Overall Survival After Treatment With First-line Osimertinib for *EGFR*-mutant Advanced NSCLC in the US

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Background and Objectives

Background

- Osimertinib is a third-generation EGFR TKI approved for 1L treatment of advanced NSCLC with common *EGFR* mutations (Ex19del or L858R)
- In the FLAURA study (ClinicalTrials.gov Identifier: NCT02296125), median OS was 38.6 months for patients treated with osimertinib, and the 2-year landmark survival was 74%[1]
- Few studies have evaluated how these clinical trial results translate into real-world, long-term outcomes
- We assessed rwOS in patients with *EGFR*-mutant NSCLC who were treated with 1L osimertinib using real-world data from 3 large, longitudinal US medical oncology databases

Objectives

- To estimate rwOS in patients with newly diagnosed advanced/metastatic *EGFR*-mutant NSCLC who were initiated on 1L osimertinib monotherapy and in patients stratified by subgroups
- To describe baseline demographic and clinical characteristics of patients in this population
- To identify risk factors for survival outcomes

1L, first-line; EGFR, epidermal growth factor receptor; Ex19del, exon 19 deletion; L858R, exon 21 L858R; NSCLC, non-small cell lung cancer; OS, overall survival; rwOS, real-world overall survival; TKI, tyrosine kinase inhibitor.

1. Ramalingam SS, et al. *N Engl J Med*. 2020;382(1):41-50.

Methods

Study design and population

- This was a retrospective new user cohort study
- Inclusion criteria
  - ≥18 years of age
  - Newly diagnosed advanced/metastatic[a] NSCLC between 2018 and 2022
  - Documented *EGFR* Ex19del or L858R mutations prior to the index date
  - Treated with 1L osimertinib monotherapy from April 2018 to October 2022 per the local label
- Exclusion criteria
  - No record of TNM stage
  - Missing *EGFR* test results
  - Documented Ex20ins or atypical mutations
- Patients were followed-up until death, loss to follow-up, or December 31, 2023, whichever occurred first

Primary endpoint

- rwOS was defined as the time from the index date until death due to any cause

Analysis

- rwOS was estimated using the Kaplan-Meier method for all patients and stratified by subgroup
- Relative risk of death in subgroups was compared using a multivariate Cox model that was adjusted for potential risk factors (eg, age, ECOG PS, brain metastasis status, liver metastasis status, *TP53*, *EGFR* L858R mutation status)
- A subgroup analysis of rwOS in clinical trial-eligible patients was conducted by applying clinical trial eligibility criteria, and weighted data were used to estimate rwOS
- Attrition rates were calculated

[a]Stages IIIb to IV or documented metastases.

1L, first-line; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Ex19del, exon 19 deletion; Ex20ins, exon 20 insertion; L858R, exon 21 L858R; NSCLC, non-small cell lung cancer; rwOS, real-world overall survival; TNM, tumor, nodes, metastisis.

Methods: Data Sources

- The 3 large, longitudinal US medical oncology databases provided a representative study population of US patients who have *EGFR*-mutant NSCLC

ConcertAI Patient360™

RWD provider that aggregates the data from EHRs of >100 US principally community–based oncology practices

Mortality data obtained from EHRs, third-party obituary data sources, the SSDI, and commercial claims

Flatiron-FMI CGDB

A nationwide, longitudinal EHR database from a network of >280 community clinics and academic institutions at >800 geographically diverse sites of care

Mortality variable created through an amalgamation of EHRs and links to external mortality sources and the SSDI

