LAURA: Osimertinib maintenance following definitive chemoradiation therapy (CRT) in patients with unresectable Stage III epidermal growth factor receptor mutation positive (EGFRm) non-small cell lung cancer (NSCLC)

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Background

• EGFR mutations are present in approximately 34% of patients with Stage III NSCLC1
• Platinum-based CRT followed by durvalumab consolidation (PACIFIC regimen) is standard of care for patients with unresectable Stage III NSCLC, without progression after platinum-based CRT2. Six percent of patients had EGFRm NSCLC in PACIFIC, and due to limited patient numbers results were inconclusive3
• While there are very limited outcome data for patients with EGFRm NSCLC receiving platinum-based CRT, there is evidence to suggest that following CRT, patients with EGFRm NSCLC have superior local, but inferior distant control, including CNS metastases, vs those with EGFR wild-type NSCLC4,5, highlighting the need for targeted therapy with activity
• Osimertinib is a third-generation, irreversible, oral EGFR-TKI that potently and selectively inhibits both EGFR-TKI sensitizing and EGFR T790M resistance mutations2,6 and has demonstrated efficacy in NSCLC CNS metastases3–5.
• In the first-line metastatic (FLAURA trial)4 and adjuvant (ADJUVANCE trial) settings, osimertinib demonstrated efficacy in patients with EGFRm NSCLC, indicating osimertinib could also provide benefits in patients with unresectable Stage III EGFRm NSCLC

Purpose of Study

The LAURA study will evaluate the efficacy and safety of osimertinib as maintenance therapy in patients with locally advanced, unresectable EGFRm Stage III NSCLC without progression during/ following definitive platinum-based CRT

Study Endpoints

• Primary: BICR PFS per RECIST 1.1
• Secondary: CNS PFS; OS; PFS by mutation status; safety and tolerability
• Exploratory: PROs; correlation of baseline tumor and plasma biomarkers with clinical outcomes

LAURA (NCT03521154): Phase III, double-blind, randomized, placebo-controlled trial

Enrollment start: July 2018 | Primary PFS analysis: estimated August 2022

Key Inclusion Criteria

• ≥18 years (≥20 years in Japan)
• Locally advanced, unresectable, Stage III NSCLC
• Ex19del or L858R EGFR mutations
• Received concurrent or sequential CRT, including ≥2 cycles of 5–7 Gy/day dose of platinum-based chemotherapy and a total dose of radiation of 60 Gy ≥10% (54–66 Gy)
• Completed CRT ≥6 weeks prior to randomization with no evidence of disease progression during or following CRT
• Creatinine ≤1.5x upper limit of normal or creatinine clearance ≥30 mL/min
• WHO performance status of 0/1

Key Exclusion Criteria

• History of interstitial lung disease before CRT
• Symptomatic pneumonitis following CRT
• Uncontrolled toxicity of CTCAE grade ≥3 from prior CRT
• Prior treatment with an EGFR-TKI, chemotherapy, radiotherapy, immunotherapy, or investigational agents for NSCLC beyond those received in the definitive setting for Stage III disease as part of CRT

Key protocol changes (February 2020)*

• Patients with squamous histology who have a pre-existing local positive EGFR test result (Ex19del/L858R) are eligible for part I screening
• The minimum value for creatinine clearance is reduced from 50 mL/min to 30 mL/min
• Prior to PFS analysis, patients may receive open-label osimertinib after BICR-confirmed progression (see Figure)
• Following PFS analysis, patients may receive open-label osimertinib after investigator-assessed disease progression (see Figure)
• Increased duration of monitoring of AE(s) of special interest during progression and survival follow-up

References


Abbreviations

BICR, blinded independent central review; CRT, chemoradiation therapy; CTCAE, Common Terminology Criteria for Adverse Events; DFS, disease-free survival; DLL, domain limited liquid biopsy; ECOG, Eastern Cooperative Oncology Group; Ex19del, exon 19 deletion; FLAURA trial, first-line osimertinib trial; HCC, hepatocellular carcinoma; IHC, immunohistochemistry; ICC, intracellular; ICC, intracellular; HR, hazard ratio; NSCLC, non-small-cell lung cancer; OS, overall survival; PFS, progression-free survival; PFS2, time from the start of osimertinib until the primary PFS2 analysis; R, cycle; SD, stable disease; TFST, time to second subsequent therapy; WHO, World Health Organization

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The original study design was previously presented: Shun Lu et al. 2018 J Thorac Oncol 13(10) suppl S437. Since then there have been no protocol changes, control arms added or descoped.

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