AdvanTIG-302: Anti-TIGIT Monoclonal Antibody Ociperlimab+Tislelizumab in Non-Small Cell Lung Cancer

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Speaker disclosures

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Background

- Monotherapy with PD-1/PD-L1 mAbs has improved clinical outcomes for patients with non-oncogenic driven NSCLC, but clinical efficacy is limited by primary and secondary resistance, and improvements in OS are required\(^1,2\)

- Ociperlimab (BGB-A1217) is a novel, humanized mAb that binds to TIGIT with high affinity and specificity, blocking the interaction with its ligands on tumor cells\(^3\)

- Tislelizumab is an anti–PD-1 mAb that has been engineered to minimize binding to FcγR on macrophages and abrogate antibody-dependent phagocytosis\(^4,5\)

- Dual targeting of tumors with anti-TIGIT and anti–PD-1 mAbs produces synergistic immune cell activation and enhanced antitumor activity in preclinical and clinical studies\(^3,6\)

Here we present the design of the ongoing phase 3 AdvanTIG-302 study (NCT04746924) investigating the efficacy and safety of ociperlimab + tislelizumab vs pembrolizumab (anti–PD-1 mAb) as a single agent in patients with PD-L1–selected, previously untreated, locally advanced, unresectable or metastatic NSCLC

**Diagram Description:**

- Ociperlimab activates T/NK cells by blocking TIGIT and ligand interaction
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  - APC or tumor cell
  - CD226 (DNAM-1)
  - Stimulatory signal
  - T cell or NK cell
  - Inhibitory signal
- PVR-L2 (CD112)
- PVR (CD155)
- TIGIT
- APC, antigen-presenting cell; DNAM-1, DNAX accessory molecule 1; FcγR, Fcγ receptor; mAb, monoclonal antibody; NK, natural killer; NSCLC, non-small cell lung cancer; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PVR, poliovirus receptor; PVR-L2, poliovirus receptor-related 2; TIGIT, T cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibition motif domain.

Enrollment sites

AdvanTIG-302: a phase 3, multicenter, international, randomized, double-blind study

Across 242 centers globally

Approximately 660 patients with PD-L1–selected, locally advanced/recurrent or untreated metastatic NSCLC

NSCLC, non-small cell lung cancer; PD-L1, programmed death-ligand 1.
AdvanTIG-302 study design

### Key eligibility criteria\(^a\)
- Metastatic nonsquamous or squamous NSCLC or locally advanced or recurrent NSCLC that is not eligible for curative surgery and/or definitive radiotherapy with or without chemoradiotherapy
- Tumor cell PD-L1 expression ≥50%
- No known EGFR-sensitizing mutations or ALK rearrangements
- No prior systemic treatment for metastatic NSCLC
- No prior checkpoint inhibitor treatment (∼N=660)

### Stratification factors
- Histology (squamous vs nonsquamous)
- Region (Asia vs non-Asia)

### Arm A:
- ociperlimab 900 mg + tislelizumab 200 mg IV Q3W (n=286)

### Arm B:
- pembrolizumab 200 mg + placebo IV Q3W (n=286)

### Arm C\(^b\):
- tislelizumab 200 mg + placebo IV Q3W (n=88)

- Treatment until lack of benefit, unacceptable toxicity, or withdrawal for other reasons
- Continued safety and survival follow-up

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\(^a\) Patients were ineligible if they had active leptomeningeal disease, an autoimmune disease or infection, a history of interstitial lung disease or diabetes, an active malignancy ≤2 years previous, a condition that required systemic treatment with steroids, hepatitis B or C, HIV, cardiovascular risk factors, a surgical procedure or live vaccine ≤28 days before randomization, or concurrent participation in clinical trial or were pregnant. \(^b\) Tislelizumab monotherapy has demonstrated activity in pretreated NSCLC and is expected to be active in patients with previously untreated NSCLC. Arm C was implemented with the intent to generate tislelizumab monotherapy data in this specific NSCLC population so that the relative contributions of tislelizumab and ociperlimab in arm A can be understood. \(^c\) The timepoint at which the investigator considers that the patient is no longer benefiting from the study treatment.
## Endpoints

### Dual primary endpoints
- Investigator-assessed PFS according to RECIST v1.1 for arm A vs B
- OS for arm A vs B

### Secondary endpoints
- PFS by BIRC<sup>a</sup> in arms A and B
- ORR by investigators<sup>a</sup> in arms A and B
- DOR by investigators<sup>a</sup> in arms A and B
- HRQOL
  - EORTC QLQ-C30<sup>b</sup>
  - EORTC QLQ-LC-13
  - EQ-5D-5L questionnaire
- Time to deterioration
- Incidence and severity of AEs

### Exploratory endpoints
- ORR and DOR by BIRC<sup>a</sup> in arms A and B
- DCR, CBR, and TTR by BIRC and investigators<sup>a</sup> in arms A and B
- PFS after next line of treatment (PFS2)
- OS, PFS, ORR, and DOR by BIRC and investigators<sup>a</sup> in arm C
- Incidence and severity of AEs in arm C
- Association between biomarkers and response or resistance
- Pharmacokinetics
- Host immunogenicity

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<sup>a</sup> According to RECIST v1.1.  
<sup>b</sup> Analyzed using the global health status scale of the QLQ-C30 tool.

AE, adverse event; BIRC, blinded independent review committee; CBR, clinical benefit rate; DCR, disease control rate; DOR, duration of response; EORTC, European Organization for Research and Treatment of Cancer; EQ-5D-5L, 5 Level EuroQol 5 Dimension; HRQOL, health-related quality of life; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PFS2, time from randomization to objective disease progression after next line of treatment or death from any cause, whichever occurs first; QLQ-C30, Quality of Life Questionnaire Core 30; QLQ-LC-13, Quality of Life Questionnaire Lung Cancer 13; RECIST, Response Evaluation Criteria in Solid Tumors; TTR, time to response.
Assessments

• All efficacy-related endpoints will be assessed in the ITT analysis set (all randomized patients)

• Radiological imaging will be performed every 9 weeks for the first year of the study and every 12 weeks thereafter

• Tumor responses will be assessed by investigators and a BIRC using RECIST v1.1

• Patient-reported HRQOL assessments will be performed at baseline, every other cycle through cycle 13, every 4 cycles thereafter, and at the end-of-treatment visit

• Safety will be assessed through monitoring of the incidence and severity of AEs (graded via NCI CTCAE v5.0), laboratory results, vital signs, ECOG PS, and other examinations

• Safety analyses will be performed using the safety analysis set (all randomized patients receiving ≥1 dose of study drug)
The dual primary endpoints of PFS and OS will be estimated using the Kaplan-Meier method, with a stratified log-rank test used to compare arm A vs B and treatment effect estimated using a Cox regression model.

An interim analysis will be performed for OS at the time of final PFS analysis.

OS, overall survival; PFS, progression-free survival.
Conclusions

- AdvanTIG-302 is an ongoing phase 3 study investigating whether ociperlimab + tislelizumab combination therapy prolongs PFS and OS vs pembrolizumab monotherapy in adults with PD-L1–high, locally advanced/recurrent or untreated metastatic NSCLC.

- This study will provide insight into the effect of dual targeting with anti-TIGIT and anti–PD-1 antibodies (ociperlimab and tislelizumab) vs anti–PD-1 monotherapy (pembrolizumab) in first-line NSCLC.
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