COTA

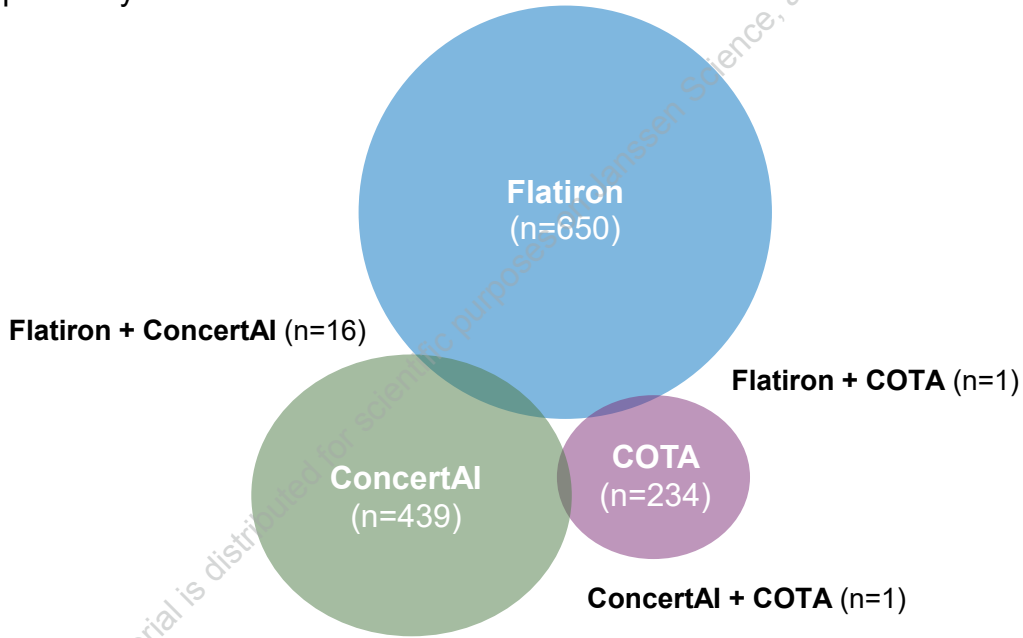
A longitudinal EHR database from academic institutions, community centers, and hospital systems that represents 500,000 patients from >200 sites of care

Mortality data obtained from documentation in EHRs and a third-party obituary data source

EGFR, epidermal growth factor receptor; EHR, electronic health record; FMI, Foundation Medicine, Inc.; NSCLC, non-small cell lung cancer; RWD, real-world data; SSDI, Social Security Death Index.

Methods: Data Sources

- Minimal overlap (1.4%) was observed across the 3 databases, underscoring the distinct nature of the patient populations captured by each database



ConcertAI, ConcertAI Patient360™; Flatiron, Flatiron/Foundation Medicine, Inc. Clinico-Genomic Database.

Results: Demographic and Clinical Characteristics

- 1323 patients who started 1L osimertinib monotherapy between April 2018 and October 2022 were included in the analysis
- Median age was 70 years (range, 35–89)
- 68.8% were female
- 17.2% of patients had an ECOG PS score ≥2
- 36.1% had brain metastases
- 15.1% had liver metastases
- 63.1% had a *TP53* co-mutation[a]

Characteristic	Pooled group (N=1323)
Median age at index (range), y	70 (35–89)
Median follow-up (Q1–Q3), mo	20.0 (10.6–31.1)
Age group, n (%)	
≥65 years	877 (66.3)
<65 years	446 (33.7)
Sex, n (%)	
Female	910 (68.8)
Male	413 (31.2)
Race, n (%)	
White	800 (60.5)
Asian	176 (13.3)
Black or African American	111 (8.4)
Other	135 (10.2)
Unknown	101 (7.6)
Body weight, n (%)	
<80 kg	893 (67.5)
≥80 kg	335 (25.3)
Unknown	95 (7.2)
EGFR mutation type, n (%)	
Exon 21 L858R	575 (43.5)
Exon 19 deletion	692 (52.3)

