

Comparative Effectiveness of Consolidation Durvalumab versus Osimertinib in Patients with Unresectable, Stage III, EGFR-Mutated Non-Small-Cell Lung Cancer: A Systematic Review

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BACKGROUND

- Stage III unresectable non-small-cell lung cancer (NSCLC) has historically been managed with definitive chemoradiotherapy (CRT) followed by consolidation immunotherapy
- The PACIFIC trial established durvalumab, a PD-L1 inhibitor, as the standard of care, significantly improving progression-free survival (PFS) and overall survival (OS)
- However, the efficacy of durvalumab in patients with epidermal growth factor receptor (EGFR) mutations, representing approximately 15-50% of NSCLC cases, has been a subject of clinical debate due to a lack of benefit
- The LAURA trial showed that consolidation with osimertinib, a third generation EGFR tyrosine kinase inhibitor (TKI), leads to a 84% reduction in the risk of disease progression or death in EGFR-mutated patients compared to placebo
- Real world clinical practice has often defaulted to durvalumab or observation due to the long standing PACIFIC standard of care
- There is a critical need to synthesize evidence comparing the effectiveness of durvalumab versus osimertinib specifically for the EGFR mutated subgroup to inform optimal treatment pathways and health outcomes

OBJECTIVES

The comparative effectiveness of consolidation therapies for unresectable stage III EGFR-mutated non-small cell lung cancer (NSCLC) remains uncertain. This systematic review compared consolidation durvalumab versus osimertinib with respect to progression-free survival (PFS).

METHODS

- Following the PRISMA framework, PubMed and Embase were systematically searched through May 2025 for studies of stage III NSCLC, EGFR mutations, durvalumab, and osimertinib
- Eligible studies included clinical trials or observational studies of adults with unresectable stage III EGFR-mutated NSCLC receiving consolidation durvalumab or osimertinib after chemoradiotherapy
- Primary outcome was median PFS
- Two independent reviewers screened records in Covidence
- Of 160 records identified, 37 underwent full-text review and 5 met inclusion criteria

RESULTS

- Total of five studies with six unique PFS comparisons were included (2 RCTs, 3 observational) (Figure 1)
- Sample size ranged from 35 to 216
- Median age was mid-60s across all cohorts

