VELOCITY-Lung Substudy-03: a phase 2 study of neoadjuvant domvanalimab + zimberelimab + chemotherapy or zimberelimab + chemotherapy followed by adjuvant domvanalimab + zimberelimab or zimberelimab in patients with resectable stage II–III non-small cell lung cancer

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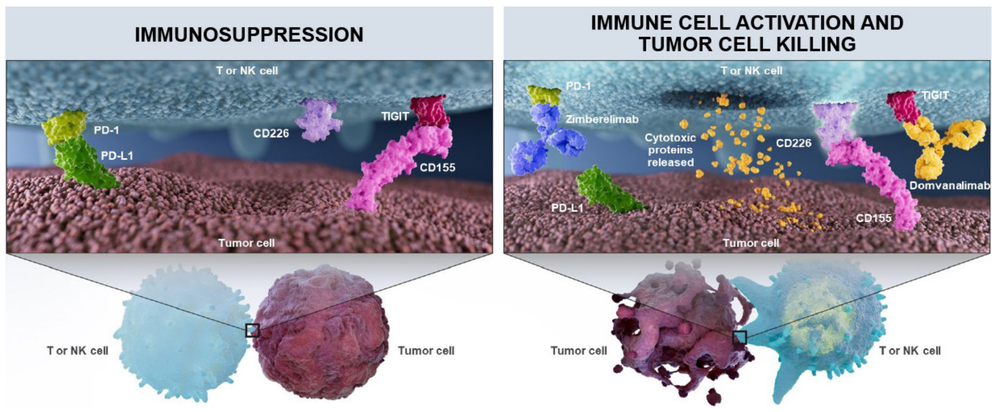
Introduction

- Management of resectable non-metastatic non-small cell lung cancer (NSCLC) includes a multimodal approach with surgery and neoadjuvant and/or adjuvant systemic therapy (including chemotherapy, immune checkpoint inhibitors, and targeted therapies), leading to improved outcomes[1]
- While immunotherapy has resulted in clinical benefit for participants with early-stage, resectable NSCLC, there remains a need to improve upon and extend event-free survival and to increase the rate of overall survival[2]
- Combination immune checkpoint inhibition with domvanalimab, an anti–T-cell immunoglobulin and immunoreceptor tyrosine-based inhibitory motif (ITIM) domain (TIGIT) antibody, and zimberelimab, an anti–programmed death protein 1 (PD-1) antibody **(Figure 1)**, has shown promising antitumor activity with a manageable safety profile in metastatic NSCLC[3]
  - This combination may provide an opportunity to improve clinical outcomes in the perioperative setting in early-stage, resectable NSCLC
- Substudy-03 of the VELOCITY-Lung platform study is evaluating novel perioperative treatment combinations in participants with newly diagnosed, resectable, stage II–III NSCLC

Figure 1. Domvanalimab and Zimberelimab and the TIGIT Pathway[3-6]

