Phase 3 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**

Why are we performing this research?

Durvalumab is a drug that blocks the activity of a protein called PD-L1, making cancer cells more susceptible to being killed by immune cells. Based on the findings of the PACIFIC study, durvalumab was established as the standard of care for patients with Stage II non-small-cell lung cancer (NSCLC) for whom surgery is not an option. The drug has been shown to delay the cancer growth or spread in the NSCLC setting, with benefit observed among patients with PD-L1 positive, unresectable Stage III NSCLC.

How are we performing this research?

Study participants will be randomly assigned in equal numbers to one of two groups (both the participants and their physicians will be unaware of which group the participant is assigned to):

• durvalumab + domvanalimab

• durvalumab + placebo (an inactive substance that looks the same and is given in the same way as domvanalimab).

All participants will remain on their assigned study treatment for up to 12 months.

The primary efficacy measure is progression-free survival, measured as the length of time that participants remain alive without cancer growing or spreading + durvalumab + domvanalimab = compared with durvalumab + placebo.

Who will participate in this study?

We aim to recruit approximately 860 patients with Stage III NSCLC for whom surgery is not an option. To be eligible, patients must have cancers that:

• have not grown or spread following concurrent chemoradiotherapy

• are positive for PD-L1

• do not have mutations in the EGFR or ALK genes.

Where can I access more information?

This study is ongoing, and no results are available. The study is expected to complete in June 2023. More information about this study can be found at https://www.clinicaltrials.gov/ct2/show/NCT05211895?term=NCT05211895&draw=1&rank=1

You may also speak to your doctor about clinical studies.


**Background**

The results of the phase 3 PACIFIC trial established consolidation therapy with durvalumab (an anti-PD-L1 mAb) for up to 12 months as SoC for patients with unresectable Stage III NSCLC and no disease progression following platinum-based cCRT (the PACIFIC regimen). 1

To further improve outcomes in this population, novel immunotherapy combinations that synergistically combine an anti-PD-L1 mAb with durvalumab are being explored – this includes combinations with anti-TIGIT, anti-CD73, and anti-MOGa2 mAbs.

**Key inclusion criteria**

• Participants (≥18 years) must present with histologically or cytologically documented unresectable Stage III NSCLC (per the IASLC Staging Manual) – In ARC

• Current or prior use of immunosuppressive medication within 14 days before the first dose of durvalumab.

• Participants with unresolved toxicity CTCAE grade >2, or grade ≥2 pneumonitis, from prior CRT.

• Participants must have received 22 doses of platinum-based chemotherapy concurrent with radiotherapy (60 Gy or the authors.

**Key exclusion criteria**

• History of another primary malignancy, with the exceptions of:

  - malignancies treated with curative intent with no known active disease 25 years before the first dose of study intervention and of low potential risk for recurrence

  - adequately resected non-melanoma skin cancer and curatively treated in situ disease

  - adequately treated carcinoma in situ or Ta tumors treated with curative intent and without evidence of disease

  - mixed small- and NSCLC histology

  - Participants who receive sequential CRT for unresectable Stage III NSCLC or who have progressed during platinum-based CRT

  - Participants with uncontrolled tumor CTCAE grade ≥2, or grade ≥2 pneumonias, from prior CRT

  - History of idiopathic pulmonary fibrosis, drug-induced pneumonitis, or idiopathic pneumonitis, regardless of time of onset prior to randomization. Evidence of active non-CRT-induced pneumonitis (grade ≥2), active pneumonitis, active interstitial lung disease

  - Active or prior documented autoimmune or inflammatory disorders (with exceptions).

  - Active EBV infection or known or suspected chronic active EBV infection at screening

  - Current or prior use of immunosuppressive medication within 14 days before the first dose of durvalumab.

**Study status**

Countries with active sites (as of May 2023)

Countries with sites that plan to participate but are not yet active

• Trial enrollment begins in February 2022 and primary completion is anticipated in June 2023

• PACIFIC-8 is currently active and plans to recruit up to 214 sites across 27 countries.

**Abbreviations**

BCIRL, blind independent central review; cCRT, concurrent chemoradiotherapy; CD73, adenosine 5'-triphosphate-diphosphohydrolase-3; CTCAE, Common Terminology Criteria for Adverse Events; EBV, Epstein–Barr virus; FcγR, Fc gamma receptor; IFN-a, interferon alpha; IL-2, interleukin-2; IHC, immunohistochemistry; IRESSA, Iressa; ICI, immune-checkpoint inhibitor; JCO, Journal of Clinical Oncology; L1, ligand B7.1; M1, macrophage type 1; M2, macrophage type 2; NSCLC, non-small-cell lung cancer; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PD-L2, programmed death-ligand 2; RECIST, Response Evaluation Criteria in Solid Tumors; TIGIT, T-cell immunoglobulin and mucin domain containing, type 1; TIM3, T-cell immunoglobulin and mucin domain containing, type 3; TCR, T-cell receptor.

**Key study endpoints**

1. PFS (BCIRL per RECIST v1.1) in patients with PD-L1 TC ≥50%.

2. PFS (BCIRL per RECIST v1.1) in patients with PD-L1 TC ≤1%.

3. Objective response rate (OSR) and DoR (BCIRL per RECIST v1.1).

4. Time from randomization to second progression (PFS2).

**Study phase**

Posterior

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