Recurrent patient-reported outcome (PRO)-based symptomatic deterioration predicts survival and disease progression in patients with resectable non-small cell lung cancer (NSCLC): Post-hoc analysis of RATIONALE-315

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ABSTRACT

Objectives: Traditional time-to-deterioration analyses do not account for the recurrent nature of PRO symptoms like dyspnea (a common NSCLC symptom). Here, we report results from a 3-component joint model (JM) analysis of the phase 3 RATIONALE-315 study (NCT04379635) that integrates longitudinal and time-to-event data to quantify the association between PROs, survival, and disease progression.

Methods: RATIONALE-315 was a randomized, double-blind study of perioperative tislelizumab vs placebo, plus neo-adjuvant chemotherapy, in patients with resectable NSCLC. In this post-hoc analysis, a 3-component JM assessed the association between PRO dyspnea scores (by linear mixed model [LMM]), dyspnea symptom deterioration events (by recurrent events [REs] frailty Cox model), and terminal events (TEs; by Cox proportional hazards model).

Results: Of 453 randomized patients, 211 in the tislelizumab arm and 208 in the placebo arm were included in this analysis. Per the LMM component, tislelizumab was associated with a non-substantial dyspnea improvement, with an estimated effect (95% CI) of 2.28 (0.41, 4.17) and *P*-value of 0.0183. Furthermore, the tislelizumab-by-day interaction indicated a protective effect of tislelizumab on dyspnea over time (estimate [95% CI] −0.01 [−0.02, 0.00]; *P*=0.0010).
In TE analyses, tislelizumab showed a 54% reduction in risk of a TE (thus a higher chance of event-free survival), with an estimate of −0.79 (95% CI: −1.49, −0.23; *P*=0.0044). Although the REs frailty Cox model was not significant, it suggested a potential association between recurrent dyspnea symptom deterioration and the risk of TEs (estimate [95% CI] 3.81 [−1.64, 7.30], *P*=0.1495), corresponding to a hazard ratio of 44.96.

Conclusions: These data demonstrated that patient-reported deterioration of dyspnea symptoms over time may be a predictor of clinically important survival events (based on TEs). Furthermore, dyspnea appears to improve with tislelizumab compared with placebo. Modeling can highlight the importance of PROs as a prognostic tool in the journey of patients with cancer.