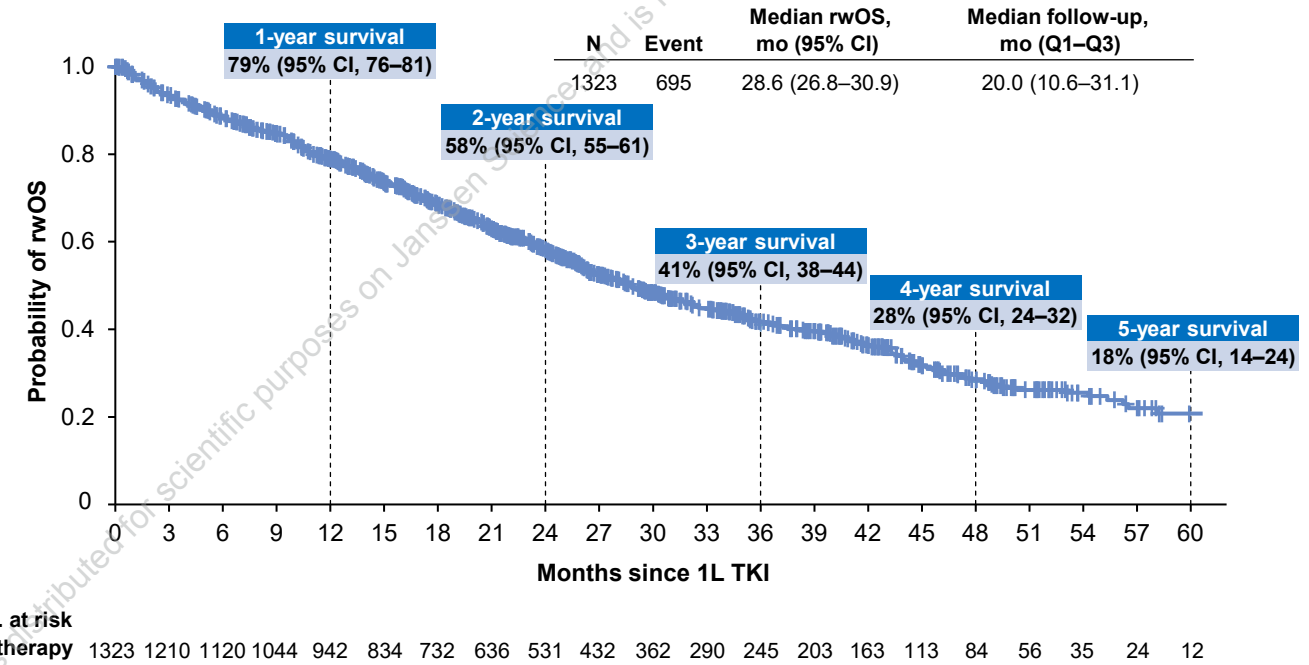
Characteristic	Pooled group (N=1323)
Stage at initial diagnosis, n (%)	
I	61 (4.6)
II	42 (3.2)
III	84 (6.3)
IV	1092 (82.5)
Unspecified	44 (3.3)
Histology, n (%)	
Non-squamous	1242 (93.9)
ECOG PS score at index, n (%)	
0	375 (28.3)
1	501 (37.9)
≥2	227 (17.2)
Unknown	220 (16.6)
Metastases at index, n (%)	
Brain	478 (36.1)
Liver	200 (15.1)
***TP53* co-mutation, n (%)[a]**	
Present	571 (63.1)
Not present	334 (36.9)

[a]*TP53* co-mutation status was available for 905 patients from Flatiron and ConcertAI.

1L, first-line; ECOG PS, Eastern Cooperative Oncology Group performance status; mo, months; Q1–Q3, interquartile range, y, years.

Results: rwOS of Patients Treated With 1L Osimertinib Monotherapy

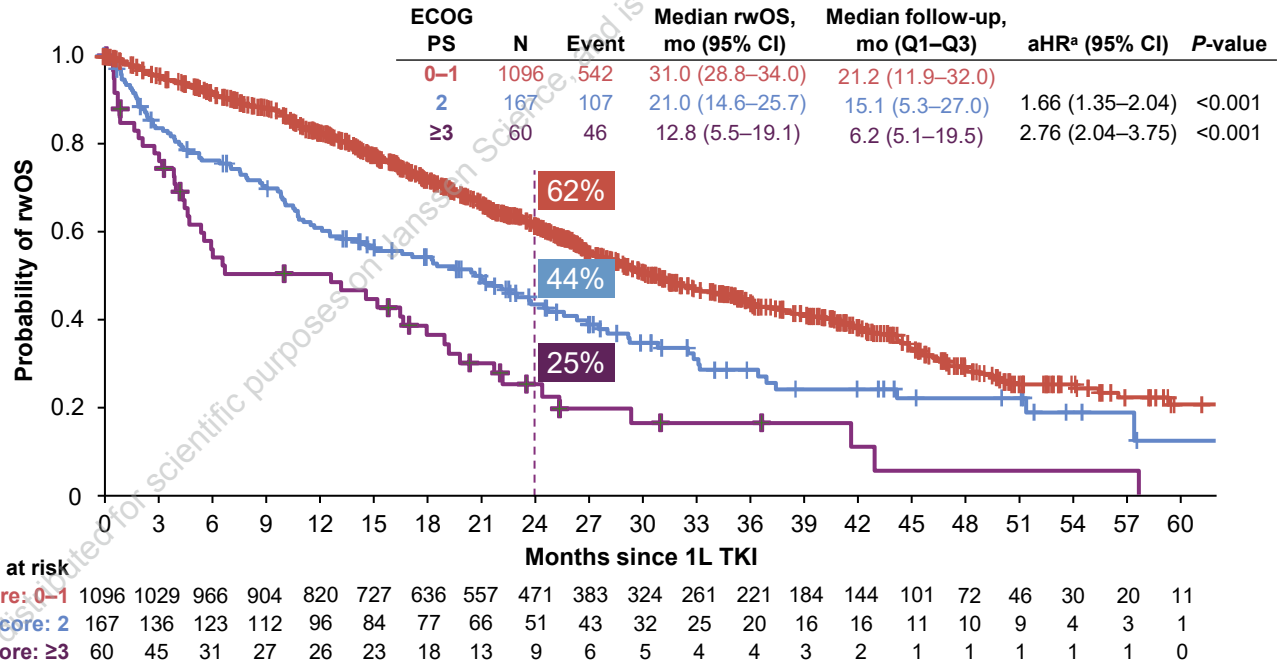
- At 24 months, rwOS was 58% (95% CI, 55–61)
- Median rwOS was 28.6 months (95% CI, 26.8–30.9)



