Phases III trial of durvalumab combined with domvanalimab following concurrent chemoradiotherapy (cCRT) in patients with unresectable Stage III NSCLC (PACIFIC-8)

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Plain language summary

A recently published 5-year update from PACIFIC demonstrated robust and sustained survival benefit following cCRT: In the PACIFIC trial, durvalumab significantly improved OS and PFS versus placebo in patients with unresectable Stage III NSCLC and thereby stopping PD-L1 mediated inhibition of T-cell activation.

Anti-TIGIT mAbs, such as domvanalimab, have previously demonstrated encouraging clinical activity in patients with metastatic NSCLC. To further improve outcomes in this population, novel immunotherapy combinations that synergistically build on the backbone of PD-L1 inhibition are being studied.

In this Phase III, randomised, double-blind, placebo-controlled, multicentre, international trial, patients with unresectable Stage III NSCLC who have not been treated with cCRT will be randomly assigned at a ratio of 1:1 to receive either domvanalimab or placebo in conjunction with cCRT. After completion of cCRT, patients will be eligible to receive either placebo or durvalumab as per investigator preference.

Study endpoints

• PFS (OS and DoR vs placebo): 13.5 months
• PFS2 (from randomisation to second progression): 6.1 months

Key inclusion criteria

• Participants must have received ≥2 cycles of platinum-based chemotherapy concurrent with radiotherapy (60 Gy)
• Participants (≥18 years) must present with histologically or cytologically documented unresectable Stage III NSCLC (per the IASLC T-Stage definition)
• No progression or clinical deterioration in pulmonary symptoms

Key exclusion criteria

• History of interstitial lung disease, including idiopathic pulmonary fibrosis and organizing pneumonia
• History of active EBV infection or known or suspected chronic active EBV infection at screening

Study status

• Phase III, randomised, double-blind, placebo-controlled, multicentre, international trial
• Participants (≥18 years) with histologically or cytologically documented unresectable Stage III NSCLC (per the IASLC T-Stage definition), no progression or clinical deterioration in pulmonary symptoms, with an estimated 42.9% of patients assigned to durvalumab remained alive at 5 years, versus 33.4% of patients assigned to placebo.
• The primary endpoint is PFS, measured as the length of time that participants remain alive without progression or death.

Disclosures

No disclosures from any of the authors.

References