AdvanTIG-301: Anti-TIGIT monoclonal antibody ociperlimab + tislelizumab + concurrent chemoradiotherapy followed by ociperlimab + tislelizumab or tislelizumab + concurrent chemoradiotherapy followed by tislelizumab versus concurrent chemoradiotherapy followed by durvalumab in previously untreated, locally advanced, unresectable non-small cell lung cancer

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Introduction

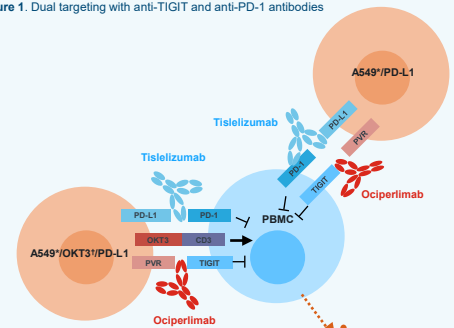
Unmet need in NSCLC

- Non-small cell lung cancer (NSCLC) accounts for approximately 85% of lung cancers, and around one third of patients with NSCLC present with Stage III, locally advanced disease at initial diagnosis.[1] This can lead to a poor long-term prognosis[2]
- Programmed cell death protein 1 (PD-1)/programmed death-ligand 1 (PD-L1)-based therapy, in combination with concurrent chemoradiotherapy (cCRT), has been shown to improve survival outcomes for patients with locally advanced, unresectable disease.[3–7] PD-L1 inhibitor durvalumab (DUR) is the current standard of care for patients whose disease had not progressed following cCRT[8]
- Despite this improvement in treatment outcomes, most patients still suffer from disease recurrence with an 18-month progression-free survival rate of approximately 44%[8,9]

Introduction to ociperlimab, tislelizumab, and the AdvanTIG-301 study

- T-cell immunoreceptor with immunoglobulin (Ig) and tyrosine-based inhibitory motif domains (TIGIT) is a co-inhibitory immune checkpoint receptor upregulated on T cells and natural killer cells in multiple solid tumors[10,11]
- The addition of an anti–TIGIT therapy to PD-1 backbone therapy could enhance antitumor responses and improve clinical outcomes for patients with non-oncogene driven NSCLC by enhancing antitumor response. Dual targeting of tumors with anti-TIGIT and anti-PD-1 monoclonal antibodies (mAbs) (**Figure 1**) produces synergistic immune cell activation and enhanced antitumor activity in preclinical and clinical studies[11,12]
- Ociperlimab (OCI; BGB-A1217) is a humanized IgG1 mAb designed to bind to TIGIT with high affinity and specificity, blocking the interaction with cluster of differentiation (CD) 155 (poliovirus receptor [PVR]) and CD112 (PVR-related 2; nectin-2) expressed by tumor cells. This leads to inhibitory signalling in T cells and natural killer cells[13,14]
- Tislelizumab (TIS) is a humanized IgG4 mAb designed to minimize Fc gamma receptor binding on macrophages to abrogate antibody-dependent phagocytosis, a potential mechanism of resistance to anti-PD-1 therapy[15,16]

Figure 1. Dual targeting with anti-TIGIT and anti-PD-1 antibodies



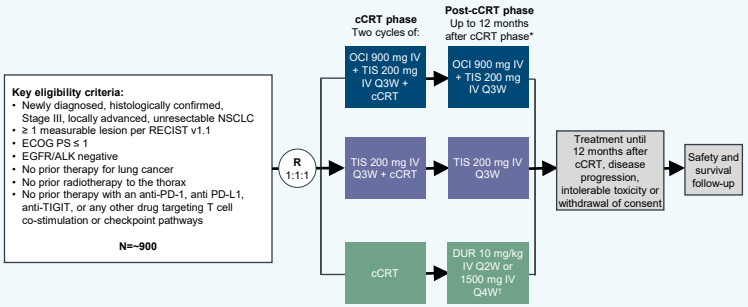
Chen X, et al. AACR (Abs 1854). PMBCs were pre-stimulated to upregulate TIGIT expression and used as effector cells. PD-L1 and T-cell engager (OS8)-positive A549 cells (A549/OS8-PD-L1) were used as target cells. IFN-γ secretion was used as the readout for T-cell activation. The combination of OCI and TIS enhanced IFN-γ production compared with OCI and TIS alone[13,14]
**PVR positive A549 cells; †anti-CD3 antibody clone; A549, adenocarcinomic human alveolar basal epithelial cells; CD3, cluster of differentiation 3; IFN-γ, interferon-gamma; OCI, ociperlimab; OKT3, muromonab-CD3; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PBMC, peripheral blood mononuclear cell; PVR, poliovirus receptor; TIGIT, T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domain; TIS, tislelizumab*