1L, first-line; CI, confidence interval; Q1–Q3, interquartile range; rwOS, real-world overall survival; TKI, tyrosine kinase inhibitor.

Results: rwOS of Patients Treated With 1L Osimertinib Monotherapy by **ECOG PS**

- rwOS was significantly lower in patients with ECOG PS 2 compared to patients with ECOG PS 0–1 (median rwOS, 21.0 mo vs 31.0 mo; *P*<0.001)
- rwOS was significantly lower in patients with ECOG PS ≥3 compared to patients with ECOG PS 0–1 (median rwOS, 12.8 mo vs 31.0 mo; *P*<0.001)

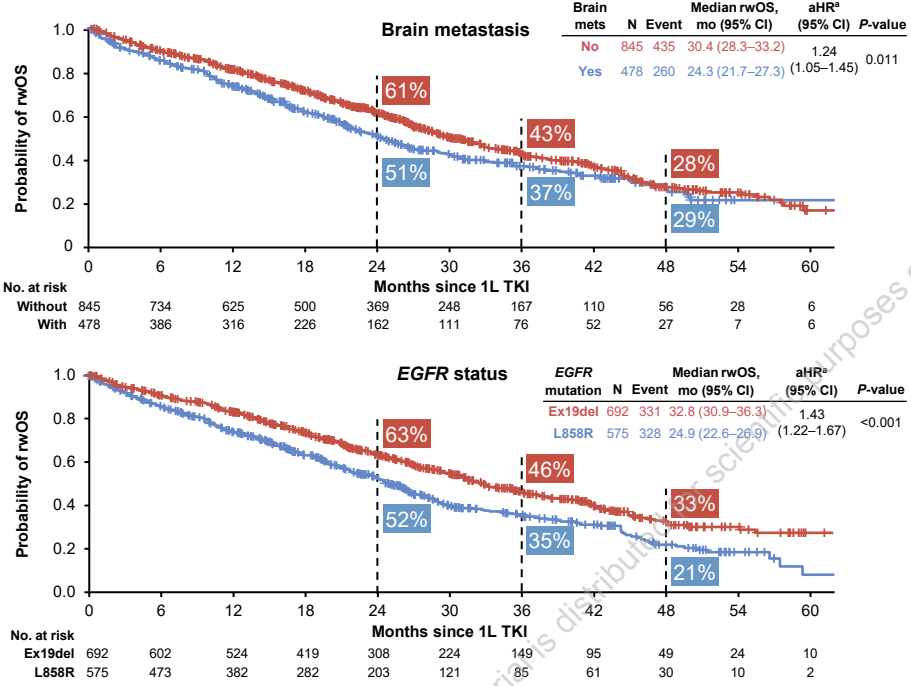


[a]Covariates for aHR: age, ECOG PS score, brain metastasis status, liver metastasis status, exon 21 L858R mutation status.

1L, first-line; aHR, adjusted hazard ratio; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; Q1–Q3, interquartile range; rwOS, real-world overall survival; TKI, tyrosine kinase inhibitor.

