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Be6A Lung-01, a phase 3 study of sigvotatug vedotin, an investigational antibody-drug conjugate versus docetaxel in patients with previously treated non-small cell lung cancer

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Objective

- To evaluate sigvotatug vedotin (SV) compared with docetaxel in adult patients with previously treated locally advanced, unresectable, or metastatic nonsquamous NSCLC.

Conclusions

- Enrollment has begun in study centers globally.

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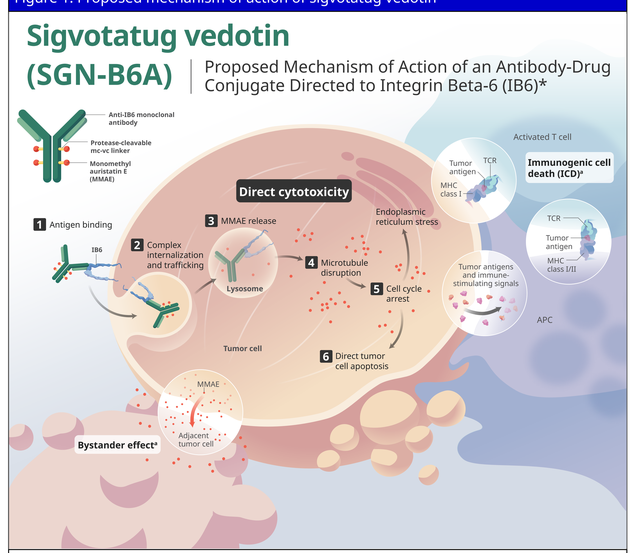
Background

- Lung cancer is a major global health problem and despite advancements in treatment options, the prognosis for patients with NSCLC remains poor.[1,2]
  - Second-line or subsequent (2L+) treatment options offer limited benefit for patients whose disease has progressed after treatment with PD-(L)1 inhibitors, platinum-based chemotherapy (PBC), and/or targeted therapy; therefore, there remains a high unmet need for patients with previously treated NSCLC.
- Integrin-beta 6 (IB6) has become an investigational target for cancer treatment as it is overexpressed in many solid tumors, and its expression is correlated with poor outcomes in several cancers.[3,4]
  - IB6 expression is a negative prognostic indicator for NSCLC,[5] and >90% of NSCLC tumors express IB6 (Pfizer data on file).
- Sigvotatug vedotin (SV, formerly known as SGN-B6A, **Figure 1**) is an IB6-directed vedotin antibody-drug conjugate that elicits antitumor activity via MMAE-mediated cytotoxicity, bystander effect, and immunogenic cell death.
- In the first-in-human trial SGNB6A-001 (NCT04389632), SV demonstrated a manageable and tolerable safety profile and encouraging activity in heavily pretreated patients with NSCLC and other solid tumors.[6,7]
  - Confirmed objective response rate:
    - NSCLC: 19.0% (95% CI: 12.3, 27.3).[7]
    - Nonsquamous, taxane-naïve NSCLC: 31.0% (95% CI: 17.6, 47.1).[7]
  - Median duration of response:
    - NSCLC: 11.3 months (range: 2.4, 24.9+).[7]
    - Nonsquamous, taxane-naïve NSCLC: 11.6 months (range: 2.4, 24.2+).[7]
- SV is currently being investigated in a phase 3 study Be6A Lung-01 (NCT06012435).

Figure 1: Proposed mechanism of action of sigvotatug vedotin



[a] Additional mechanisms of action and their potential to complement the direct cytotoxicity of some MMAE-based antibody-drug conjugates are currently under investigation.
* Sigvotatug vedotin (SGN-B6A) is an investigational agent, and its safety and efficacy have not been established.
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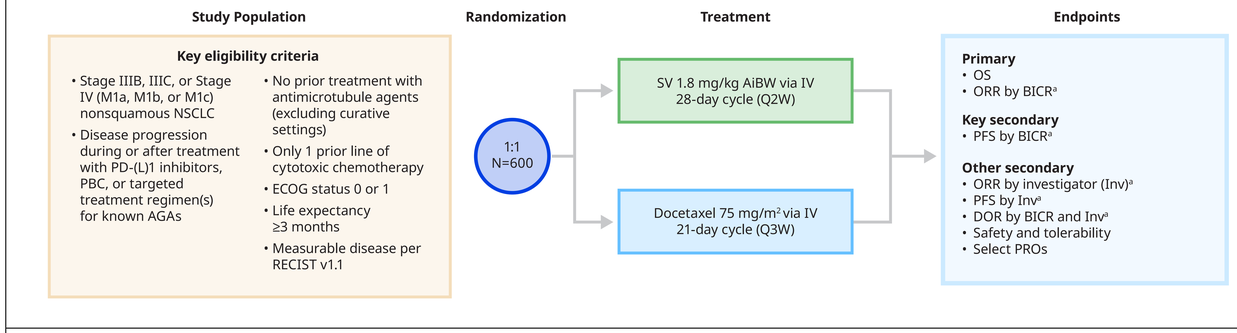
Figure 2: Study schema



[a] RECIST v1.1 will be used for DOR, ORR, and PFS assessed by BICR or Inv.

