

P3.196: Outcomes of Oligoprogression Managed with Local Ablative Therapy During First-Line Osimertinib in EGFR-Mutated NSCLC

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INTRODUCTION

- First-line osimertinib is a standard of care in advanced EGFR-mutated NSCLC, but virtually all patients eventually progress.
- A relevant proportion of these progressions are **oligoprogressive (OPD)** — limited to a small number of lesions — and may be amenable to local treatment.
- Continuing EGFR-TKI beyond progression combined with **local ablative therapy (LAT)** is widely used and endorsed by ESMO/ASCO guidance, but the evidence comes mainly from retrospective series and from the randomised phase II NORTHSTAR trial.
- Dedicated real-world data in the first-line osimertinib setting are scarce.
- Objective:** to describe the frequency, management and outcomes of OPD during first-line osimertinib in a multicentre real-world cohort, and to explore the impact of LAT.

METHODS

Design. Multicentre, retrospective, observational cohort study conducted in 11 public hospitals of eastern Spain (GIDO group).

Population. Adults with advanced EGFR-mutated NSCLC (classical or uncommon mutations; exon 20 insertions excluded) starting first-line osimertinib between June 2021 and December 2024. No prior first- or second-generation EGFR-TKI.

OPD definition. Progression in ≤ 5 lesions, assessed by the treating investigator using RECIST v1.1.

Endpoints in the OPD cohort.

- PFS2** — from osimertinib start to second progression or death.
- OS** — from osimertinib start to death from any cause.
- PFSBOP** — from the start of osimertinib beyond progression to second progression or death.

Exploratory comparison. Patients managed with LAT (plus osimertinib beyond progression) versus those continuing osimertinib without radical local treatment.

Statistics. Kaplan–Meier estimates, log-rank test and Cox hazard ratios with 95% CI (R v2025.09.1). Given the sample size and the risk of selection and immortal-time bias, all LAT analyses are considered exploratory.

Ethics. Approved by the Research Ethics Committee of La Fe University and Polytechnic Hospital (GIDO/2024/01); conducted according to the Declaration of Helsinki.

DISCUSSION AND CONCLUSION

Actionable Take-Away Message

- About **one in four** patients progressing on first-line osimertinib had oligoprogressive disease.
- In routine practice OPD was almost always managed by continuing osimertinib (90.2%) and adding LAT (82.4%), mainly radical radiotherapy.
- LAT was associated with markedly longer post-progression disease control (mPFSBOP 8.97 vs 2.07 months; HR 0.21) and a favourable but non-significant OS trend.
- Osimertinib beyond progression plus LAT is a pragmatic option for selected patients with OPD.

Future Direction for Research

- Findings are exploratory: retrospective design, small no-LAT group, and potential selection and immortal-time bias.
- Prospective validation is warranted, building on randomised data (NORTHSTAR) and ongoing trials in the pure first-line setting (LAT-FLOSI).
- The role of LAT alongside intensified first-line regimens (FLAURA2, MARIPOSA) remains to be defined.

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RESULTS

268

patients started first-line osimertinib

180

progressed on osimertinib (67.2%)

51

developed oligoprogression (28.3%)

46/51

continued osimertinib beyond progression (90.2%)

42/51

received local ablative therapy (82.4%)

Table 1. Baseline characteristics, overall cohort (N=268)

Characteristic	n (%)
Age, median years (range)	72 (31–96)
Female sex	182 (67.9)
Never-smoker	163 (60.8)
ECOG PS ≥ 2	74 (27.6)
Stage IV at osimertinib start	260 (97.0)
Brain metastases at baseline	114 (42.5)
Adenocarcinoma	263 (98.1)
EGFR exon 19 deletion	165 (61.6)
EGFR exon 21 L858R	96 (35.8)
Uncommon EGFR mutation	7 (2.6)
EGFR testing by NGS	167 (62.3)
TP53 co-mutation (NGS subset)	25 (24.8)

Table 2. Survival outcomes in the oligoprogressive cohort

Whole OPD cohort (n=51)	Median, months (95% CI)
PFS2	25.0 (21.5–45.1)
OS	46.5 (34.4–NE)
PFSBOP	7.62 (5.19–11.8)

Exploratory analysis: LAT vs no LAT

Outcome	LAT (n=42)	No LAT (n=9)	HR (95% CI)
PFSBOP, median months (95% CI)	8.97 (6.8–16.4)	2.07 (1.02–NE)	0.21 (0.09–0.47) p<0.001
OS, median months (95% CI)	46.5 (43.7–NE)	39.7 (14.6–NE)	0.46 (0.19–1.1) p=0.08

LAT modality: radical radiotherapy in 40/42 patients (95.2%); surgery in 2/42 (4.8%), both discontinuing osimertinib.