Results: rwOS by **Subgroups**

- Patients with brain metastasis, liver metastasis, L858R mutation, or *TP53*+ mutation had significantly lower rwOS versus patients without these characteristics

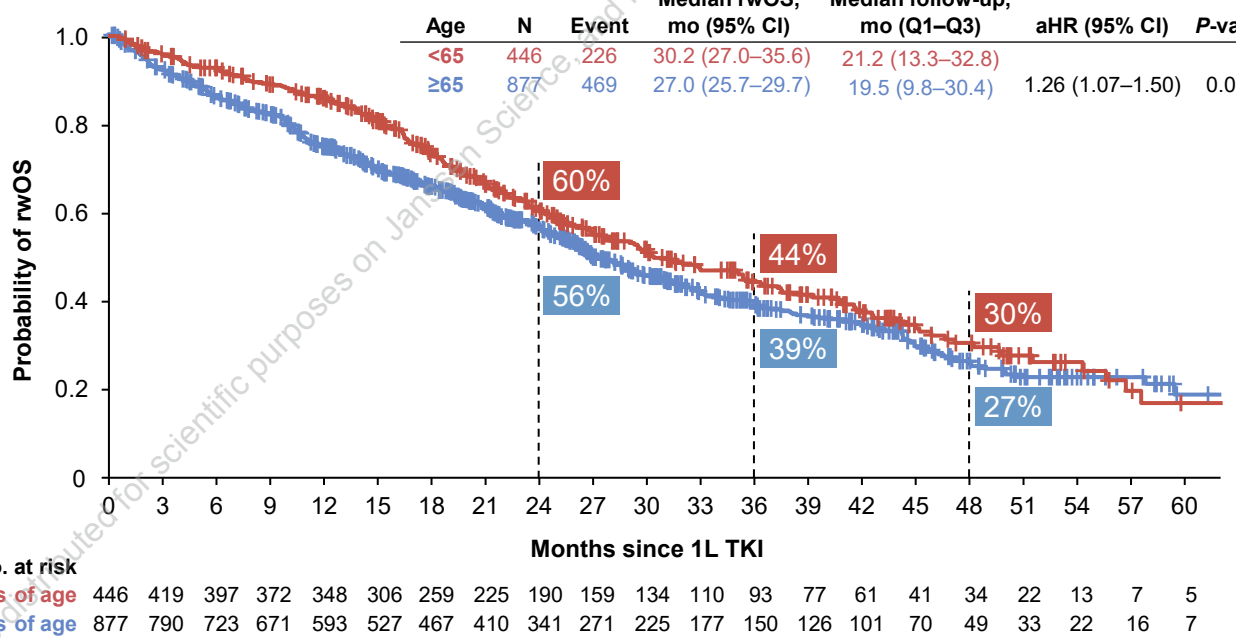


[a]Covariates for aHR: age, ECOG PS score, brain metastasis status, liver metastasis status, exon 21 L858R mutation status.

1L, first-line; aHR, adjusted hazard ratio; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; *EGFR*, epidermal growth factor receptor; Ex19del, exon 19 deletion; L858R, exon 21 L858R; mets, metastasis; rwOS, real-world overall survival; TKI, tyrosine kinase inhibitor.

Results: rwOS of Patients Treated With 1L Osimertinib Monotherapy by **Age Group**

- rwOS was significantly lower in patients aged 65 years or older (median rwOS, 27.0 mo vs 30.2 mo; *P*=0.007)