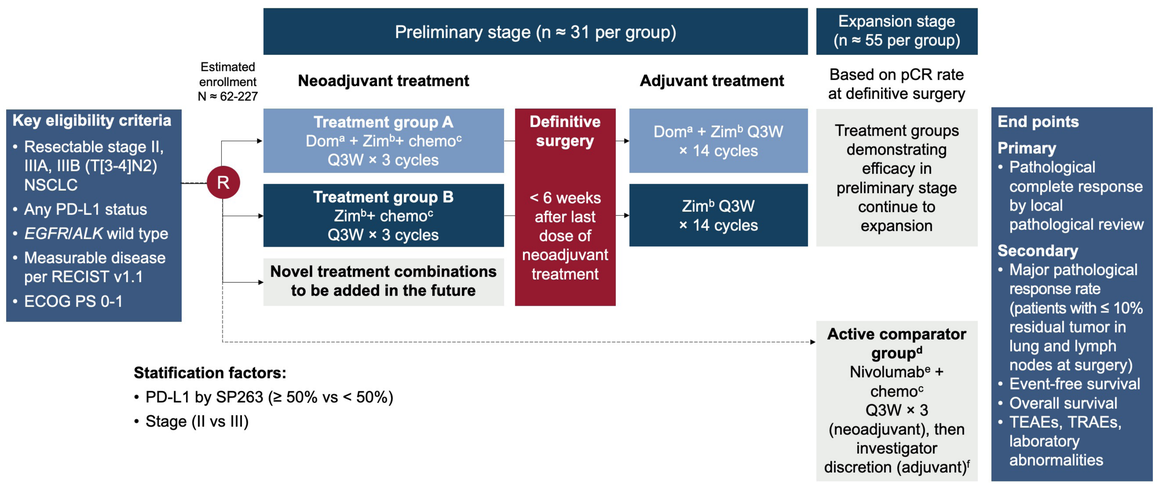


CD, cluster of differentiation; NK, natural killer; PD-L1, programmed death ligand-1.

Study Design

- VELOCITY-Lung (NCT05633667) is an open-label, multicenter, phase 2 platform study with 3 ongoing substudies evaluating novel treatment combinations in participants with NSCLC
- Substudy-03 will evaluate the efficacy, safety, and tolerability of perioperative domvanalimab- and zimberelimab-containing treatments in participants with previously untreated, resectable, stage II–III NSCLC **(Figure 2)**
  - At the preliminary stage, approximately 31 participants will be enrolled into each treatment group for the preliminary phase
  - Based on pathological complete response rates at definitive surgery, approximately 55 participants will be enrolled into each experimental treatment group that enters the expansion stage, with approximately 55 participants enrolled initially into the comparator group

Figure 2. VELOCITY-Lung Substudy-03 Study Design



[a]1200 mg IV.
[b]360 mg IV.
[c]Platinum-based chemo dependent on histology. Participants with nonsquamous histology will receive carboplatin AUC 5 with pemetrexed 500 mg/m^2 as part of neoadjuvant treatment. Participants with squamous histology will receive carboplatin AUC 6 with paclitaxel 200 mg/m^2.
[d]The comparator 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.
[e]360 mg IV.
[f]Participants may receive optional platinum-based chemo with or without radiotherapy as adjuvant treatment per the investigator's discretion.
ALK, anaplastic lymphoma kinase; AUC, area under the curve; chemo, chemotherapy; Dom, domvanalimab; ECOG PS, Eastern Cooperative Oncology Group performance status; *EGFR*, epidermal growth factor receptor; IV, intravenous; Q3W, every 3 weeks; R, randomization; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; Zim, zimberelimab.

Table 2. Primary, Secondary, and Exploratory End Points

Primary end point	Secondary end points	Exploratory end points
Pathological complete response[a]	Major pathological response rate[b]	Proportion of delayed or canceled surgery, duration of surgery, length of hospital stays, surgical approach, incidence of AEs/serious AEs associated with surgery
	Event-free survival[c]	Clinical response rate prior to definitive surgery[d]
	Overall survival[e]	Biomarker change and correlation with clinical responses
	Incidence of TEAEs,TRAEs, and laboratory abnormalities	Pharmacokinetics and immunogenicity

[a]Percentage of participants with no residual invasive cancer in resected lung specimens and lymph nodes, assessed by local pathology review.
[b]Percentage of participants with ≤ 10% residual tumor in lung and lymph nodes at surgery.
[c]Time from randomization until any of the following events: any progression precluding surgery or preventing completion of surgery, progression or recurrence of disease after surgery (local or distant) as assessed by investigator per RECIST v1.1, or death due to any cause, whichever occurs first. Participants who do not undergo surgery for reasons other than progression will be considered to have had an event at progression based on investigator assessment per RECIST v1.1 or at death.
[d]Percentage of participants with complete response or partial response as their best overall investigator-assessed radiological response.
[e]Time between the date of randomization and the date of death due to any cause.
AE, adverse event