Conclusions

- **AdvanTIG-301 is an ongoing Phase 3 study investigating the efficacy and safety of ociperlimab plus tislelizumab plus cCRT followed by ociperlimab plus tislelizumab or tislelizumab plus cCRT followed by tislelizumab vs cCRT followed by durvalumab in patients with locally advanced, unresectable NSCLC**
- **This study will provide insight into the effect of dual targeting with anti-TIGIT and anti-PD-1 antibodies (ociperlimab and tislelizumab) in combination with cCRT**

Methods

Figure 2. Study design



**For patients without disease progression or unacceptable toxicity; †1500 mg Q4W dosage required approval by a local health authority*
ALK, anaplastic lymphoma kinase; cCRT, concurrent chemoradiotherapy; DUR, durvalumab; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EGFR, epidermal growth factor receptor; IV, intravenously; NSCLC, non-small cell lung cancer; OCI, ociperlimab; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; Q2W, every 2 weeks; Q3W, every 3 weeks; Q4W, every 4 weeks; R, randomized; RECIST V1.1, response evaluation criteria in solid tumors version 1.1; TIGIT, T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domain; TIS, tislelizumab

Figure 3. Current study locations

Study design and treatment

- AdvanTIG-301 is a Phase 3, multicenter, international, randomized, open-label study (NCT04866017)
- Approximately 900 patients with newly diagnosed, histologically confirmed, locally advanced, Stage III unresectable NSCLC will be enrolled (**Figure 2**) (aged ≥ 18 years)
- Study enrollment has begun, and recruitment is ongoing. Current study locations are presented in **Figure 3**
- Eligible patients will be randomized 1:1:1 to:
  - **Arm A:** Two cycles of OCI 900 mg intravenously (IV) + TIS 200 mg IV every 3 weeks (Q3W) + cCRT followed by OCI 900 mg IV + TIS 200 mg IV Q3W for up to 12 months after cCRT
  - **Arm B:** Two cycles of TIS 200 mg IV Q3W + cCRT followed by TIS 200 mg IV Q3W for up to 1 year after cCRT
  - **Arm C:** Two cycles of cCRT followed by DUR 10 mg/kg IV every 2 weeks (or 1500 mg IV every 4 weeks) for up to 1 year after cCRT
- Study endpoints are outlined in **Table 1.** Safety and efficacy will be monitored by an independent Data Monitoring Committee
- Tumor imaging will be performed approximately every 9 weeks from randomization for the first 54 weeks, and every 12 weeks thereafter based on RECIST v1.1

Table 1. AdvanTIG-301 study endpoints

Primary endpoints	• PFS and CRR by IRC per RECIST v1.1 in the ITT analysis set
Secondary endpoints	**ITT and PD-L1 positive analysis sets** • OS • ORR assessed by both IRC and the investigator per RECIST v1.1 • DoR assessed by both IRC and the investigator per RECIST v1.1 • PFS by the investigator per RECIST v1.1 • Time to death or distant metastasis by IRC • HRQoL • Safety and tolerability • Serum concentrations of ociperlimab and tislelizumab • Immunogenic responses to ociperlimab and tislelizumab • Evaluation of PD-L1 and TIGIT expression
Exploratory endpoints	• Biomarkers and patient-reported outcomes

CRR, complete response rate; DoR, duration of response; HRQoL, health-related quality of life; IRC, independent review committee; ITT, intent-to-treat; ORR, overall response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; RECIST v1.1, response evaluation criteria in solid tumors version 1.1; TIGIT, T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domain

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