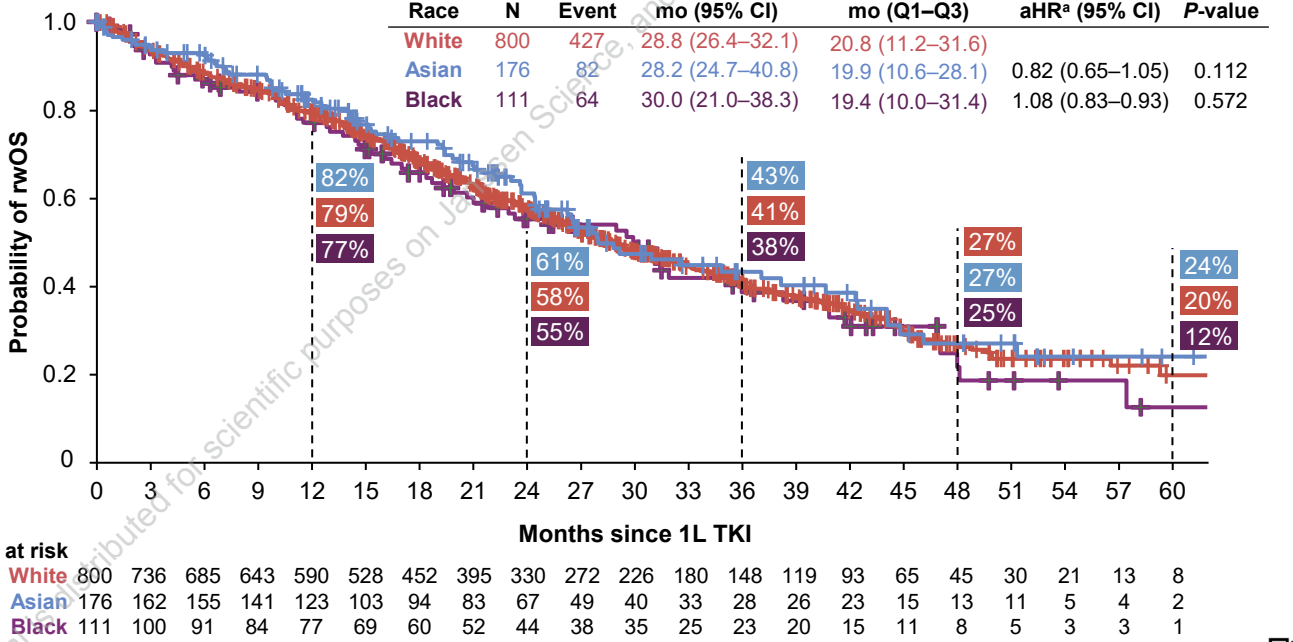


1L, first-line; aHR, adjusted hazard ratio; CI, confidence interval; Q1–Q3, interquartile range; rwOS, real-world overall survival; TKI, tyrosine kinase inhibitor.

Results: rwOS of Patients Treated With 1L Osimertinib Monotherapy by **Race**

- No significant difference in rwOS was observed among racial subgroups

Race	N	Event	Median rwOS, mo (95% CI)	Median follow-up, mo (Q1–Q3)	aHR[a] (95% CI)	*P*-value
White	800	427	28.8 (26.4–32.1)	20.8 (11.2–31.6)		
Asian	176	82	28.2 (24.7–40.8)	19.9 (10.6–28.1)	0.82 (0.65–1.05)	0.112
Black	111	64	30.0 (21.0–38.3)	19.4 (10.0–31.4)	1.08 (0.83–0.93)	0.572