Methods

OVERALL STUDY DESIGN

- Be6A Lung-01 is a randomized, phase 3, open-label, global study evaluating the efficacy and safety of SV compared with docetaxel in adult patients with previously treated NSCLC (**Figure 2**).
  - Approximately 600 patients will be enrolled across 250 centers.
  - Randomization will be stratified by:
    - ECOG performance status: 0 vs 1.
    - AGAs: known *EGFR* or *ALK* alterations; present vs absent or unknown.
    - Regions: North America and Western Europe vs Asia Pacific vs rest of world.
  - The maximum time on study is up to 5 years for each patient.

ELIGIBILITY

Key Inclusion Criteria

- ≥18 years old.
- Histologically or cytologically confirmed NSCLC (IIIB-IVB).
- Patients without AGAs:
  - Received prior treatment and progressed during or after PBC (or within 6 months of the last dose of PBC in the adjuvant, neoadjuvant, or chemoradiotherapy setting) and a concurrent or sequential anti-PD-(L)1 therapy.
- Patients with AGAs:
  - Received at least 1 AGA-targeted therapy and a PBC (or progressed within 6 months of the last dose of PBC in the adjuvant, neoadjuvant, or chemoradiotherapy setting).
- Measurable disease per RECIST v1.1, as determined by investigator.
- ECOG performance status score of 0 or 1 and adequate organ function.

Key Exclusion Criteria

- Life expectancy <3 months.
- History of another malignancy within 3 years or residual disease from a previous malignancy (excluding those with negligible risk of metastasis or death).
- Respiratory conditions, including:
  - Noninfectious interstitial lung disease or pneumonitis.
  - Diffusing capacity of the lung for carbon monoxide <50%.
  - Grade ≥3 pulmonary disease unrelated to underlying malignancy.
- Active and untreated central nervous system lesions.
- Pre-existing grade ≥2 peripheral neuropathy or uncontrolled diabetes mellitus.
- Prior treatment with: antimicrotubule agents (excluding curative settings), >1 line of cytotoxic chemotherapy, radiotherapy >30 Gray to lung parenchyma within 6 months of first study dose.

ASSESSMENTS

Efficacy

- Radiographic tumor evaluation per RECIST v1.1 every 9 weeks from randomization (every 12 weeks after Week 72).
- Survival follow-up every 12 weeks.

Patient-Reported Outcomes

- HR-QoL assessment at protocol-specified timepoints:
  - EQ-5D-5L, EORTC QLQ-C30, EORTC QLQ-LC13, PGI-C, and PGI-S.

Safety

- Adverse events, concomitant medications, physical examination findings, and laboratory tests.

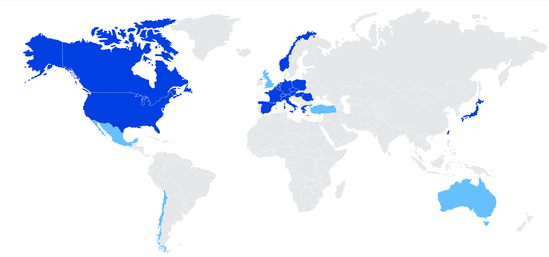
PK

- PK analysis, biomarker analysis, and immunogenicity assessments will be carried out.

Summary

- Be6A Lung-01 (NCT06012435) is evaluating the efficacy and safety of SV compared with docetaxel in patients with previously treated locally advanced, unresectable, or metastatic nonsquamous NSCLC.
- Enrollment has begun in study centers globally (**Figure 3**).
- Other SV trials include:
  - NCT04389632: a phase 1 study investigating SV as monotherapy or in combination with pembrolizumab, with or without chemotherapy, in advanced solid tumors.[6,7]
  - NCT06549816: an open-label, phase 1 study to investigate the safety and PK of SV in Chinese patients with advanced solid tumors.

Figure 3: Participating regions of study Be6A Lung-01 (NCT06012435)



Abbreviations: AE=adverse event; AGA=actionable genomic alteration; AiBW=adjusted ideal body weight; APC=antigen-presenting cell; BICR=blinded independent central review; DOR=duration of response; ECOG=Eastern Cooperative Oncology Group; EORTC QLQ-C30=European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; EORTC QLQ-LC13=EORTC QLQ-Lung Cancer 13; EQ-5D-5L=the EuroQol 5 Dimensions 5 Levels; HR-QoL=health-related quality of life; IB6=integrin beta-6; Inv=investigator; IV=intravenously; mc-vc=maleimidocaproyl-valine-citrulline; MHC=major histocompatibility complex; MMAE=monomethyl auristatin E; NSCLC=non-small cell lung cancer; ORR=objective response rate; OS=overall survival; PBC=platinum-based chemotherapy; PD-(L)1=programmed cell death receptor 1 and programmed cell death ligand 1; PFS=progression-free survival; PGI-C=Patient Global Impression of Change; PGI-S=Patient Global Impression of Severity; PROs=patient-reported outcomes; Q2W=once every 2 weeks; Q3W=once every 3 weeks; SV=sigvotatug vedotin, SGN-B6A; TCR=T-cell receptor; TTD=time to deterioration.