

Real-World Treatment Duration and Outcomes Among Patients With Early-Stage NSCLC Receiving Adjuvant Osimertinib: A Retrospective Cohort Study

Eric K. Singhi^{1*}, Xinran Ma², Catherine Rinaldi², Lana Kovacevic³, Yi Liang⁴, Daniel Simmons⁴, Martyna Lupicka⁴, İlker Arslan⁴, Martin Sandelin⁵, Joanna Pye⁶, Danny Nguyen⁷

¹The University of Texas MD Anderson Cancer Center, Houston, TX, USA; ²Flatiron Health, New York, NY, USA; ³Flatiron Health, Durham, NC, USA; ⁴AstraZeneca, Gaithersburg, MD, USA; ⁵AstraZeneca, Södertälje, Stockholm, Sweden; ⁶AstraZeneca, Macclesfield, UK; ⁷City of Hope, Huntington Beach and Irvine, CA, USA⁴

Objective

- This study aimed to quantify real-world duration of therapy (rwDOT), assess real-world disease-free survival (rwDFS), examine association between early treatment discontinuation and outcomes, and explore potential drivers of discontinuation among US patients with resected NSCLC receiving adjuvant osimertinib.

Conclusions

- In US real-world practice, a substantial proportion of patients discontinued adjuvant osimertinib before completing the recommended 3-year course, with only one third remaining on treatment at 36 months.
- Early discontinuation was associated with more than a two-fold higher risk of recurrence or death, reinforcing the importance of maintaining the full recommended treatment duration.
- Proactive adverse-event management and effective clinician-patient communication on the benefits and risks of continuing therapy are critical to support treatment persistence and improve patient outcomes.

Patient-friendly summary

Why did we perform this research?

Although osimertinib is recommended for 3 years after surgery for early-stage epidermal growth factor receptor (EGFR)-mutated non-small cell lung cancer (NSCLC), little was known about how long patients actually stay on treatment in routine clinical practice in the US and whether stopping early affects patient outcomes.

How did we perform this research?

We used the Flatiron Health Research Database to analyze real-world electronic health records from 822 US patients with Stage I–IIIA EGFR-mutated NSCLC who started osimertinib after surgery between 2021 and 2024.

What were the findings of this research?

Half of patients stayed on treatment for approximately 33 months or less, falling short of the recommended 3 years. About 75% were still receiving treatment at 1 year, 62% at 2 years, and 33% at 3 years. The study also found that patients who stopped treatment early had a higher chance of cancer returning or dying compared with those who stayed on treatment. Patients who stopped before 12 months had about a 2.3 times higher risk, and those who stopped before 24 months had about a 2.7 times higher risk of cancer returning or dying. Among patients who stopped treatment before 24 months, possible side effects were reported more often than cancer recurrence when treatment was stopped, suggesting that side effects may have played a role in stopping treatment early.

What are the implications of this research?

Stopping osimertinib early after lung cancer surgery was associated with significantly worse outcomes for patients. This suggests it is important for doctors and patients to work closely together to manage side effects early and maintain good communication, so patients have the best chance of completing the full 3 years of treatment and achieving the best possible outcomes.