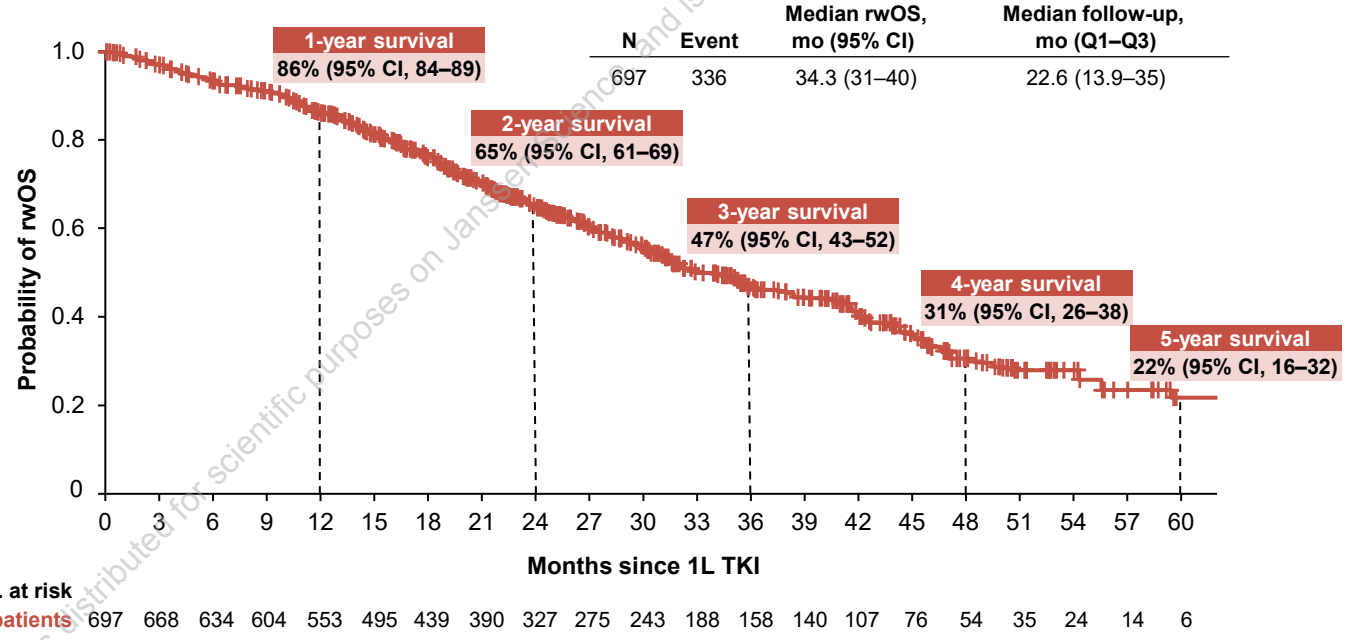


[a]Covariates for aHR: age, ECOG PS score, brain metastasis status, liver metastasis status, exon 21 L858R mutation status.

1L, first-line; aHR, adjusted hazard ratio; CI, confidence interval; Q1–Q3, interquartile range; rwOS, real-world overall survival; TKI, tyrosine kinase inhibitor.

Results: rwOS of Trial-Eligible Patients[a] Treated With 1L Osimertinib Monotherapy (Weighted Analysis[b])

- At 24 months, rwOS was 65% (95% CI, 61–69)
- Median rwOS was 34.3 months (95% CI, 31–40)
  - Median rwOS was comparable to that observed in the FLAURA trial (34.3 mo [95% CI, 31–40] vs 38.6 mo (95% CI, 34.5–41.8)[1]



[a]Trial-eligible patients were matched as closely as possible to inclusion criteria for patients in the FLAURA[1] trial (teatment-naïve for therapies other than osimertinib monotherapy, non-squamous NSCLC, ECOG PS score 0-1 without other malignancies, major surgery, or severe comorbidities).[b]In this analysis, median age was weighted from 69 years in the real-world data set to 64 years; also weighted by sex, histology, brain metastases, and *EGFR* mutation type.

1L, first-line; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group performance status; NSCLC, non-mall cell lung cancer; Q1–Q3, interquartile range; rwOS, real-world overall survival; TKI, tyrosine kinase inhibitor.

1. Ramalingam SS, et al. *N Engl J Med*. 2020;382(1):41-50.

Results: Multivariate Cox Regression Analysis of Risk Factors for All-cause Death

- 95% of patients had ≥1 risk factor for poor survival
  - 33% of patients had 2 risk factors
  - 26% of patients had 3 risk factors

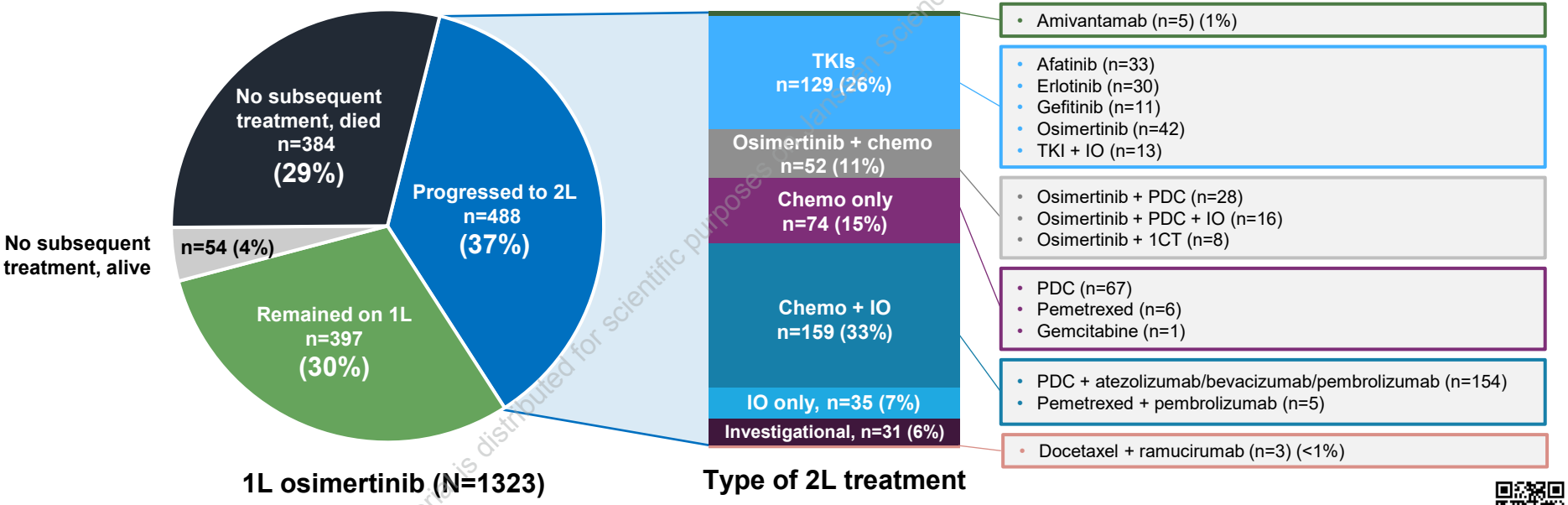
Risk factor	Prevalence	HR (95% CI)	*P*-value
≥65 years of age	66%	1.18 (1.00–1.38)	0.045
Brain metastases	36%	1.24 (1.05–1.45)	0.011
TP53+	64%	1.35 (1.06–1.60)	0.011
EGFR L858R[a]	43%	1.43 (1.22–1.67)	<0.001
Liver metastases	15%	1.80 (1.47–2.20)	<0.001
ECOG PS score ≥2	17%	1.93 (1.61–2.30)	<0.001

