WCLC 2018: PACIFIC Trial: Overall Survival With Durvalumab After Chemo-Radio therapy in Unresectable Stage III NSCLC

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Key Points

- Durvalumab significantly improved overall survival vs placebo after concurrent chemoradiation.
- Median overall survival was not reached vs 28.7 months.

As reported at the current International Association for the Study of Lung Cancer 19th World Conference on Lung Cancer (Abstract PL02.01) and in *The New England Journal of Medicine* by Antonia et al, the phase III PACIFIC trial has shown significantly improved overall survival—a co-primary endpoint—with durvalumab (Imfinzi) vs placebo after chemoradiotherapy in unresectable stage III non–small cell lung cancer (NSCLC). An earlier report from the trial supported the approval of durvalumab in this setting in February 2018 on the basis of improved progression-free survival.

Study Details

In the international double-blind trial, 709 patients were randomized 2:1 between May 2014 and April 2016 to receive durvalumab 10 mg/kg intravenously (IV) (n = 473) or IV placebo every 2 weeks (n = 236) for up to 12 months as consolidation in patients with unresectable stage III NSCLC without progression after ≥ 2 cycles of definitive platinum-based chemoradiation. Randomization was performed at 1 to 42 days after receipt of chemoradiotherapy and was stratified according to age, sex, and smoking history.

The primary endpoints were progression-free survival assessed by blinded independent central review and overall survival.

Overall Survival

As of data cutoff in March 2018, median follow-up for overall survival was 25.2 months. Overall survival at 24 months was 66.3% in the durvalumab group vs 55.6% in the placebo group (*P* = .005). Median overall survival was not reached (95%

confidence interval [CI] = 34.7 months–not reached) vs 28.7 months (95% confidence interval [CI] = 22.9 months–not reached). The stratified hazard ratio (HR) for overall survival for durvalumab vs placebo was 0.68 (*P* = .0025). The overall survival benefit with durvalumab was observed across all prespecified subgroups.

Updated analysis showed median progression-free survival of 17.2 vs 5.6 months (stratified HR = 0.51, 95% CI = 0.41–0.63). After discontinuation of study treatment, 41.0% of the durvalumab group and 54.0% of the placebo group received additional anticancer therapy. Median time to death or distant metastasis was 28.3 months in the durvalumab group vs 16.2 months in the placebo group (stratified HR = 0.53, 95% CI = 0.41–0.68). New brain metastases were found in 6.3% vs 11.8% of patients. Investigator-assessed median time to second progression or death was 28.3 months vs 17.1 months (stratified HR = 0.58, 95% CI = 0.46–0.73).

Safety Profile

Safety profiles were similar to those previously reported. Grade 3 or 4 adverse events occurred in 30.5% of the durvalumab group vs 26.1% of the placebo group. Adverse events led to treatment discontinuation in 15.4% vs 9.8% of patients, with the most common cause being pneumonitis in both groups (4.8% vs 2.6%). Adverse events of special interest occurred in 66.7% vs 49.1% (grade 1 or 2 in 56.8% vs 43.6%). Serious adverse events occurred in 29.1% vs 23.1% of patients, and adverse events led to death in 4.4% vs 6.4%.

The investigators concluded, “[This] trial showed a survival advantage with durvalumab therapy after concurrent chemoradiation therapy in patients with stage III, unresectable NSCLC…. No new safety signals were identified.”

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