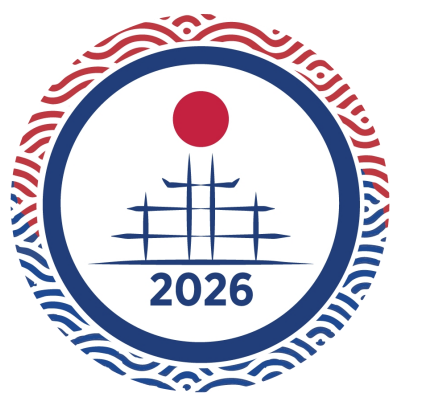


Biomarker-Directed Therapy for Distant Recurrence after Adjuvant Osimertinib in EGFRm Resectable Stage IB-IIIA NSCLC (REVIVE)

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IASLC 2026 World
Conference on Lung Cancer
SEPTEMBER 12 - 15, 2026
SEOUL, REPUBLIC OF KOREA

Background

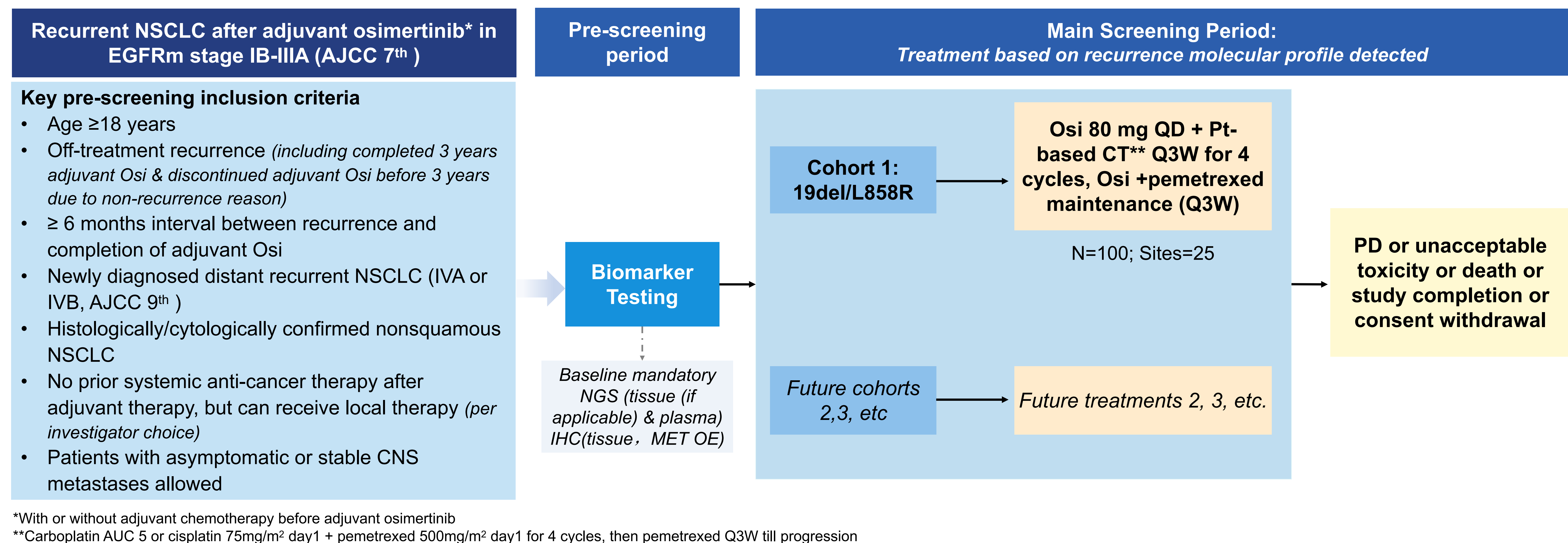
- In the phase III ADAURA study, adjuvant osimertinib (Osi) significantly improved disease-free survival (DFS) and overall survival (OS) versus placebo in patients with resected EGFRm stage IB–IIIA NSCLC¹⁻³. Osi is now the standard of care in this setting and was approved by the NMPA in April 2021.
- Since the approval of adjuvant Osi, patients with recurrence during or after adjuvant Osi have emerged in real-world clinical practice. In ADAURA, at a median follow-up of 44.2 months, 27% of patients in the Osi arm experienced disease recurrence, most of which occurred after treatment discontinuation².
- However, there is a lack of guidance for managing patients post-recurrence, underscoring the needs to explore the molecular profiles and optimal treatment strategy after adjuvant Osi.

