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

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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**

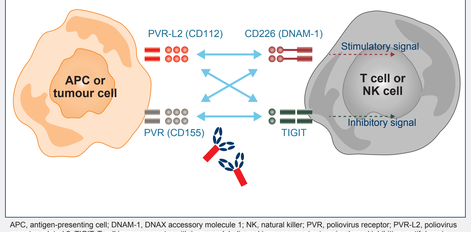
Introduction

- Monotherapy with programmed cell death protein-1 (PD-1)/ programmed death-ligand 1 (PD-L1) monoclonal antibodies (mAbs) has improved clinical outcomes for patients with non-oncogenic driven non-small cell lung cancer (NSCLC), but clinical efficacy is limited by primary and secondary resistance, and improvements in overall survival (OS) are required[1,2]
- T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domain (TIGIT) is upregulated in the tumour microenvironment in multiple malignancies, and is often co-expressed with PD-1[3]
- Dual targeting of tumours with anti-TIGIT and anti-PD-1 mAbs produces synergistic immune cell activation and enhanced antitumour activity in preclinical and clinical studies[4,5]

Introduction to ociperlimab, tislelizumab, and the AdvanTIG-302 study

- Ociperlimab (BGB-A1217) is a novel, humanised mAb that binds TIGIT with high affinity and specificity, blocking the interaction with its ligands on tumour cells (**Figure 1**)[4]
- Tislelizumab is an anti-PD-1 mAb that has been engineered to minimise binding to FcγR on macrophages and abrogate antibody-dependent phagocytosis[6,7]
- Here we report 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

Figure 1. Ociperlimab activates T/NK cells by blocking TIGIT and ligand interaction



APC, antigen-presenting cell; DNAM-1, DNAX accessory molecule 1; NK, natural killer; PVR, poliovirus receptor; PVR-L2, poliovirus receptor-related 2; TIGIT, T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibition motif domain.

Methods

Study Design and Treatment

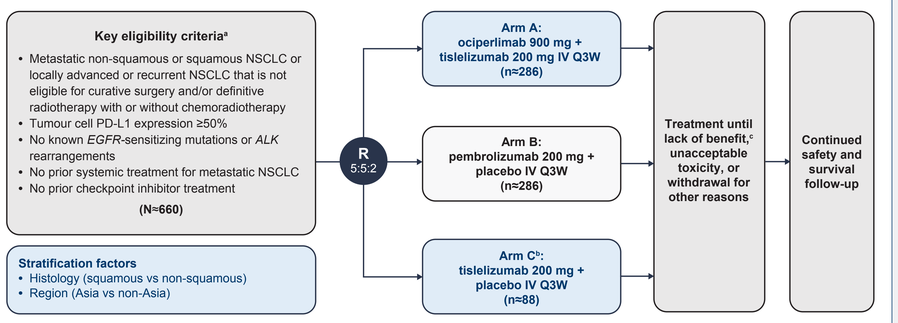
- AdvanTIG-302 is a phase 3, multicentre (242 centres globally), international (across 17 countries), randomised, double-blind study (**Figure 2**)
- Approximately 660 patients with PD-L1−selected, locally advanced/recurrent or untreated metastatic NSCLC will be enrolled in the study (**Figure 3**)
- Patients will be randomly assigned 5:5:2 to receive ociperlimab 900 mg + tislelizumab 200 mg IV every 3 weeks (Q3W) (Arm A),pembrolizumab 200 mg + placebo IV Q3W (Arm B), or tislelizumab 200 mg + placebo IV Q3W (Arm C)
  - Randomisation will be stratified by histology (squamous vs non-squamous) and region (Asia vs non-Asia)
- Treatment will be administered until disease progression, loss of clinical benefit, unacceptable toxicity, or withdrawal for other reasons, before continued safety and survival follow-up
- Study enrolment has begun, and recruitment is ongoing

Study Population

- Key eligibility criteria included the following:
  - Histologically or cytologically confirmed metastatic non-squamous or squamous NSCLC, or locally advanced or recurrent NSCLC that is not eligible for curative surgery and/or definitive radiotherapy with or without chemoradiotherapy
  - Tumours with PD-L1 expressed in ≥50% tumour cells
  - No known *EGFR*-sensitising mutations or *ALK* rearrangements
  - No prior systemic treatment for metastatic NSCLC
  - No prior therapy with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-TIGIT, or any other antibody or drug specifically targeting T-cell co-stimulation or checkpoint pathways.
  - Patients must agree to provide archival tumour tissue or be willing to undergo fresh tumour biopsy
  - ≥1 measurable lesion as defined by Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1)
  - Eastern Cooperative Oncology Group performance status (ECOG PS) of ≤1

Figure 2. Enrollment sites

Figure 3. Study Design



[a]Patients are ineligible if they have untreated brain metastases, an active autoimmune disease or infection, a history of interstitial lung disease, another active malignancy ≤5 years previously, a condition that required systemic treatment with steroids, active hepatitis B or C, HIV, cardiovascular risk factors, a surgical procedure or live vaccine ≤28 days before randomisation, concurrent participation in a 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
ALK, anaplastic lymphoma kinase; *EGFR*, epidermal growth factor receptor; IV, intravenous; NSCLC, non-small cell lung cancer; PD-1, programmed death-ligand 1; Q3W, every 3 weeks; R, randomisation.

Endpoints and Assessments

- The dual primary endpoints are investigator-assessed progression-free survival (PFS; per RECIST v1.1) and OS for Arm A vs Arm B
  - PFS and OS will be estimated using the Kaplan-Meier method, with a stratified log-rank test used to compare Arm A vs Arm B and treatment effect estimated using a Cox regression model
  - An interim analysis for OS will be performed at the time of the final PFS analysis
- Secondary and exploratory endpoints are listed in **Table 1**
- All efficacy endpoints will be assessed in the intention-to-treat analysis set (all randomised patients)
- Radiological imaging will be performed every 9 weeks for the first year of the study, and every 12 weeks thereafter
- Tumour responses will be assessed by investigators and a blinded independent review committee using RECIST v1.1
- Patient-reported health-related quality-of-life 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 adverse events (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 randomised patients receiving ≥1 dose of study drug

Table 1. Study Endpoints

Primary endpoint	• Investigator-assessed PFS (per RECIST v1.1) for Arm A vs Arm B • OS for Arm A vs Arm B
Secondary endpoints	• PFS by BIRC in Arms A and B • ORR by investigators in Arms A and B • DOR by investigators in Arms A and B • HRQoL – EORTC QLQ-C30 – EORTC QLQ-LC-13 – EQ-5D-5L questionnaire • Time to deterioration • Incidence and severity of AEs
Exploratory endpoints	• ORR and DOR by BIRC in Arms A and B • DCR, CBR, and TTR by BIRC and investigators in Arms A and B • PFS after next line of treatment (PFS2) • OS, PFS, ORR, and DOR by BIRC and investigators in Arm C • Incidence and severity of AEs in Arm C • Association between biomarkers and response or resistance • Pharmacokinetics • Host immunogenicity

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

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