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Poster

Plain language summary

Mobile-friendly poster

Narrated poster video

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* Corresponding author email address: eksinghi@mdanderson.org
Corresponding author Twitter handle: @lungoncdoc
[‡] Affiliation at the time of the study
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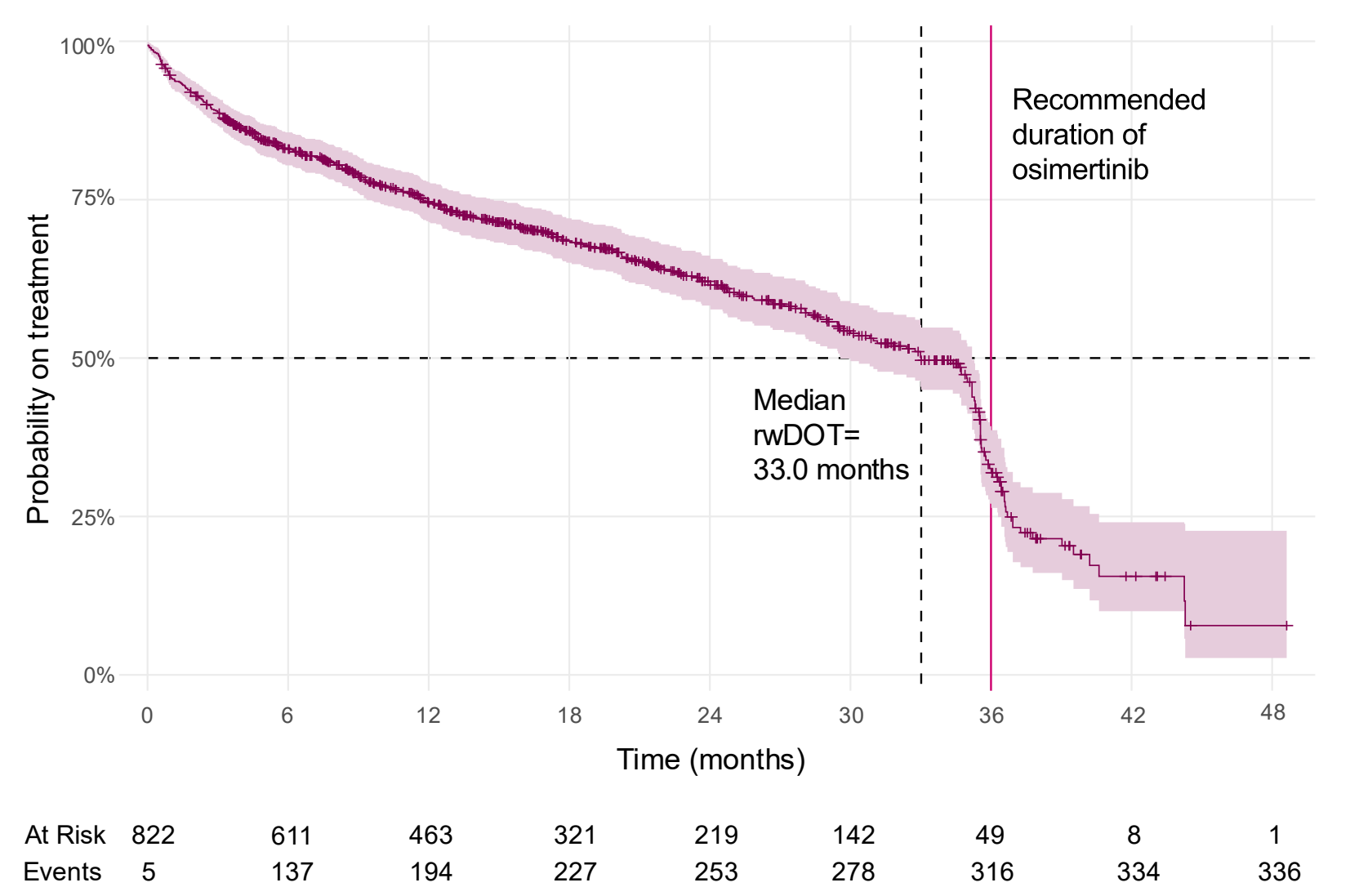
Introduction

- Lung cancer is the second most common cancer, and the leading cause of cancer deaths in the US.¹
- Approximately 30% of patients with NSCLC present with resectable disease. Adjuvant cisplatin-based chemotherapy offers modest benefit, with recurrence and death rates after surgery remaining high in this population.²
- Adjuvant osimertinib demonstrated significant disease-free and overall survival benefits in patients with resectable EGFR-mutated (EGFRm) NSCLC in the ADAURA trial, establishing 3 years as the recommended duration of therapy.^{3,4}
- However, in real-world clinical practice, treatment may be discontinued earlier than intended; in ADAURA, the most common reasons for early discontinuation were low-grade adverse events and patient choice.⁵
- To date, no published data have characterized rwDOT for adjuvant osimertinib in US real-world populations; and there is a lack of data on the impact of early discontinuation on clinical outcomes.

