

Overall Survival of 2nd-Line Chemotherapy-Containing Regimens After 1st-Line Osimertinib in EGFR-Mutated Advanced NSCLC

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Key Takeaway

These real-world data show that one-third of patients received no subsequent therapy after progression on 1L Osi, and that outcomes with 2L chemotherapy-based regimens (i.e., chemo-only, chemo-IO, and Osi-chemo) remain poor.

Conclusions

Median rwOS following 2L chemo-only, chemo-IO, and Osi-chemo was consistently below one year.

These real-world outcomes suggest that more meaningful improvements may be achieved by altering the underlying disease biology with 1L treatment. 2L chemo-only, chemo-IO, and Osi-chemo following progression on 1L Osi provided only limited benefit. In contrast, early, disease-modifying strategies may delay resistance and preserve subsequent treatment options.

Collectively, these findings reinforce the complex nature of EGFR-mutated NSCLC and the need for more effective, durable, and disease modifying frontline treatment strategies.

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Disclosures

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Introduction

- Osimertinib (Osi) was commonly used first-line (1L) treatment for advanced non-small cell lung cancer (NSCLC) with EGFR mutations (Ex19del or L858R) before the recent adoption of combination regimens as standard of care.
- Evidence guiding therapeutic sequence following 1L Osi remains limited, with recent literature emphasizing that available data are largely retrospective and heterogeneous^{1-2,6}.
- Real-world studies evaluating second-line (2L) chemotherapy after 1L Osi, including multi-center and institutional cohorts, consistently report modest outcomes and heterogeneous chemotherapy treatment patterns, and highlight constraints such as small sample sizes and inefficient subgroup detail for specific strategies¹⁻⁷. A national study from Taiwan similarly notes suboptimal 2L outcomes following 1L Osi³.
- In this context of evolving approvals of novel and combination therapies, this retrospective, multi-database study evaluated real-world overall survival (rwOS) outcomes for patients receiving 2L chemotherapy-containing regimens (i.e., chemotherapy monotherapy (chemo-only), chemotherapy plus immunotherapy (chemo-IO), or Osi-chemo) following 1L Osi monotherapy to help inform treatment sequencing decisions.

Results

Patient Characteristics

- One-third (438/1323, 33%) of 1L Osi patients did not receive 2L treatments.
- A total of 285 patients received 2L chemo-containing regimens: chemo-only (n=74), chemo-IO (n=159), and Osi-chemo (n=52) (**Table 2**).
- Age distributions and baseline rates of liver metastases appeared similar between chemo-only and chemo-IO-treated patients (**Table 1**).
- Patients who received 2L Osi-chemo were younger and had a higher proportion of brain or liver metastases at baseline than those on other 2L regimens (**Table 1**).
- Median 1L Osi duration was longer among patients who went on to receive 2L Osi-chemo than those who received 2L chemo-only or chemo-IO (**Table 1**).

Table 1. Baseline Characteristics of Patients who Progressed to 2L Chemotherapy-containing Regimens

