated clinical trial investigators and their devoted team members for participating in the VELOCITY-Lung study
- This study is sponsored by Gilead Sciences, Inc.
- Editorial support was provided by Team 9 Science, and funded by Gilead Sciences, Inc.

VELOCITY-Lung Contacts

- Enrollment for VELOCITY-Lung Trial (NCT05633667) is currently ongoing
- For more information, please visit www.clinicaltrials.gov
- Contact email: mmm@gilead.com

Copies of this poster obtained through Quick Response (QR) code are for personal use only and may not be reproduced without written permission of the authors

Presented at the American Association for Cancer Research Annual Meeting, April 14-19, 2023