Results

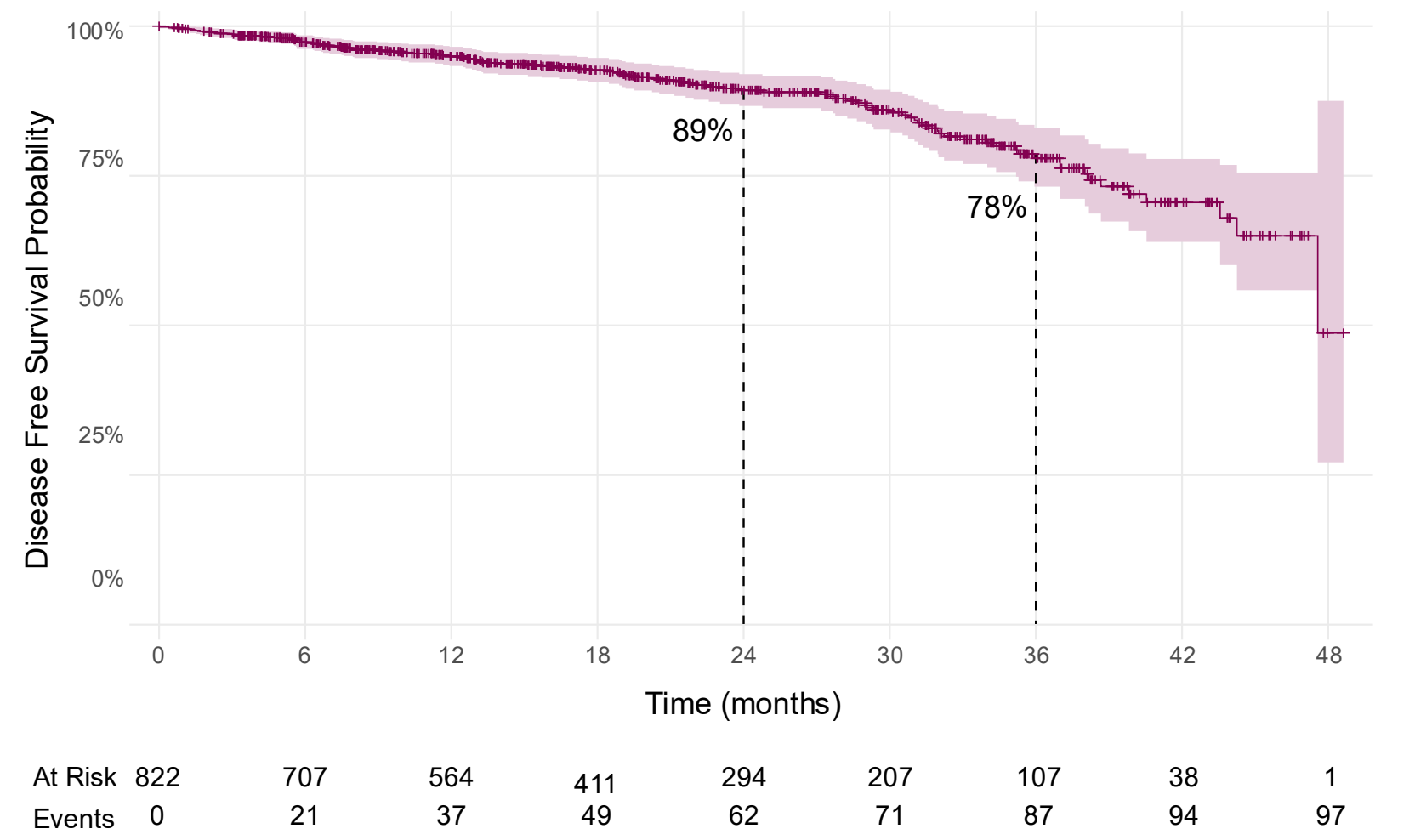
- A total of 822 patients met the study eligibility criteria. Baseline demographic and clinical characteristics for the study population are reported in **Table 1** and **Figure 3**.
- The observed median rwDOT was 33.0 months (95% Confidence Interval [CI]: 29.6–35.2), indicating only 50% remained on therapy at 33 months. K-M estimated probability of remaining on therapy: 75% at 12, 62% at 24, and 33% at 36 months (**Figure 4**).
- K-M estimated disease free survival probability: 95% at 12, 89% at 24, and 78% at 36 months (**Figure 5**). Disease-free survival rates at 24 and 36 months are comparable to those observed in ADAURA (90% and 85%).³
- Patients with discontinuation prior to the 12-month and 24-month landmarks had a higher risk of recurrence or death compared with those continuing therapy, after adjusting for patient demographic and clinical characteristics (12-month Hazard Ratio [HR] **2.34, 95% CI 1.28–4.29**; 24-month **HR 2.74, 95% CI 1.22–6.13**) (**Figure 6**).
- Among patients who discontinued therapy (N=336), 39 (12%) had a documented recurrence within 30 days before or after discontinuation. Among 297 patients without recurrence during this period, 154 (51.9%) had a documented real-world adverse event (rwAE), and 143 (48.1%) had neither within the same time window. Recurrence and rwAEs of interest within 30 days of discontinuation (potential drivers of discontinuation) by timing of discontinuation are presented in **Figure 7**.
 - Fatigue (23%), loss of appetite (16%), diarrhea (15%), rash (15%), and nausea/vomiting (12%) were the most common rwAEs in the overall population (**Figure 8**).
- The exploratory multi-state survival analysis results were consistent with the landmark analyses, with a faster rate of recurrence observed after treatment discontinuation (**Figure 9**). Cumulative hazards for all transitions by year are presented in **Table 2**.

Figure 4. Kaplan-Meier estimates of rwDOT in the overall cohort



Median rwDOT was 33.0 months (95% CI, 29.6–35.2), indicating only 50% remained on therapy at 33 months.

Figure 5. Kaplan-Meier estimates of rwDFS in the overall cohort



Disease-free survival rates at 24 and 36 months were 89% and 78%, respectively, and were comparable to those observed in ADAURA (90% and 85%).³