Variables	Chemo-only (N=74)	Chemo-IO (N=159)	Osi-chemo (N=52)
Demographics			
Median age at 1L initiation (IQR), years	67 (59-72)	66 (58-74)	62.5 (57-70.5)
Age group, n (%)			
≥75 years	12 (16.2)	36 (22.6)	7 (13.5)
<75 years	62 (83.8)	123 (77.4)	45 (86.5)
Sex, n (%)			
Female	57 (77.0)	103 (64.8)	40 (76.9)
Male	17 (23.0)	56 (35.2)	12 (23.1)
Race, n (%)			
White	42 (56.8)	96 (60.4)	37 (71.2)
Asian	13 (17.6)	13 (8.2)	5 (9.6)
Black or African American	7 (9.5)	19 (12)	
Other	7 (9.5)	16 (10.1)	8 (15.4)
Unknown	5 (6.8)	15 (9.4)	2 (3.9)
Clinical Characteristics			
EGFR mutation type, n (%)			
Exon 21 L858R	32 (43.2)	68 (42.8)	20 (38.5)
Exon 19 deletion	42 (56.8)	91 (57.2)	32 (61.5)
TP53 mutation at 1L initiation, n (%)			
Positive	29 (39.2)	78 (49.1)	36 (69.2)
Negative	29 (39.2)	49 (30.8)	10 (19.2)
Unknown	16 (21.6)	32 (20.1)	6 (11.5)
Stage at initial diagnosis, n (%)			
I	1 (1.4)	2 (1.3)	3 (5.8)
II	1 (1.4)	1 (0.6)	
III	4 (5.4)	6 (3.8)	3 (5.8)
IV	67 (90.5)	145 (91.2)	46 (88.5)
Unspecified	1 (1.4)	5 (3.1)	
ECOG PS score at 1L initiation, n (%)			
0	22 (29.7)	51 (32.1)	20 (38.5)
1	35 (47.3)	67 (42.1)	18 (34.6)
≥2	6 (8.1)	17 (10.7)	6 (11.5)
Unknown	11 (14.9)	24 (15.1)	8 (15.4)
Brain Metastases at 1L initiation, n (%)	24 (32.4)	63 (39.6)	26 (50)
Liver Metastases at 1L initiation, n (%)	13 (17.6)	24 (15.1)	12 (23.1)
Median follow-up (IQR), months	7.6 (2.6-15.5)	7.4 (3.5-13.6)	8.8 (4.8-13.1)
Median duration of 1L Osi (IQR), months	13.0 (8.2-18.2)	11.9 (7.3-13.7)	16.6 (9.5-22.8)
Median duration of 2L treatment (IQR), months	2.2 (0.8-4.8)	4.1 (1.8-7.6)	5.3 (1.8-7.4)
Median time from start 1L to start 2L (IQR), months	13.5 (8.4-19.5)	12.2 (7.6-19.4)	16.6 (9.5-22.8)
Median treatment gap (IQR), months	0.0 (0.0-0.7)	0.1 (0.0-0.5)	0.0 (0.0-0.0)

References

1. Robinson ND, et al. Clin Lung Cancer. 2025;26(1):9–17.e3.
2. Attili i, Corvaja C, et al. Cancers. 2024; 16(14):2589.
3. Wu, S. Ann Oncol. 2025; Conference abstract P46.6.
4. Gómez-Riancho J, et al. Lung Cancer. 2025; 209:108797
5. Hettinger G CN, et al. Clin Lung Cancer. 2025.
6. Cheung WY et al. Curr Oncol. 2024; 31(8), 4382-4396.
7. Girard et al. Adv Ther. 2026; 43(4):1601-1621.
8. Sabari JK, et al. J Thorac Oncol. 2024; Conference abstract EP.12A.03 [Presentation Slides].

Methods

Study Design and Data Sources

- This retrospective, observational cohort study analyzed previously collected electronic medical record (EMR) and linked genomic data to assess outcomes in clinical practice.
- Data were aggregated from three US medical oncology databases: ConcertAI Patient360™, Flatiron-FMI CGDB, and COTA.

Patient Population

- Adults with EGFR Ex19del or L858R mutated advanced NSCLC who initiated 1L Osi monotherapy between April 2018 and October 2022 and progressed to 2L chemotherapy-containing regimens were included.
- Patients were followed up until death, loss to follow-up, or December 31, 2023, whichever occurred first.
- The 2L regimens included chemo-only, chemo-IO, and Osi-chemo.

