Presentation: O56-6

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

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Speaker disclosures

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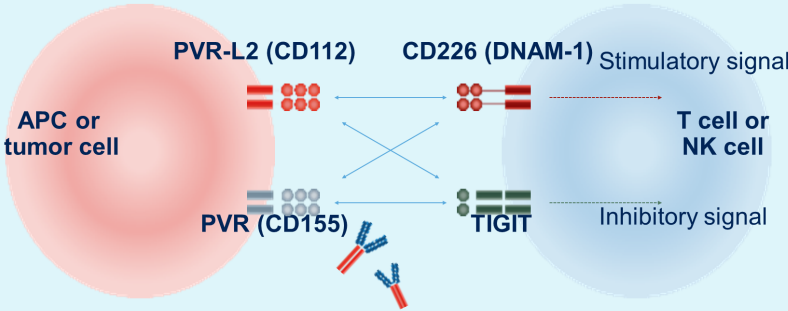
Background

- 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]

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

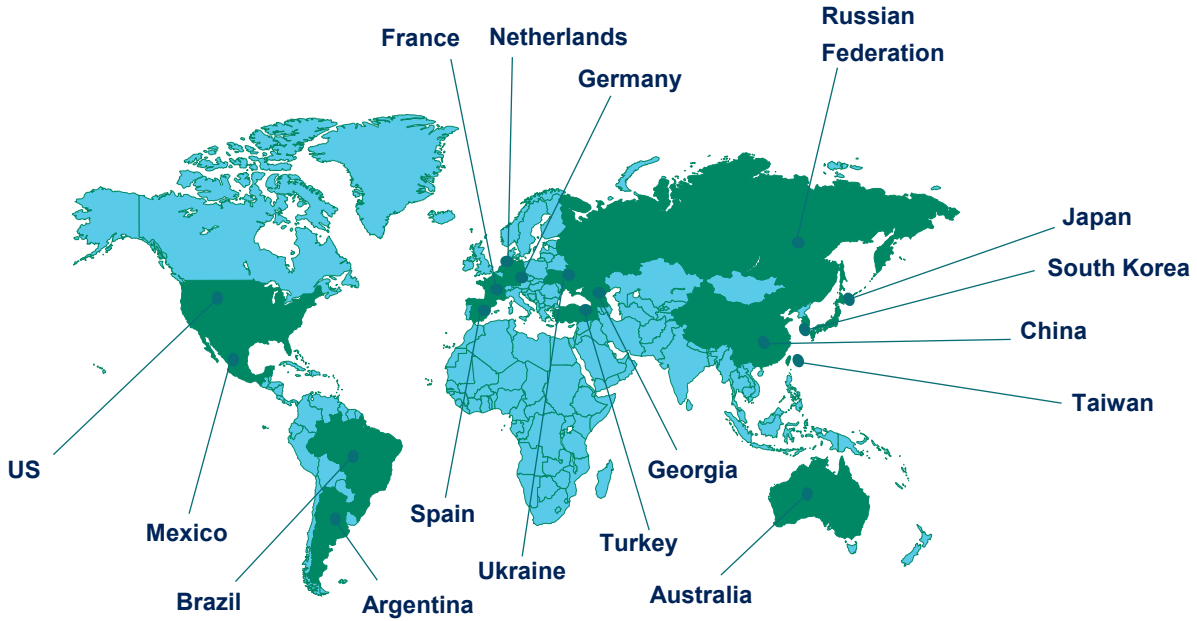


Here we present the design of the ongoing phase 3 AdvanTIG-302 study (NCT04746924) investigating the efficacy and safety of ociperlimab + tislelizumab vs pembrolizumab (anti–PD-1 mAb) as a single agent in patients with PD-L1–selected, previously untreated, locally advanced, unresectable or metastatic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

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.

1. Santini FC and Hellman MD. *Cancer J*. 2018;24:15-19. 2. Sui H, et al. *J Immunol Res*. 2018;2018:6984948. 3. Chen X, et al. Data presented at AACR Congress 2021. Poster 1854. 4. Qin S, et al. *Future Oncol*. 2019;15:1811-1822. 5. Zhang T, et al. *Cancer Immunol Immunother*. 2018;67:1079-1090. 6. Rodriguez-Abreu D, et al. *J Clin Oncol*. 2020;38:9503.