Methods

- Study Design & Data Source:** Retrospective cohort study conducted using the US Flatiron Health Research Database, a de-identified nationwide database derived from electronic health records (EHR).
- Inclusion Criteria:** Patients aged ≥18 years with stage I-IIIA EGFRm NSCLC who underwent surgical resection and initiated adjuvant osimertinib between Jan 1, 2021, and Nov 30, 2024. Patients were required to have documented EGFR mutation status and ≥3 months of potential follow-up.
- Index Date and Follow-up:** Index date was the date of adjuvant osimertinib treatment initiation. Follow-up was the time from index date until the earliest of death, loss to follow-up, or end of data availability.
- Outcomes and Censoring Events:** rwDOT (time from index date to adjuvant osimertinib discontinuation) and rwDFS (time from index date to recurrence or death). Censoring events were last known adjuvant osimertinib treatment date (rwDOT) and last confirmed EHR activity (rwDFS).
- Statistical Methods:** rwDOT and rwDFS were estimated using the Kaplan–Meier (K-M) method. Associations between discontinuation and rwDFS were assessed via adjusted Cox proportional hazards models, with landmark analyses at 12, 24, and 34 months to mitigate immortal time bias (**Figure 2**). The 34-month landmark was chosen to allow a 2-month grace period in real-world practice when defining early discontinuation for a 36-month therapy. Potential discontinuation drivers were explored by summarizing recurrence and adverse events of interest within 30 days before or after discontinuation (events may not represent confirmed discontinuation reasons). A multistate survival analysis with Cox proportional hazards models estimated hazard ratios across key transition states, with Nelson-Aalen cumulative hazard curves characterizing hazard accumulation over follow-up.

Table 1. Demographic characteristics of study population	
Variable	Overall, N = 822
Age at index (years), median (IQR)	71.0 (64.0, 76.0)
Female, n (%)	604 (73.5%)
Race	
Asian	87 (10.6%)
White	504 (61.3%)
Other	103 (12.5%)
Unknown	128 (15.6%)
Community practice, n (%)	638 (77.6%)
Socioeconomic Status (SES) Index: 4+*, n (%)	404 (49.1%)
History of smoking, n (%)	388 (47.2%)
Follow-up (months)**, median (IQR)	18.7 (10.0, 31.1)

*SES Index: 4+ represents the fourth and fifth quintile of socioeconomic status, where 1 = Lowest SES and 5 = Highest SES.
**Follow-up time is the time from index date to earliest of last confirmed activity, death date, or data cutoff (Feb 28, 2025).

