AdvanTIG-204: Anti-TIGIT Monoclonal Antibody Ociperlimab Plus Anti-PD-1 Monoclonal Antibody Tislelizumab Plus Concurrent Chemoradiotherapy in Patients With Untreated Limited-Stage Small Cell Lung Cancer

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Conclusions

AdvanTIG-204 is a **Phase 2** study designed to investigate the **efficacy and safety of OCI in combination with TIS plus cCRT,** vs **TIS plus cCRT and cCRT alone,** in patients with **untreated LS-SCLC**

Background

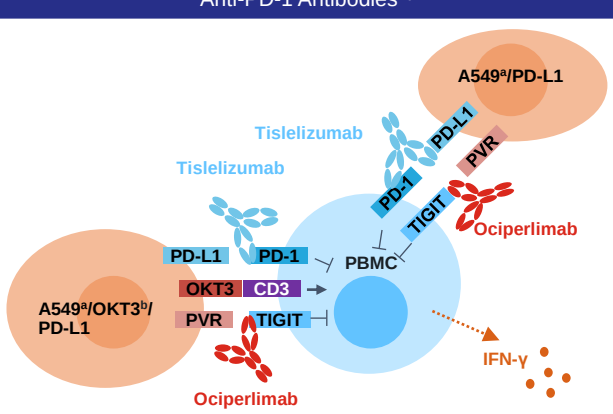
Unmet Need in Limited-Stage Small Cell Lung Cancer

- Small cell lung cancer (SCLC) is a highly aggressive neuroendocrine tumor that accounts for approximately 13% of lung cancers.[1,2] SCLC is classified into two stages, limited stage (LS-SCLC) and extensive stage (ES-SCLC).[2] It is estimated approximately 30% of patients with SCLC will have LS-SCLC at the time of diagnosis[2]
- The current standard of care for patients with LS-SCLC is concurrent chemoradiotherapy (cCRT).[2,3] Up to now, there are no approved novel therapeutic agents that improve clinical outcomes, including targeted therapy and immunotherapy[4]
- Despite high response rates with cCRT, patients' outcomes are poor, and most patients experience disease relapse; the median overall survival has been reported as 25-30 months, with a 5-year survival rate of 25-35%[5-9]
- Upregulation of immune checkpoint molecules, such as programmed cell death protein 1 (PD-1), represents a key mechanism through which tumors inhibit anticancer immune responses[10-12]
- Immune checkpoint inhibitors in combination with standard therapy have shown clinical benefit as a first-line treatment for ES-SCLC.[13] However, a trial investigating the role of checkpoint inhibitors in LS-SCLC is ongoing[8]

Introduction to Ociperlimab, Tislelizumab, and AdvanTIG-204 Study

- T-cell immunoreceptor with immunoglobin and immunoreceptor tyrosine-based inhibitory motif domain (TIGIT) is a co-inhibitory immune checkpoint receptor that is upregulated on T cells and natural killer cells in multiple solid tumors, which can cause tumor escape from immune surveillance[14,15]
- Ociperlimab (OCI) is a humanized immunoglobin G1 (IgG1) monoclonal antibody (mAb) designed to bind to TIGIT with high specificity, blocking the interaction with CD155 (poliovirus receptor [PVR]) and CD112 (PVR-L2) ligands on tumor cells[16]
- Programmed death-ligand 1 (PD-L1) is an immune checkpoint protein that is overexpressed on the surface of tumor and immune cells in the tumor microenvironment.[17] Interactions between PD-L1 and PD-1 on T cells play an important role in suppressing antitumor activity[17]
- Tislelizumab (TIS) is a humanized IgG4 PD-1 inhibitor mAb with high affinity and binding specificity for PD-1 and was engineered to minimize Fc gamma receptor binding to abrogate antibody-dependent cellular phagocytosis, which is a mechanism of resistance to anti-PD-1 therapy.[17,18] TIS has been approved for treating multiple tumor types in China, including non-small cell lung cancer, and has demonstrated clinical activity in patients with ES-SCLC[19,20]
- Dual targeting of tumors with anti-TIGIT and anti-PD-1 mAbs (**Figure 1**) has shown synergistic immune activation and enhanced antitumor activity in the phase 1 AdvanTIG-105 trial, which demonstrated OCI plus TIS was well tolerated in patients with advanced solid tumors and preliminary antitumor activity was observed.[21] A study investigating their clinical activity in LS-SCLC is ongoing[8]

