First-line (1L) tislelizumab (TIS) + chemotherapy (CT) vs placebo (PBO) + CT in extensive-stage small cell lung cancer (ES-SCLC): long-term follow-up (LTFU) of RATIONALE-312

Authors: Ying Cheng,[1]* Yun Fan,[2] Yanqiu Zhao,[3] Dingzhi Huang,[4] Jun Zhao,[5] Tai Qin,[6] Chunyu Wang,[6] Chenqi Chen,[7] Pu Sun,[8] Kirsha Naicker,[9] Yong Song[10]

Corresponding/presenting author*

Affiliations: [1]Department of Thoracic Oncology, Jilin Cancer Hospital, Changchun, China; [2]Department of Thoracic Oncology, Zhejiang Cancer Hospital, Hangzhou, China; [3]Department of Medical Oncology, The Affiliated Cancer Hospital of Zhengzhou University and Henan Cancer Hospital, Zhengzhou, China; [4]Department of Pulmonary Oncology, Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; [5]Department I of Thoracic Oncology, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Peking University Cancer Hospital and Institute, Beijing, China; [6]Clinical Development – Solid Tumors, BeOne Medicines (Beijing) Co., Ltd., Beijing, China; [7]Statistics, BeOne Medicines USA, Inc., New York City, USA; [8]Clinical Biomarkers, BeOne Medicines (Beijing) Co., Ltd., Beijing, China; [9]Clinical Development – Solid Tumors, BeOne Medicines UK, Ltd., London, UK; [10]Department of Respiratory and Critical Care Medicine, Jinling Hospital, Nanjing Medical University, Nanjing, China

ABSTRACT (1846/2000 characters)

Background: In the final analysis of the phase 3 RATIONALE-312 trial (NCT04005716), patients (pts) with ES-SCLC treated with 1L TIS + CT experienced a significant improvement in overall survival (OS) with tolerable safety vs PBO + CT. We report LTFU data in the ITT population and in tumour PD-L1 expression subgroups.

Methods: Eligible pts with previously untreated ES-SCLC were randomised (1:1) to 4 induction cycles of IV TIS 200 mg or PBO once every 3 weeks + investigator's choice of CT (IV carboplatin or cisplatin + etoposide), followed by TIS or PBO maintenance. The primary endpoint was OS. Exploratory OS analyses in PD-L1–evaluable pts was performed centrally using a validated immunohistochemistry assay.

Results: With a median follow-up of 39.8 and 36.4 months (data cutoff: Dec 29, 2023), respectively, OS benefit was maintained with TIS + CT (n=227) vs PBO + CT (n=230; 15.5 vs 13.5 months; HR=0.78 [95% CI: 0.63, 0.95]) in the ITT population, and the 3-year OS rates were 22.1% and 13.1%, respectively. The 4-year OS rate in the TIS + CT arm was 18.9% with 7 pts still at risk while no pts remained at risk in the PBO + CT arm. Median OS was not reached (95% CI: 44.8 months, not estimable) among 44 pts treated with >16 cycles of TIS. In the PD-L1–evaluable pts, the OS benefit with TIS + CT (n=60) over PBO + CT (n=65; 20.7 vs 13.5 months; HR=0.71 [95% CI: 0.48, 1.06]) was consistent with that in the ITT population. A consistent OS improvement favouring TIS + CT vs PBO + CT was observed across all PD-L1 subgroups. Grade ≥3 treatment-related adverse events (TRAEs) were reported in 85.5% and 86.5% of pts in the TIS + CT and PBO + CT arms, respectively. The most frequent TRAEs were alopecia (78.4% vs 79.5%, respectively), anaemia (76.7% vs 78.6%, respectively), and neutropenia (68.7% vs 70.3%, respectively). In the TIS + CT vs PBO + CT arms, 66.5% vs 79.1% pts, respectively, reported use of subsequent systemic anticancer therapy.

Conclusion: LTFU data from RATIONALE-312 showed pts with ES-SCLC treated with 1L TIS + CT had clinically meaningful and sustained improvements in OS vs PBO + CT in the ITT and PD-L1–evaluable population. The safety profile of TIS + CT was tolerable with no new signals.

Clinical trial number: NCT04005716