Figure 3. Clinical characteristics of study population

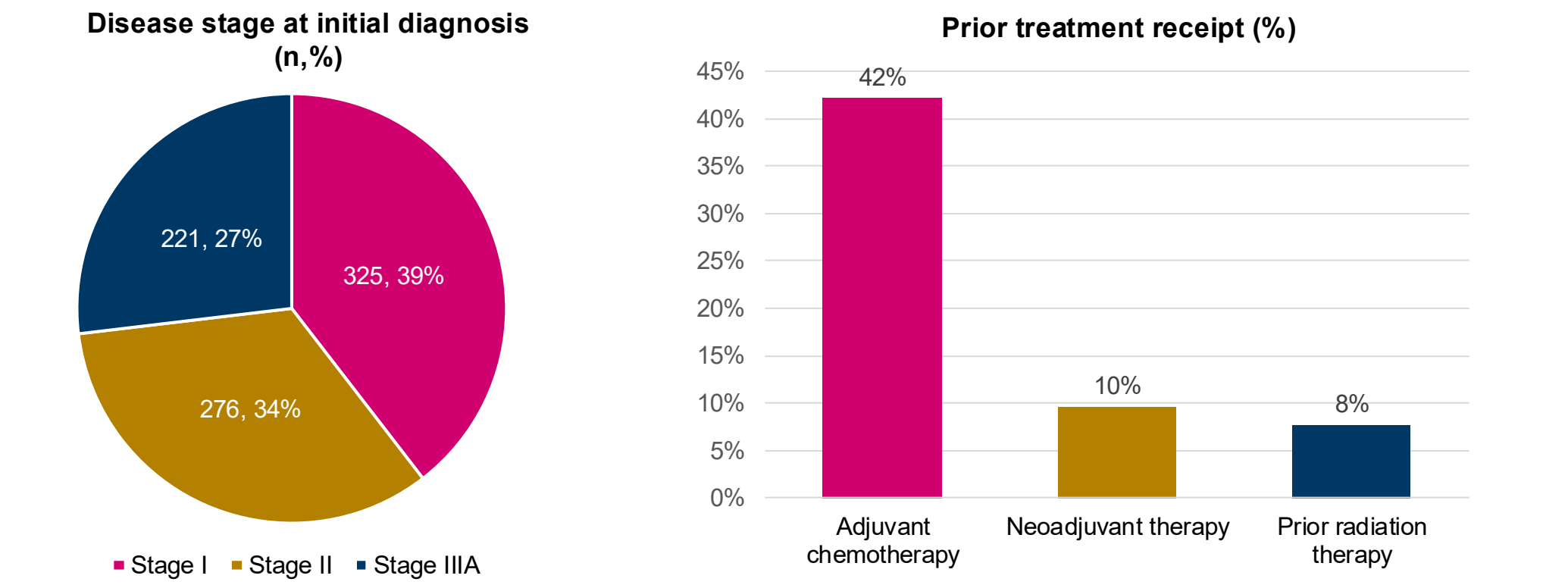
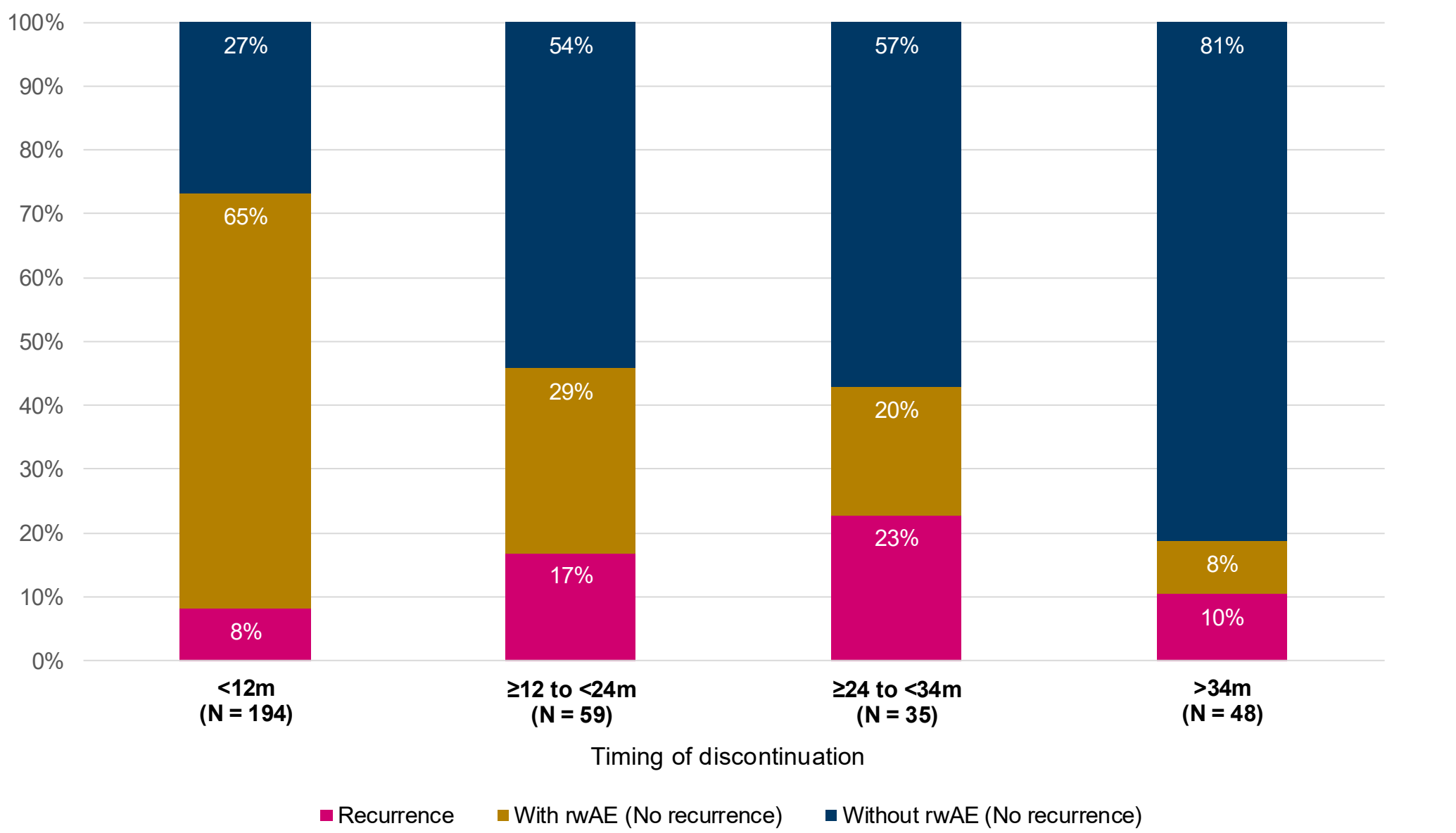


Figure 7. Recurrence and rwAEs within 30 days of osimertinib discontinuation, by timing of discontinuation



Among patients who discontinued osimertinib prior to 24 months, higher proportion of patients had rwAEs documented at discontinuation than recurrence, underscoring the importance of AE management to support rwDOT.

Figure 8. AEs within 30 days of discontinuation among patients without recurrence at discontinuation

Characteristic	Overall, N = 297	<12 m, N = 178	≥12 to <24 m, N = 49	≥24 to ≤34 m, N = 27	>34 m, N = 43
Fatigue	22.9%	36.0%	4.1%	3.7%	2.3%
Loss of appetite	15.8%	21.3%	10.2%	11.1%	2.3%
Diarrhea	15.2%	21.9%	10.2%	0.0%	2.3%
Rash	14.5%	22.5%	6.1%	0.0%	0.0%
Nausea/vomiting	11.8%	17.4%	8.2%	0.0%	0.0%
Musculoskeletal pain	11.4%	16.3%	2.0%	14.8%	0.0%
Anemia	9.4%	14.6%	2.0%	0.0%	2.3%
Pneumonitis	6.7%	8.4%	8.2%	3.7%	0.0%
Constipation	6.4%	9.0%	6.1%	0.0%	0.0%
Pneumonia	5.4%	5.6%	8.2%	7.4%	0.0%

Fatigue, loss of appetite, diarrhea, rash, and nausea/vomiting were the most common rwAEs in the overall population and among those who discontinued within 12 months.