Figure 1. PRISMA Flow Diagram of Study Selection

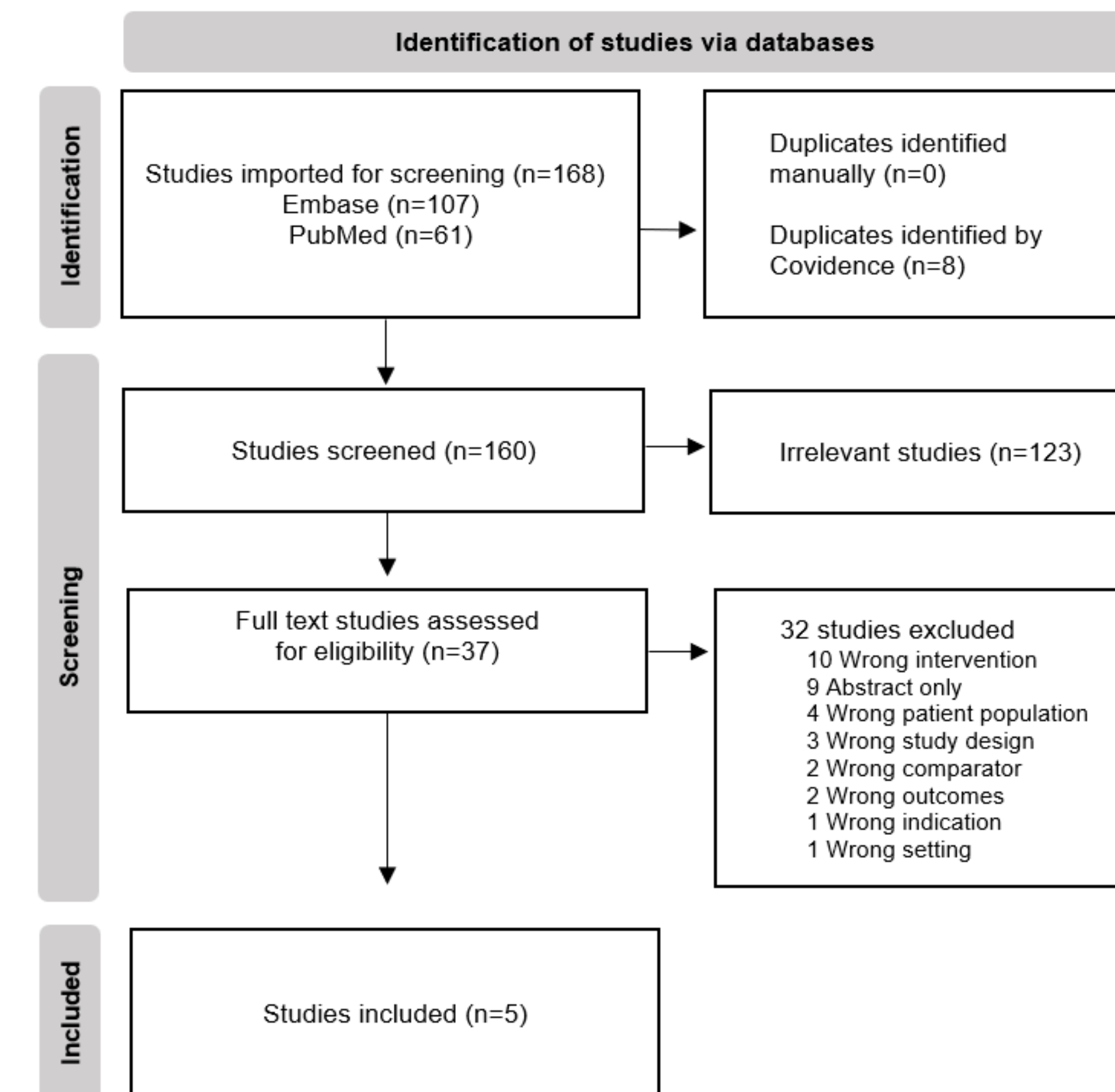


Table 1. Clinical Outcomes and Study Characteristics of Consolidation Therapy in EGFR-Mutated Stage III NSCLC

| Study | Design | Treatment Arms | Median PFS (months) | HR | Risk of Bias |
|--|--|---|--|--|--------------|
| Aredo et al., 2021 | Multicenter retrospective cohort | CRT + durvalumab vs. CRT alone vs. CRT + EGFR TKI | CRT + durvalumab 10.3 CRT alone 6.9 CRT+EGFR TKI 26.1 | CRT + durvalumab vs. CRT alone: HR 1.06 (95% CI: 0.44-2.52) p = 0.993 CRT+EGFR TKI vs. CRT alone: HR 0.16 (95% CI: 0.03-0.73) CRT+EGFR TKI vs. CRT + durvalumab: HR 0.15 (95% CI: 0.03-0.72) p=0.023 | High |
| Huang et al., 2022 | Single center retrospective cohort | CCRT + durvalumab vs. CCRT alone | CCRT + durvalumab 17.5 (95% CI: 11.3-NR) CCRT alone 8.9 (95% CI: 5.8-16.3) EGFR+ subgroup on durvalumab: 17.5 CCRT alone: 10.9 p=0.907 | CCRT + durvalumab vs. CCRT alone: HR 0.47 (95% CI: 0.23-0.96), p=0.038 | High |
| Lu et al., 2024 (LAURA Trial — Primary: BICR-Assessed PFS) | Phase 3, double-blind, placebo-controlled RCT | Osimertinib 80 mg PO QD vs. placebo Randomized post-CRT | Osimertinib 39.1 (95% CI: 31.5-NC) Placebo 5.6 (95% CI: 3.7-7.4) | HR 0.16 (95% CI: 0.10-0.24), p<0.001 | Low-Moderate |
| Lu et al., 2024 (LAURA Trial — Sensitivity: Investigator-Assessed PFS) | Phase 3 RCT — Sensitivity/secondary analysis | Same as above | Osimertinib 38.9 (95% CI: 26.7-NC) Placebo 7.3 (95% CI: 5.5-10.3) | HR 0.19 (95% CI: 0.12-0.29) | Low-Moderate |
| Naidoo et al., 2023 (PACIFIC Trial — Post Hoc EGFRm Subgroup) | Post hoc exploratory subgroup analysis of Phase 3 double-blind, placebo-controlled RCT | Durvalumab vs. placebo Randomized post-CRT | Durvalumab 11.2 (95% CI: 7.3-20.7) Placebo 10.9 mo (95% CI: 1.9-NE) | HR 0.91 (95% CI: 0.39-2.13) no significant difference | Very High |
| Nassar et al., 2024 | Multicenter retrospective cohort | Osimertinib vs. Durvalumab vs. Observation alone Randomized post-CRT | Durvalumab rwPFS 12.7 mo (95% CI: 10.5-15.5) 24-mo rwPFS: 30% Osimertinib rwPFS NR 24-mo rwPFS: 86% Observation rwPFS: 9.7 | Osimertinib vs Durvalumab: HR 0.20 (95% CI: 0.09-0.49) Durvalumab vs Observation: HR 0.67, p=0.083 Durvalumab vs Observation: HR 0.14, p < 0.001 | High |