Figure 1. Dual Targeting With Anti-TIGIT and Anti-PD-1 Antibodies[16]



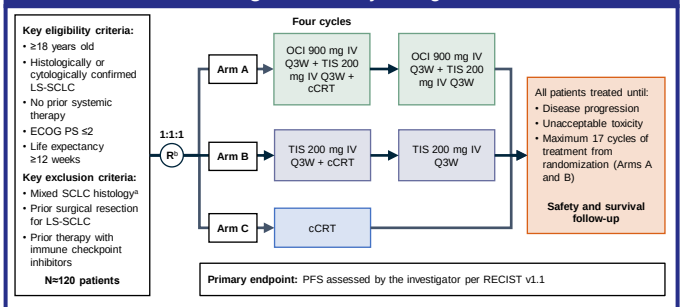
Chen X, et al. Data presented at AACR 2021 (Abs 1854).
[a] PVR positive A549 cells; [b] anti-CD3 antibody clone.
Abbreviations: IFN, interferon; PBMC, human peripheral blood mononuclear cells; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PVR, poliovirus receptor; TIGIT, T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domain.

Methods

Study Design and Treatments

- AdvanTIG-204 is a phase 2, randomized, multicenter, open-label study (NCT04952597). The first patient was enrolled on July 15, 2021, and the study is ongoing
- Approximately 120 patients aged ≥18 years, with untreated histologically or cytologically confirmed LS-SCLC will be enrolled (**Figure 2**)
- Eligible patients will be randomized 1:1:1 to:
  - **Arm A:** OCI 900 mg intravenously (IV) once every 3 weeks (Q3W) plus TIS 200 mg IV Q3W and cCRT for four cycles, followed by OCI 900 mg IV Q3W plus TIS 200 mg IV Q3W
  - **Arm B:** TIS 200 mg IV Q3W and cCRT for four cycles, followed by TIS 200 mg IV Q3W
  - **Arm C:** cCRT only for four cycles
- Prophylactic cranial irradiation is permitted at the investigator's discretion

Figure 2. Study Design



[a] Mixed SCLC with the component of neuroendocrine carcinoma origin is considered eligible; [b] Stratification factor: Stage (2/3 vs 3) per AJCC 8th edition.
Abbreviations: AJCC, American Joint Committee on Cancer; cCRT, concurrent chemoradiotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; LS-SCLC, limited-stage small cell lung cancer; OCI, ociperlimab; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors; SCLC, small cell lung cancer; TIS, tislelizumab.

Endpoints and Assessments

- The primary, secondary, and exploratory endpoints of the AdvanTIG-204 study are listed in **Table 1**
- Baseline tumor imaging will be performed ≤28 days before randomization
- Tumor response will be evaluated 12 weeks (±7 days) from the date of randomization, then every 6 weeks (±7 days) for the next 54 weeks, and then every 12 weeks (±7 days) thereafter, per RECIST v1.1
- Safety analyses will be performed using the safety analysis set (includes all randomized patients receiving ≥1 dose of the study treatment)
- Safety will be assessed through monitoring the incidence and severity of adverse events (graded according to National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0, vital signs, and clinical laboratory results)

Table 2. Endpoints of the Study

AdvanTIG-204 endpoints	
Primary endpoint	• PFS assessed by the investigator per RECIST v1.1 in the ITT analysis set
Secondary endpoints	• CR rate, ORR, DoR, and DMFS, all assessed by the investigator per RECIST v1.1 in the ITT analysis set • OS in the ITT analysis set • ORR, PFS, and OS assessed in subgroups based on PD-L1 and TIGIT expression levels • Safety
Exploratory endpoints	• Biomarker analysis • HRQoL using EORTC QLQ-C30 and QLQ-LC13 • ctDNA level changes before, during, or after treatment • Serum concentrations of OCI and TIS at specified timepoints • Immunogenicity of OCI and TIS by determining the incidence of ADAs