Key Eligibility Criteria

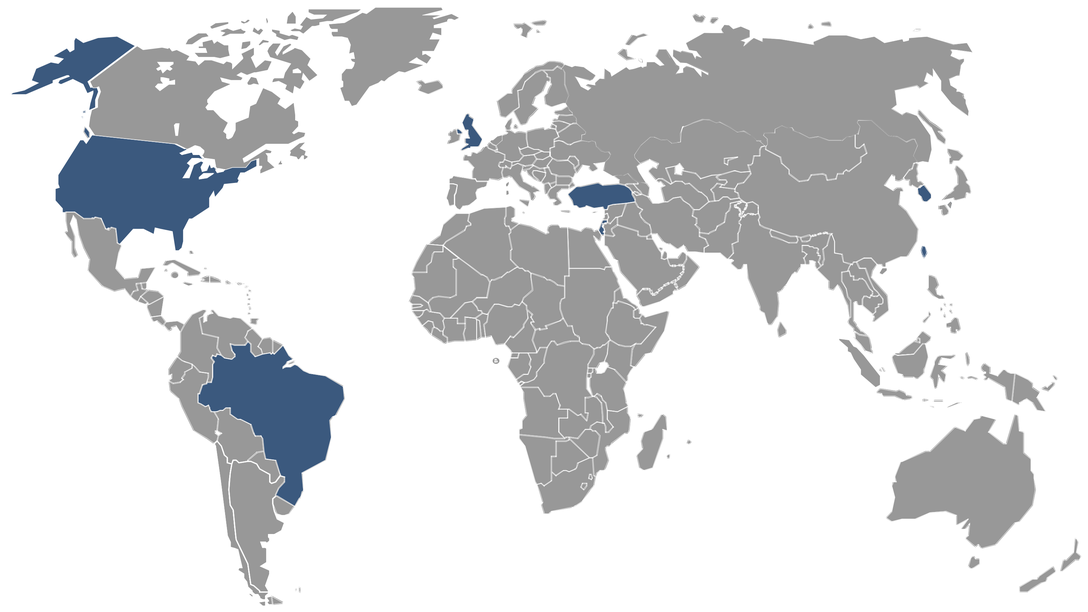
Table 2. Key Inclusion and Exclusion Criteria

Inclusion	Exclusion
• Age ≥ 18 years • Histologically/cytologically confirmed stage II, IIIA, or IIIB (T[3-4]N2) squamous or nonsquamous NSCLC per American Joint Committee on Cancer (edition 8), considered resectable with curative intent • R0 resection is achievable as determined by a thoracic surgeon, and planned surgery prior to enrollment must be lobectomy, sleeve lobectomy, or bilobectomy • Measurable disease by CT or MRI per RECIST v1.1. For participants with nonsquamous histology, central lab testing is required if *EGFR* or *ALK* status is unknown • Centrally confirmed tumor PD-L1 status by Ventana (SP263) assay • ECOG PS 0-1 • Adequate hematologic counts, adequate hepatic function, and creatinine clearance	• NSCLC previously treated with systemic therapy or radiotherapy • Actionable *EGFR* or *ALK* genomic alterations in participants with nonsquamous NSCLC • Mixed small-cell lung cancer and NSCLC histology • Received prior treatment with any anti–PD-(L)1 or other immune checkpoint inhibitors • Active second malignancy, serious infection, or autoimmune disease • History of or current noninfectious pneumonitis/interstitial lung disease

CT, computed tomography; MRI, magnetic resonance imaging.

Study Sites/Enrollment

Figure 3. Participating Countries



As of January 2024, the VELOCITY-Lung Substudy-03 (NCT05633667) is currently enrolling participants globally. There are sites in Brazil, Israel, South Korea, Taiwan, Turkey, United Kingdom, and United States.

For more information, please visit:
https://clinicaltrials.gov/ct2/show/NCT05633667

Plain Language Summary

- Participants with non-small cell lung cancer (NSCLC) that has not yet spread may have surgery to remove the tumor
  - They often receive drugs before surgery to make the tumor smaller
  - They often receive drugs after surgery to prevent the cancer from returning
- Researchers observed that the combination of domvanalimab and zimberelimab shrank NSCLC tumors in participants whose cancer had already spread throughout the body
  - Researchers think this combination may help if participants receive it before and after surgery
- Researchers want to understand if giving domvanalimab + zimberelimab + chemotherapy or zimberelimab + chemotherapy will help if given before or after surgery
  - Researchers will assess if cancer cells remain in the tissue, how long participants live, and if the combinations are safe

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