Figure 1. Study design diagram

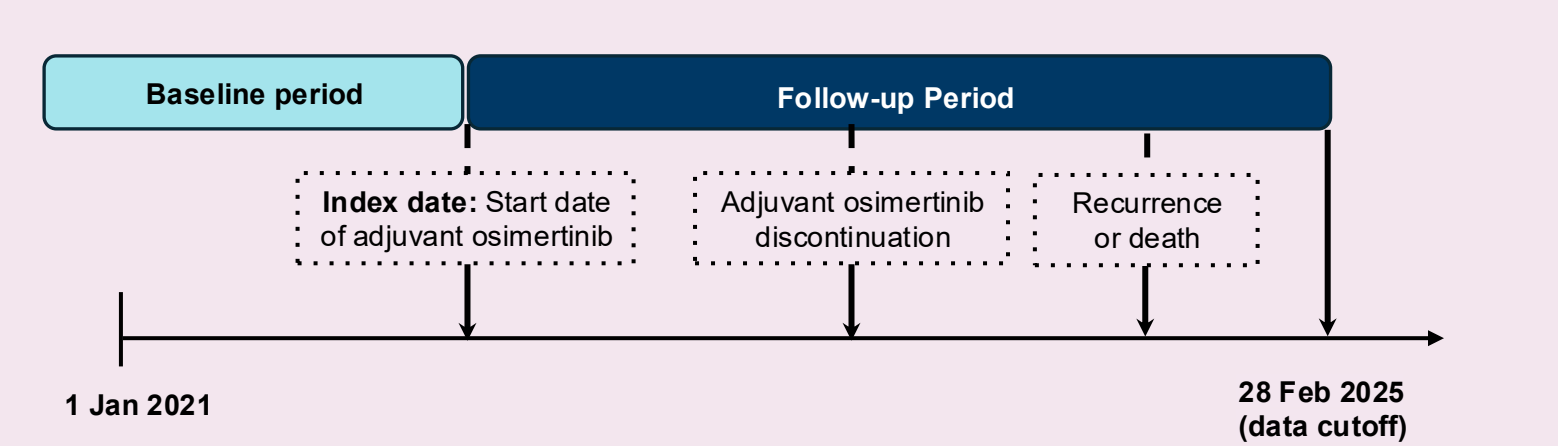


Figure 2. 24-month landmark