Table 2. Distribution of 2L Treatments by Chemo-Containing Regimen*	
Chemo-only	74
PDC	67
Pemetrexed	6
Gemcitabine	1
Chemo-IO	159
PDC + atezolizumab/bevacizumab/pembrolizumab	154
Pemetrexed + pembrolizumab	5
Osi-chemo	52
Osimertinib + PDC	28
Osimertinib + PDC + IO	16
Osimertinib + 1CT	8

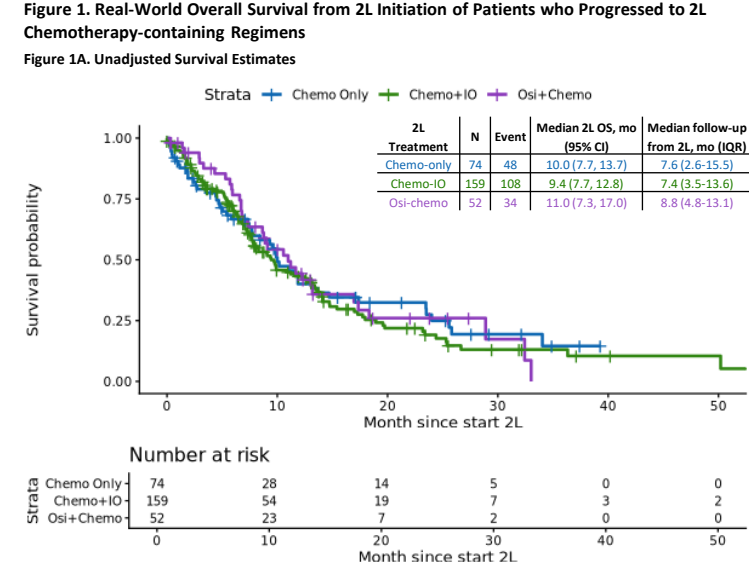
Abbreviations: chemo, chemotherapy; PDC, platinum-doublet chemotherapy; IO, immunotherapy; 1CT, one chemotherapy; *Regimen classification adapted from Sabari et al. WCLC 2024 presentation⁸

2L rwOS starting from 2L initiation date

- Median unadjusted rwOS (95% CI) from 2L was 10.0 months (7.7, 13.7) for chemo-only, 9.4 (7.7, 12.8) for chemo-IO, and 11.0 (7.3, 17.0) for Osi-chemo (**Figure 1A**).
- Median adjusted rwOS (95% CI) from 2L was 10.0 months (7.7, 13.7) for chemo-only, 9.4 (7.7, 13.0) for chemo-IO, and 9.0 (6.6, 11.2) for Osi-chemo (**Figure 1B**).

1L rwOS starting from 1L initiation date

- Median adjusted rwOS (95% CI) from 1L was 29.0 months (22.5, 40.0) for chemo-only, 26.9 (24.9, 32.1) for chemo-IO, and 23.6 (19.5, 27.4) for Osi-chemo (**Figure 2**).
- Among those who progressed to 2L chemo-containing regimens (n=285), median rwOS from 1L initiation (26.8 months) trended similarly to the 28.6-month rwOS previously reported for the overall 1L Osi population (Sabari et al., 2024), underscoring that the sequence of 1L Osi monotherapy followed by 2L chemo/IO or Osi-chemo yields suboptimal long-term survival outcomes and highlighting the critical unmet need for more effective sequencing strategies.



Data Analysis

- Descriptive baseline characteristics including age, sex, race, EGFR mutation subtype, ECOG performance status, and the presence of brain or liver metastases were assessed at 1L initiation.
- 2L rwOS was estimated using the Kaplan-Meier (KM) method. Index date was defined as the start of 2L treatment.
- Adjusted rwOS curves were generated using Inverse Probability of Treatment Weighting (IPTW). Propensity scores were estimated with a multinomial logistic regression including the following covariates: age, sex, race, EGFR mutation type, ECOG performance status, brain metastases, liver metastases, and 1L Osi treatment duration. IPTWs were calculated, stabilized, and applied to the survival curves. Covariate balance was assessed by standardized mean differences (SMDs) before and after weighting.
- Exploratory analysis: 1L rwOS was explored using the KM method, and adjusted curves were generated using IPTW, consistent with the approach for the primary analysis.

