Associations between patient-reported outcomes (PROs) and progression-free survival (PFS) in patients with extensive-stage small cell lung cancer (ES-SCLC): results from the RATIONALE-312 trial

Authors and Affiliations: Dingzhi Huang, Pulmonary Oncology Department, Tianjin Medical University Cancer Institute and Hospital, Tianjin, China[1] Bryant Barnes, BeOne Medicines, Ltd., San Mateo, CA, USA[2] Tai Qin, BeOne Medicines (Beijing) Co., Ltd., Beijing, China[3] Chenqi Chen, BeOne Medicines (Beijing) Co., Ltd., Beijing, China[4] Gisoo Barnes, BeOne Medicines, Ltd., San Mateo, CA, USA[5] Timothy Victor, BeOne Medicines, Ltd., San Mateo, CA, USA; University of Pennsylvania, Philadelphia, PA USA[6]

ABSTRACT

Background: PROs, including disease-specific symptoms and functioning, may have prognostic potential for PFS, yet their role in guiding clinical decision-making is underutilized. This study explored whether patient-reported, disease-specific symptoms are prognostic of PFS in patients with first-line (1L) ES-SCLC from the RATIONALE-312 trial.

Methods: 433 patients (n=216 tislelizumab + chemo [T+C]; n=217 placebo + chemo [P+C]) were analyzed using the EORTC-QLQ-C30 and lung cancer-specific QLQ-LC13 instruments. A 3-component joint model (JM) was fit, consisting of a 1) linear mixed model (LMM) to evaluate longitudinal change from baseline in domain-specific PRO scores, 2) a Cox model for the risk of recurrent symptomatic deterioration (RS-D) events, and 3) a Cox model to evaluate the treatment effect of PFS. JMs were adjusted for ECOG Performance status (0 vs 1), brain metastasis, and investigator-chosen chemotherapy (cisplatin vs carboplatin).

Results: In the LMM, T+C was associated with significantly lower symptom deterioration for QLQ-LC13 chest pain (P=0.0158) compared to P+C. In the recurrent event Cox model, significant longitudinal associations were observed across all PRO domains (HRs: 0.95–1.66), with better GHS and physical functioning linked to a reduced risk of an RS-D event (HR<1) and worsening symptoms linked to increased risk (HR>1). In the PFS Cox model, T+C was significantly associated with a 39-41% reduction in the risk of disease progression across all PRO domains as compared to P+C (HRs: 0.59–0.60; all P<0.05). Increasing RS-D events for physical functioning was significantly associated with a higher risk of PFS events, irrespective of treatment (P=0.0180).

Conclusions: T+C was associated with lower chest pain and a reduced disease progression in patients with ES-SCLC compared to P+C. RS-D in physical functioning was a leading prognostic indicator for risk of disease progression. These findings suggest that patient-reported symptoms and functioning are directly linked to PFS and are important prognostic factors in the treatment of 1L ES-SCLC patients.