analysis illustration

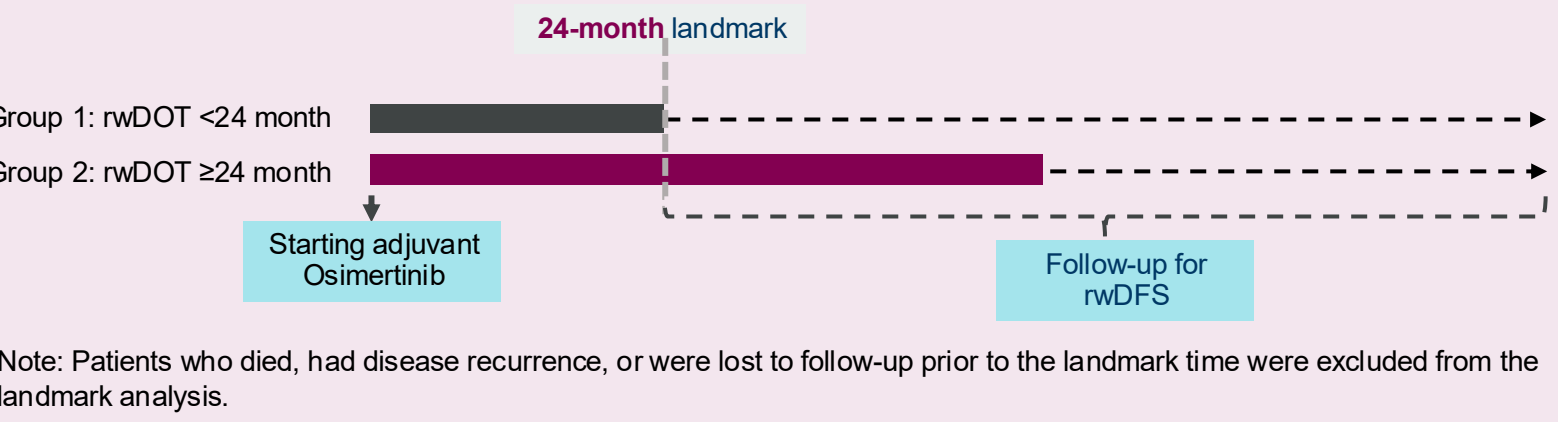
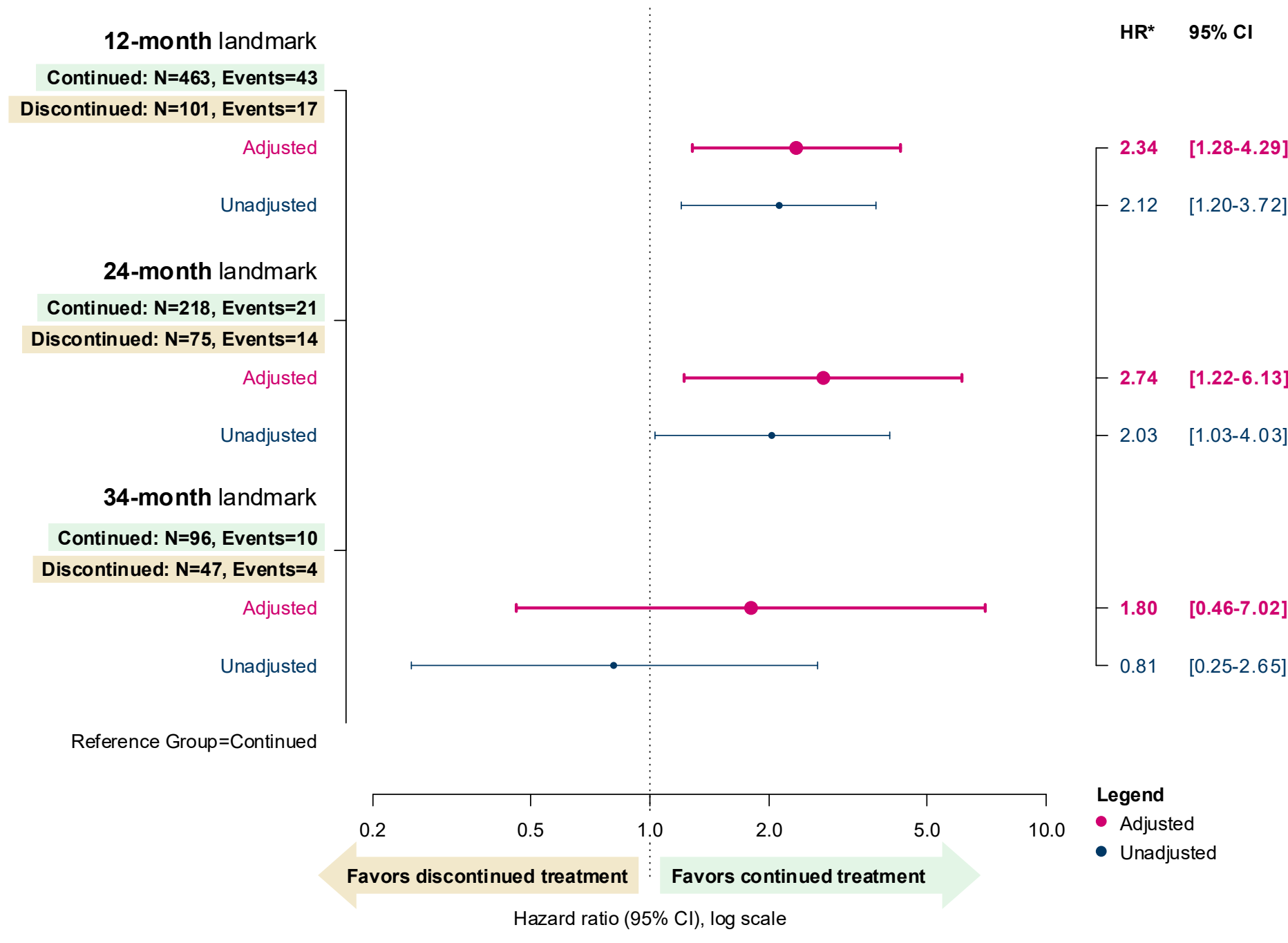


