VELOCITY-Lung (Substudy-01): A Phase 2 Study Evaluating Safety and Efficacy of Domvanalimab + Zimberelimab + Sacituzumab Govitecan or Etrumadenant + Domvanalimab + Zimberelimab, or Etrumadenant + Zimberelimab in Patients With Treatment-Naïve Metastatic Non-Small Cell Lung Cancer

Poster TPS9155

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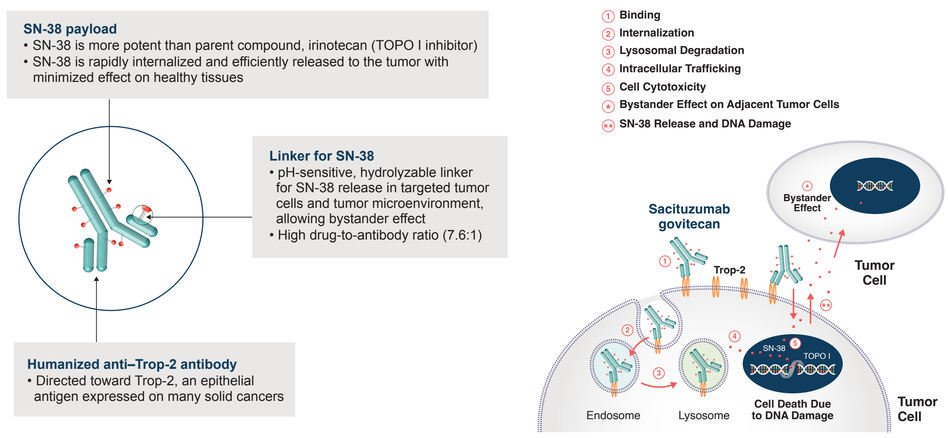
Introduction

- Despite recent improvements in the outcomes of patients with metastatic non-small cell lung cancer (mNSCLC) with the introduction of immune checkpoint inhibitors, the 5-year overall survival of these patients remains poor[1,2]
- Sacituzumab govitecan is an antibody-drug conjugate (Figure 1) approved by the US Food and Drug Administration (FDA) for patients with unresectable locally advanced or metastatic triple-negative breast cancer who received ≥ 2 prior systemic therapies (≥ 1 for metastatic disease) and has FDA accelerated approval for patients with locally advanced or metastatic urothelial cancer who have previously received a platinum-containing chemotherapy and a programmed death (ligand) 1 (PD-[L]1) inhibitor[3]
- Sacituzumab govitecan monotherapy demonstrated clinical activity with a manageable safety profile in heavily pretreated patients with mNSCLC,[4] and an ongoing phase 2 study is assessing sacituzumab govitecan in combination with pembrolizumab with or without platinum-based agents in patients with previously untreated mNSCLC (NCT05186974)
- Zimberelimab (anti–PD-1 monoclonal antibody [mAb]), etrumadenant (dual adenosine A2A/A2B receptor antagonist), and domvanalimab (Fc-silent anti–TIGIT mAb; Figure 2) combinations are currently being investigated in the phase 2 ARC-7 study (NCT04262856) and have demonstrated initial antitumor activity in mNSCLC[5]
- Given the encouraging activity of combination therapy with anti–PD-1 and anti–TIGIT antibodies in mNSCLC, the addition of sacituzumab govitecan provides an opportunity for improved clinical outcomes

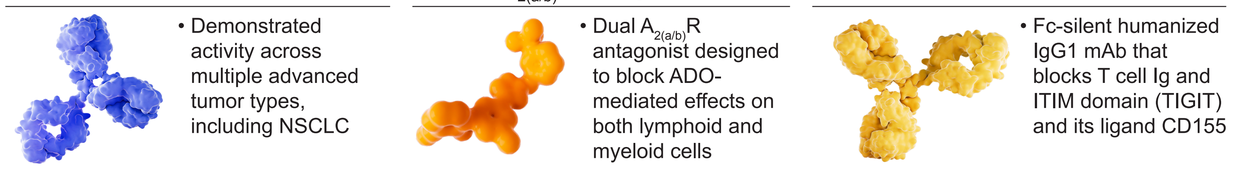
Figure 1. Sacituzumab govitecan: a novel antibody-drug conjugate[6-9]



TOPO I, topoisomerase I; Trop-2, trophoblast cell surface antigen 2.

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/.

Figure 2. Zimberelimab, etrumadenant, and domvanalimab[5,10,11]



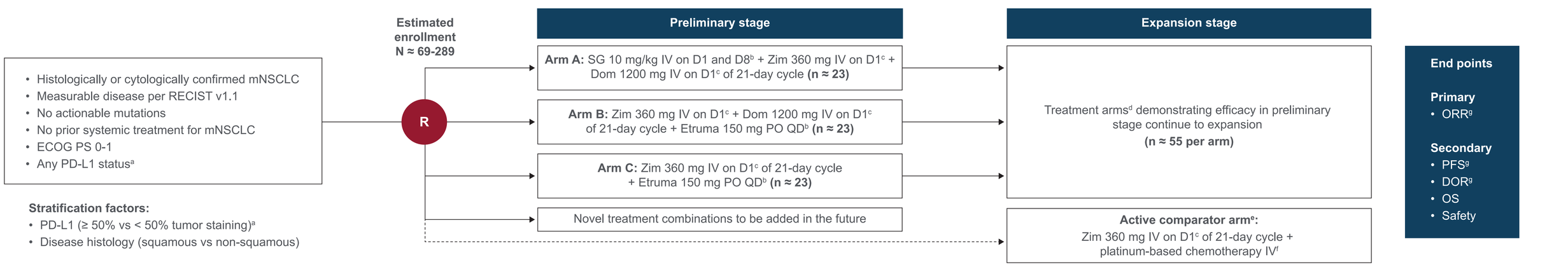
ADO, adenosine; Ig, immunoglobulin; mAb, monoclonal antibody; NSCLC, non-small cell lung cancer; PD-1, programmed death 1.