NE, not estimable; OPD, oligoprogressive disease; PFS2, progression-free survival 2; PFSBOP, progression-free survival beyond osimertinib progression.

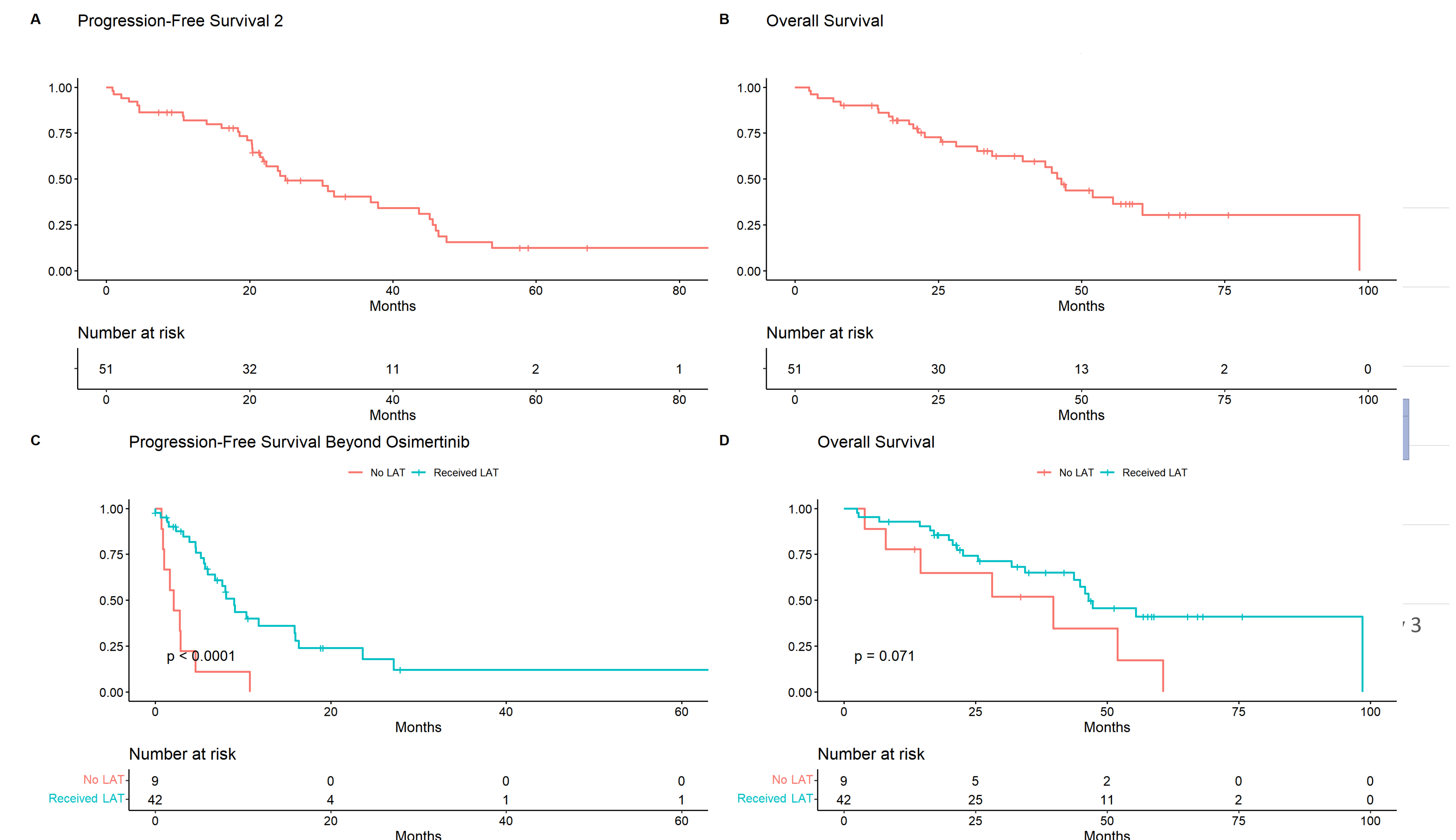


Figure 1. Kaplan–Meier estimates in the oligoprogressive cohort: (A) PFS2 and (B) OS in the whole OPD cohort; (C) PFSBOP and (D) OS according to receipt of local ablative therapy.