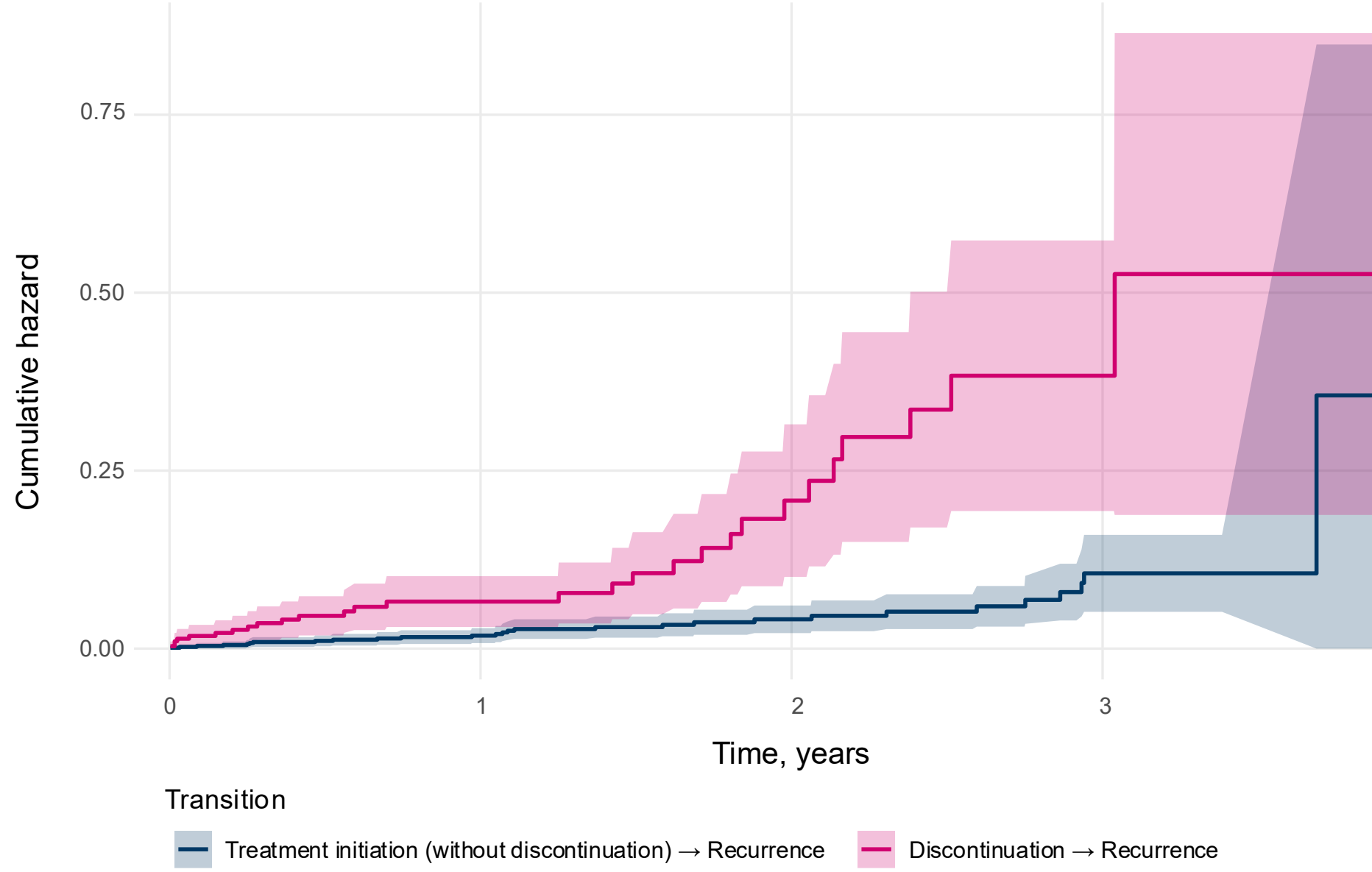
Figure 6. Association between treatment discontinuation and rwDFS: forest plot of unadjusted and adjusted Cox regression landmark analyses



*Models were adjusted for age at index date, NSCLC stage, receipt of prior adjuvant therapy, receipt of neoadjuvant therapy, receipt of prior radiation, and smoking history. Additionally, the 12- and 24-month models were also adjusted for SES.

- In the landmark analyses, early discontinuation before 12 or 24 months was associated with a 2.3-fold or 2.7-fold higher adjusted risk of recurrence or death, respectively, compared with patients who continued treatment.
- At 34 months, the result was not significant, likely due to limited post-landmark follow-up and fewer events.

Figure 9 Nelson-Aalen estimates of cumulative transition hazards



Across follow-up, the cumulative hazard for recurrence was higher after osimertinib discontinuation than during treatment, suggesting increased recurrence risk after discontinuation.

Table 2. Cumulative transition hazard (95% CI), by year of follow-up

Time (year)	Treatment initiation → Discontinuation	Treatment initiation (without discontinuation) → Recurrence	Discontinuation → Recurrence	Discontinuation (without recurrence) → Death	Recurrence → Death
Year 1	0.27 (0.23–0.31)	0.02 (0.01–0.03)	0.07 (0.03–0.10)	0.13 (0.08–0.18)	0.37 (0.16–0.57)
Year 2	0.43 (0.37–0.49)	0.04 (0.02–0.06)	0.21 (0.10–0.32)	0.21 (0.12–0.29)	0.46 (0.19–0.73)
Year 3	1.00 (0.82–1.18)	0.11 (0.05–0.16)	0.38 (0.19–0.57)	0.21 (0.12–0.29)	0.79 (0.09–1.50)
Year 4	2.05 (1.27–2.83)	0.36 (0.00–0.85)	0.53 (0.19–0.86)	0.21 (0.12–0.29)	0.79 (0.09–1.50)

Limitations

Limitations include the absence of explicit reasons for treatment discontinuation (with recurrence and rwAEs reported near discontinuation used as a proxy measure); the potential for residual confounding due to unmeasured factors; incomplete capture of selected clinical and demographic variables (e.g., EGFR mutation subtypes, race, Eastern Cooperative Oncology Group [ECOG] performance status); and limited generalizability beyond the US community oncology setting.