Study Objective

- Substudy-01 of the VELOCITY-Lung phase 2 platform study will evaluate the efficacy and safety of novel treatment combinations in patients with treatment-naïve mNSCLC

Study Design

Figure 3. An open-label, multicenter, randomized, phase 2 platform study of novel treatment combinations in patients with treatment-naïve mNSCLC (NCT05633667)



D, day; Dom, domvanalimab; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; Etruma, etrumadenant; IV, intravenous; mNSCLC, metastatic non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PO, orally; PD-L1, programmed death ligand-1; PFS, progression-free survival; QD, once daily; R, randomized; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SG, sacituzumab govitecan; Zim, zimberelimab. [a]Centrally assessed using the Ventana PD-L1 (SP263) assay. [b]Until progressive disease (PD) or unacceptable toxicity by investigator assessment. [c]Up to 35 cycles. [d]Treatment arms with minimal clinical activity or unacceptable toxicity will not proceed to the expansion stage. [e]The comparator arm may be modified if a new standard of care regimen is established during the course of the study or if the expansion stage is conducted in a biomarker-selected subgroup. [f]Choice of chemotherapy in comparator arm is dependent on histology. Non-squamous histology: cisplatin 75 mg/m^2 or carboplatin area under the curve (AUC) 5 on D1 with pemetrexed 500 mg/m^2 on D1 of 21-day cycle. Cisplatin and carboplatin will be administered for a maximum of 4 treatment cycles. Pemetrexed is continued after 4 cycles until PD or unacceptable toxicities. Squamous histology: carboplatin AUC 6 on D1 with paclitaxel 200 mg/m^2 on D1 or nab-paclitaxel 100 mg/m^2 on D1, D8, and D15 of 21-day cycle. Carboplatin, paclitaxel, and nab-paclitaxel will be administered for a maximum of 4 treatment cycles. [g]Response assessed by investigator per RECIST v1.1.

Key Eligibility Criteria

Table 1. Key inclusion and exclusion criteria

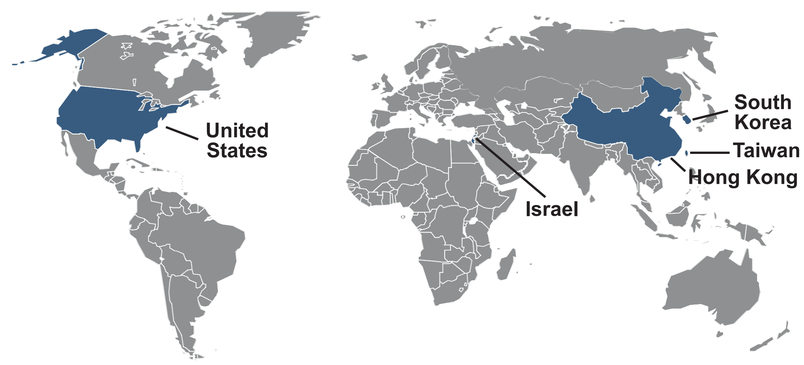
Inclusion	Exclusion
Age ≥ 18 years	Mixed small-cell lung cancer and NSCLC histology
Histologically or cytologically confirmed NSCLC with documented evidence of Stage IV disease at start of study treatment	Active CNS metastases and/or carcinomatous meningitis
Measurable disease by CT or MRI per RECIST v1.1	Active second malignancy, serious infection, or autoimmune disease
Negative test result for *EGFR* or *ALK* mutations for patients with non-squamous histology	Received anticancer therapy ≤ 4 weeks prior to enrollment
No known actionable mutations with approved therapies	Received radiotherapy ≤ 2 weeks prior to first dose of study treatment
No prior systemic treatment of metastatic NSCLC[a]	Arm A: Prior topoisomerase I inhibitors or Trop-2–targeted therapy
ECOG PS 0-1 and adequate organ function	Arms B and C: Inability to swallow oral medications or current malabsorption condition

ALK, anaplastic lymphoma kinase; CNS, central nervous system; CT, computerized tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; MRI, magnetic resonance imaging; NSCLC, non-small cell lung cancer; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1. [a]Patients who completed adjuvant or neoadjuvant therapy ≥ 12 months prior to study start are eligible.

Study Sites/Enrollment

- Study enrollment for VELOCITY-Lung began in December 2022 and is ongoing (Figure 4)
- For more information, please visit: https://clinicaltrials.gov/ct2/show/NCT05633667
- Contact email: GileadClinicalTrials@gilead.com

Figure 4. VELOCITY-Lung active study sites



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