Cyberknife or a VMAT approach. Adverse events at each dose level are monitored carefully by an independent Data Safety Monitoring Committee (DSMC).

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Time to deterioration of symptoms with durvalumab in stage III, locally advanced, unresectable NSCLC: Post-hoc analysis of PACIFIC patient-reported outcomes

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Background: Along with improving efficacy outcomes such as progression-free survival (PFS) after concurrent chemoradiotherapy (cCRT) in locally advanced, unresectable NSCLC, it is critical that new therapies are well tolerated in the curative intent setting. We studied the impact of 12 mo of durvalumab on disease symptoms in this setting using patient-reported outcomes (PROs). In a post-hoc analysis of time to deterioration, we adjusted for transient symptom changes by requiring two consecutive deterioration recordings.

Methods: Patients whose disease did not progress after ≥2 cycles of platinum-based cCRT were randomised 2:1 1–42 days post-cCRT to durvalumab 10 mg/kg i.v. or placebo every 2 weeks for up to 12 mo/progression. Co-primary endpoints were PFS and overall survival. PROs were assessed using EORTC QLQ-C30 v3 and QLQ-LC13. Time to deterioration was defined as time from randomisation until the first clinically relevant deterioration (≥10 point change); in the post-hoc analysis, deterioration confirmation was required at the next time point. Hazard ratios (HR) and 95% confidence intervals (CIs) were estimated using a stratified Cox proportional-hazards model.

Results: In the pre-specified analysis, there was no difference between treatment arms in time to deterioration besides other pain, which favoured durvalumab vs placebo (HR 0.72; 95% CI 0.58–0.89). Our post-hoc analysis indicated notable delays in deterioration of overall pain (HR 0.75; 95% CI 0.60–0.93), chest pain (HR 0.74; 95% CI 0.57–0.97), arm/shoulder pain (HR 0.74; 95% CI 0.58–0.95), nausea/vomiting (HR 0.72; 95% CI 0.54–0.97), insomnia (HR 0.75; 95% CI 0.58–0.97) and haemoptysis (HR 0.70; 95% CI 0.50–0.99) in favour of durvalumab, with no between-group differences for other items.

Conclusions: PACIFIC primary analysis showed that durvalumab significantly improved PFS vs placebo (16.8 mo vs 5.6 mo, respectively) in the post-cCRT setting, and was well tolerated, largely without PRO deterioration. Our post-hoc analysis indicates a delay in several PROs with durvalumab not observed in the pre-specified analysis. Confirmation of worsening may provide a more precise picture of deterioration than one time point alone.

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