Abbreviations: ADA, antidrug antibody; CR, complete response; ctDNA, circulating tumor DNA; DMFS, distant metastasis-free survival; DoR, duration of response; EORTC QLQ-C, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core; HRQoL, health-related quality of life; ITT, intent-to-treat; OCI, ociperlimab; ORR, overall response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; RECIST; Response Evaluation Criteria in Solid Tumors; TIGIT, T-cell immunoreceptor with immunoglobin and immunoreceptor tyrosine-based inhibitory motif domain; TIS, tislelizumab.

References

1. Howlander N, et al. *SEER Cancer Stats Rev*. 1975-2014. Accessed January 21, 2022.
2. Farago AF, et al. *Transl Lung Cancer Res.* 2018;7:69-79.
3. Zhao H, et al. *Thoracic Cancer*. 2018;9:769-774.
4. Toh TS, et al. *Radiation*. 2021;1:317-333.
5. Stinchcombe TE, et al. *The Oncol.* 2010;15:187-195.
6. Higgins KA, et al. *Transl Lung Cancer Res.* 2019;8:S147-S152.
7. Islam KM, et al. *JSM Clin Oncol Res.* 2020;8:1062.
8. Faivre-Finn C, et al. *Lancet Oncol.* 2017;18:1116-1126.
9. Senan S, et al. *Clin Lung Cancer*. 2020;21:e84-e88.
10. Johnston RJ, et al. *Cancer Cell.* 2014;26:923-937.
11. Chauvin JM, et al. *J Clin Invest.* 2015;125:2046-2058.
12. Lei Q, et al. *Front Cell Dev Biol.* 2020;8:672.
13. Horn L, et al. *N Engl J Med.* 2018;379:23.
14. Manieri NA, et al. *Trends Immunol.* 2017;38:20-28.
15. Harjunpää H and Guillerey C. *Clin Exp Immunol.* 2020;200:108-119.
16. Chen X, et al. AACR 2021 (Abs 1854).
17. Desai J, et al. *JITC.* 2020;8:e000453.
18. Zhang T, et al *Cancer Immunol.* 2018;67:1079-1090.
19. BioSpace. China NMPA approves tislelizumab as second- or third-line treatment for patients with locally advanced or metastatic non-small cell lung cancer. Available at: https://www.biospace.com/article/releases/china-nmpa-approves-tislelizumab-as-second-or-third-line-treatment-for-patients-with-locally-advanced-or-metastatic-non-small-cell-lung-cancer. Accessed February 1, 2022.
20. Wang Z, et al. *Lung Cancer*. 2020;147:259-268.
21. Frentzas S, et al. ASCO 2021 (Abs 2583).

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COI Disclosure Information

YL has received advisory fees and research grants from AstraZeneca, Bristol-Myers Squibb, Merck Sharp & Dohme, Pfizer, and Roche/Genentech. YL is also an invited speaker, project lead, and leading principle investigator of the AdvanTIG-204 clinical trial at BeiGene, Ltd. YG and J-HK have no COI to declare. YZ, XC, XL, JZ are employees of BeiGene, Ltd. HB is a consultant for BMS, Lilly, Genentech, Pfizer, Merck, EMD-Serono, Boehringer Ingelheim, AstraZeneca, Novartis, Genmab, Regeneron, BioNTech, Amgen, Abbvie, Axiom, PharmaMar, Takeda, Mirati, Daiichi, Guardant, Natera, Oncocyte, BeiGene, iTEO, Jazz, Janssen, and Da Volterra. HB is also a DSMB member for University of Pennsylvania, CAR T Program, Takeda, Incyte, and Novartis and holds stock options in Sonnetbio, Inspira (formerly Rgenix), and Nucleai.