Rationale (Cohort 1)

- Studies of first-generation EGFR-TKIs suggest that tumors recurring after treatment discontinuation may retain sensitivity to EGFR-TKI rechallenge, as supported by the SELECT study and retrospective data from MSKCC^{4,5}.
- However, there is limited data on rechallenging Osi post-recurrence, with only a few case reports highlighting its potential benefit. These cases suggest that patients might retain sensitivity to Osi despite disease recurrence⁶⁻⁸.
- Osi, alone or combined with chemotherapy, is globally approved as first-line treatment for locally advanced or metastatic NSCLC with EGFR exon 19 deletion or exon 21 L858R mutation. In advanced EGFR-mutated NSCLC, Osi plus chemotherapy demonstrated superior progression-free survival and OS versus Osi monotherapy^{9,10}.
- Given these data, Osi plus chemotherapy may provide greater clinical benefit than Osi in patients with EGFR mutations who experienced distant recurrence after adjuvant Osi for resected EGFRm NSCLC.
- This study's Cohort 1 will further characterize recurrence gene profiles after discontinuation of adjuvant Osi and evaluate the efficacy and safety of Osi plus chemotherapy in patients with EGFR mutations who experienced distant recurrence after adjuvant Osi for resected EGFRm stage IB-IIIA NSCLC.

REVIVE study design

- REVIVE (NCT07279935) is a multicenter, multi-cohort, prospective, biomarker-guided interventional study designed to characterize recurrence mechanisms in EGFRm NSCLC with distant relapse after adjuvant Osi and to evaluate the clinical benefit of a molecularly guided treatment strategy after disease recurrence.
- This study was initiated with Cohort 1 of patients with EGFR 19del/L858R-mutated NSCLC with distant recurrence after adjuvant Osimertinib, and enrollment started at the end of January 2026. Additional cohorts may be added based on emerging biomarkers.



Key inclusion criteria for Main screening (Cohort 1)

- EGFR mutation (Exon 19del/Exon 21 L858R)-reconfirmed for study entry (mandatory undergo NGS by plasma, and tissue if applicable).
- Life expectancy >12 weeks at Day 1
- At least one measurable lesion per RECIST 1.1 (≥10 mm in longest diameter, or ≥15 mm short axis for lymph nodes), suitable for repeated measurement; if solitary, it must not have been previously irradiated or biopsied within 14 days before baseline imaging
- ECOG PS 0-1

Key exclusion criteria (Cohort 1)

- Only local/regional recurrence
- Adjuvant osimertinib therapy was discontinued due to the occurrence of severe adverse events
- On-treatment recurrence patients who received R0 resection and adjuvant osimertinib
- Prior with other adjuvant EGFR-TKIs (excluding osimertinib).

Study endpoints

- Primary endpoints**
 - PFS (By investigator per RECIST 1.1)
- Secondary endpoints**
 - Objective response rate (ORR)
 - Disease control rate (DCR), Duration of Response (DoR)
 - 3 years OS rate
 - Treatment discontinuation or death (TTD)
 - Depth of response
- Safety endpoints**
 - Safety & tolerability
- Exploratory endpoints**
 - Time to recurrence of previous adjuvant osimertinib (by different adjuvant duration)
 - Recurrence molecular profile of previous adjuvant osimertinib
 - Molecular profile on patients receiving osimertinib +chemotherapy progression

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Acknowledgments

This study is sponsored by AstraZeneca and conducted at Peking University People's Hospital and participating centres across China; the authors thank all patients, investigators, and site staff contributing to the REVIVE study.

Disclosures

- All authors have declared no conflicts of interest.