Enrollment sites



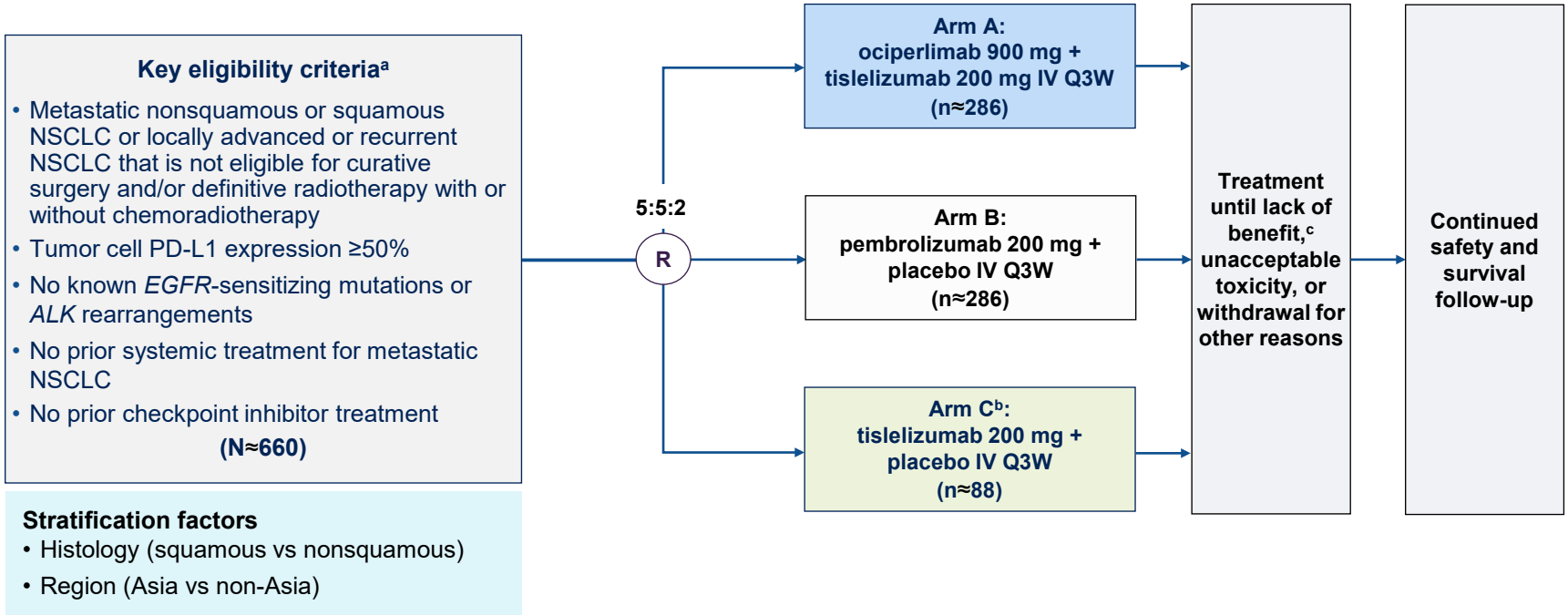
AdvanTIG-302:
a phase 3, multicenter, international, randomized, double-blind study

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



ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; IV, intravenously; NSCLC, non-small cell lung cancer; Q3W, every 3 weeks; PD-1, programmed death-ligand 1; R, randomization.

[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[a] in arms A and B
• ORR by investigators[a] in arms A and B
• DOR by investigators[a] in arms A and B
• HRQOL
  ○ EORTC QLQ-C30[b]
  ○ EORTC QLQ-LC-13
  ○ EQ-5D-5L questionnaire
• Time to deterioration
• Incidence and severity of AEs

Exploratory endpoints
• ORR and DOR by BIRC[a] in arms A and B • DCR, CBR, and TTR by BIRC and investigators[a] in arms A and B • PFS after next line of treatment (PFS2) • OS, PFS, ORR, and DOR by BIRC and investigators[a] 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 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.

[a] According to RECIST v1.1. [b] Analyzed using the global health status scale of the QLQ-C30 tool.

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)

AE, adverse event; BIRC, blinded independent review committee; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQOL, health-related quality of life; ITT, intent to treat; NCI CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; RECIST, Response Evaluation Criteria in Solid Tumors.

Statistical analysis

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

NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1.

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