AdvanTIG-204: A phase 2, multicenter, randomized, 3-arm, open-label study investigating the preliminary efficacy and safety of ociperlimab (anti-TIGIT) + tislelizumab (anti-PD-1) + concurrent chemoradiotherapy (cCRT) in patients with untreated limited-stage small cell lung cancer (SCLC)

Authors: Youling Gong[1], Qingsong Pang[2], Rong Yu[3], Zhengfei Zhu[4], Jiangqiong Huang[5], Yufeng Cheng[6], Diansheng Zhong[7], Hongbo Wu[8], Seung Soo Yoo[9], Tracy Dobbs[10], Zinan Bao[11], Yunxia Zuo[12], Boxian Wei[13], Pu Sun[14], You Lu[1*]

Affiliations:

[1]*Thoracic Oncology Ward, Cancer Center, West China Hospital, Sichuan University, Chengdu, China,*

[2]*Radiotherapy Department, Tianjin Medical University Cancer Institute & Hospital, Tianjin, China,*

[3]*Department of Radiotherapy, Beijing Cancer Hospital, Beijing, China,*

[4]*Department of Radiotherapy, Fudan University Shanghai Cancer Center, Shanghai, China,*

[5]*Department of Radiotherapy, Medical University Affiliated Tumor Hospital, Guangxi, China,*

[6]*Department of Radiation Oncology, Qilu Hospital of Shandong University, Jinan, China,*

[7]*Medical oncology Department, Tianjin Medical University General Hospital, Tianjin, China ,*

[8]*Henna Cancer Hospital, Zhengzhou, China,*

[9] *Department of Internal Medicine, School of Medicine, Kyungpook National University, Kyungpook National University Hospital, Daegu, Republic of Korea, Daegu, Republic of Korea,*

[10]*Medical Oncology, Tennessee Cancer Specialist, Knoxville, TN, US,*

[11]*Solid Tumors, BeiGene (Shanghai) Co., Ltd., Shanghai, China,*

[12]*Clinical Development, BeiGene (Shanghai) Co., Ltd., Shanghai, China,*

[13]*Statistics, BeiGene (Beijing) Co., Ltd., Beijing, China,*

[14]*Clinical Biomarkers, BeiGene (Shanghai) Co., Ltd., Shanghai, China,*

Abstract

Background: Despite a high response rate to cCRT, patients with limited-stage SCLC generally experience recurrence of disease after a few months and survival remains poor. Immunotherapy has shown benefit in many tumor types, including SCLC. In preclinical and clinical studies of solid tumors, co-inhibition of T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitor motif domains (TIGIT) and PD-1 enhanced antitumor activity of anti-PD-1. AdvanTIG-204 (NCT04952597) investigated the efficacy and safety of ociperlimab + tislelizumab + cCRT in patients with untreated limited-stage SCLC.

Methods: Patients with limited-stage SCLC and no prior systemic therapy were randomized 1:1:1 to Arm A (ociperlimab [900 mg IV Q3W] + tislelizumab [200 mg IV Q3W] + cCRT for 4 cycles, then ociperlimab + tislelizumab), Arm B (tislelizumab + cCRT for 4 cycles, then tislelizumab), or Arm C (cCRT for 4 cycles). Study drugs (Arms A and B) were continued for up to 12 months or until progression, unacceptable toxicity, or withdrawal. Primary endpoint: investigator-assessed PFS per RECIST v1.1. Secondary analyses included additional efficacy and safety endpoints in the ITT population, and efficacy in patient subgroups by PD-L1 and TIGIT expression (both <1% vs ≥1%), using tumor area positivity (PD-L1) and immune cell scoring (TIGIT). No hypothesis testing was predefined (p-value for descriptive purposes only). Descriptive comparisons were conducted for Arm A vs C, B vs C, and A vs B.

Results: As of July 26, 2023, 126 patients (median age, 61.5 years) were randomized to Arm A (n=41), Arm B (n=42), or Arm C (n=43). Median follow-up: ~18 months (all arms). There was a trend of improvement in median PFS in Arm A (12.6 months) and Arm B (13.2 months) vs Arm C (9.5 months); HR (95% CI): Arm A vs C, 0.84 (0.46-1.52; *p*=0.2793); Arm B vs C, 0.80 (0.45-1.44; *p*=0.2414). ORR was 85.4% (3 CR) in Arm A, 88.1% (4 CR) in Arm B, and 76.7% (1 CR) in Arm C. Median DoR was 10.1 months in Arm A, 11.5 months in Arm B, and 8.2 months in Arm C. Median OS was not reached in any arm. Analyses showed that PD-L1 or TIGIT expression did not correlate with efficacy, however, small subgroup size limits interpretability. All patients experienced ≥1 treatment-related adverse event (TRAE); rates of grade ≥3 TRAEs were 73.2%, 78.6% and, 65.1% in Arms A, B, and C, respectively. The most common TRAEs included anemia (80.5% in Arm A vs 83.3% in Arm B vs 81.4% in Arm C), nausea (80.5% vs 76.2% vs 65.1%), and WBC count decreased (78.0% vs 76.2% vs 62.8%). Rates of TRAEs leading to any treatment discontinuation were 26.8%, 21.4%, and 4.7% in Arms A, B, and C, respectively. One patient in each arm experienced a TRAE leading to death.

Conclusion: In patients with untreated limited-stage SCLC, tislelizumab + cCRT yielded a trend of improvement in PFS and ORR vs cCRT; addition of ociperlimab did not show detectable improvement. The overall safety profile of the treatments was tolerable, manageable, and generally consistent with the known risks of ociperlimab, tislelizumab, and cCRT.