Osimertinib

- LAURA trial resulted in median PFS of 39.1 months vs 5.6 months for placebo
- Nassar study showed 24 month PFS of 86% vs 27% with observation alone
- Across both studies, osimertinib consistently demonstrated substantial and statistically significant PFS benefit in EGFR-mutated NSCLC

LIMITATIONS

- No head-to-head RCT comparing osimertinib vs. durvalumab directly, cross-study comparisons are indirect
- Only RCT-level durvalumab data come from a post hoc subgroup of 35 patients but was underpowered for definitive conclusions
- Retrospective studies subject to selection bias, treatment choice at physician discretion
- Follow up was shorter in osimertinib cohorts, limiting mature OS comparisons

CONCLUSION

Consolidation osimertinib is associated with a longer observed median PFS than consolidation durvalumab in patients with unresectable, stage III, EGFR-mutated NSCLC, supporting osimertinib as preferred consolidation therapy.

Durvalumab

- Median PFS ranged from 10 to 17 months across studies
- PACIFIC post hoc subgroup analysis (EGFR-mutated, n=35): median PFS of 11.2 vs. 10.9 months for placebo (HR 0.91); findings are exploratory given the small sample size
- Aredo study had a median PFS of 10.3 months vs 6.9 months with CRT alone, but this did not reach statistical significance
- Huang used RWD and showed a significant overall PFS benefit in population but in the EGFR mutant subgroup, benefit was not significant
- Durvalumab demonstrated limited, inconsistent PFS benefit in EGFR-mutated patients

REFERENCES

- Ramalingam SS, et al. (2024). Osimertinib after Definitive Chemoradiotherapy in Patients with Unresectable Stage III EGFR-Mutated NSCLC. *New England Journal of Medicine*. 391(6):485-497. doi:10.1056/NEJMoa2402614.
- Antonia SJ, et al. (2017). Durvalumab after Chemoradiotherapy in Stage III Non-Small-Cell Lung Cancer. *New England Journal of Medicine*. 377(20):1919-1929. doi:10.1056/NEJMoa1709937.
- Falvre-Finn C, et al. (2024). Durvalumab after Chemoradiotherapy in Unresectable Stage III EGFR-mutant NSCLC: A Post-Hoc Subgroup Analysis from PACIFIC. *Journal of Thoracic Oncology*. 19(11):1625-1632. (or similar update).
- National Comprehensive Cancer Network (NCCN). (2025). NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer. Version 1.2025.
- Moher D, et al. (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Medicine*. 6(7):e1000097.
- Aredo JV, Mambetsariev I, Hellyer JA, et al. Durvalumab for Stage III EGFR-Mutated NSCLC After Definitive Chemoradiotherapy. *J Thorac Oncol*. 2021;16(6):1030-1041. doi:10.1016/j.jtho.2021.01.1628
- Huang Y, Zhao JJ, Soon YY, et al. Real-world experience of consolidation durvalumab after concurrent chemoradiotherapy in stage III non-small cell lung cancer. *Thorac Cancer*. 2022;13(22):3152-3161. doi:10.1111/1759-7714.14667
- Lu S, Kato T, Dong X, et al. Osimertinib after Chemoradiotherapy in Stage III EGFR-Mutated NSCLC. *N Engl J Med*. 2024;391(7):585-597. doi:10.1056/NEJMoa2402614
- Naidoo J, Antonia S, Wu YL, et al. Brief Report: Durvalumab After Chemoradiotherapy in Unresectable Stage III EGFR-Mutant NSCLC: A Post Hoc Subgroup Analysis From PACIFIC. *J Thorac Oncol*. 2023;18(5):657-663. doi:10.1016/j.jtho.2023.02.009
- Nassar AH, Kim SY, Aredo JV, et al. Consolidation Osimertinib Versus Durvalumab Versus Observation After Concurrent Chemoradiation in Unresectable EGFR-Mutant NSCLC: A Multicenter Retrospective Cohort Study. *J Thorac Oncol*. 2024;19(6):928-940. doi:10.1016/j.jtho.2024.01.012