[a]Versus exon 19 deletion.

CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HR, hazard ratio; L858R, exon 21 L858R.

Results: Patient Attrition During 1L Osimertinib and Treatment Sequence

- 33% of patients didn't receive 2L treatment (median follow-up, 20 months)



1CT, one chemotherapy; 1L, first-line; 2L, second-line; chemo, chemotherapy; IO, immunotherapy; PDC, platinum-doublet chemotherapy; TKI, tyrosine kinase inhibitor.

Conclusions

Key takeaways

- rwOS for patients with advanced/metastatic *EGFR*-mutated NSCLC was 10 months lower than that observed in the clinical trial setting (28.6 mo vs 38.6 mo)[1]
  - 58% of patients were alive at 2 years compared with 74% seen in the FLAURA trial[1]
  - Fewer than 1 in 5 patients (18%) were estimated to be alive at 5 years in the current analysis
- 1 in 3 patients did not receive 2L treatment, indicating a need for improved 1L treatments
- Risk factors, such as *TP53* mutations, *EGFR* L858R mutations, ECOG PS score 2+, and liver and brain metastases, are associated with poor survival outcomes
  - 95% of patients had ≥1 risk factor, and 33% of patients had 2 risk factors and 26% had 3 risk factors

Despite advances in TKI monotherapy treatments, long-term (5-year) survival of patients with common *EGFR*-mutant advanced NSCLC remains poor

1L, first-line; 2L, second-line; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; L858R, exon 21 L858R; NSCLC, non-small cell lung cancer; rwOS, real-world overall survival.

1. Ramalingam SS, et al. *N Engl J Med*. 2020;382(1):41-50.

Other Amivantamab Presentations at WCLC 2024

MARIPOSA

Longer follow-up of amivantamab + lazertinib vs osimertinib in first-line *EGFR*-mutant advanced NSCLC

Sunday, Sep 8 10:47-10:57am
(OA02.03; Gadgeel)

MARIPOSA

Patient-relevant outcomes of amivantamab + lazertinib vs osimertinib in first-line *EGFR*-mutant advanced NSCLC

Tuesday, Sep 10 1:55-2:00pm
(MA12.07; Nguyen)

MARIPOSA

Lazertinib vs osimertinib in first-line *EGFR*-mutant advanced NSCLC

Sunday, Sep 8 11:07-11:17am
(OA02.05; Lee)

PAPILLON

High-risk biomarker subpopulations from patients with *EGFR* Ex20ins in PAPILLON

Tuesday, Sep 10 1:50-1:55pm
(MA12.06; Goldman)

PALOMA-3

Subcutaneous vs intravenous amivantamab: patient satisfaction and resource utilization results

Monday, Sep 9 11:07-11:17am
(OA09.05; Alexander)

SKIPPirr

Preventing infusion-related reactions with intravenous amivantamab: primary results

Tuesday, Sep 10 2:00-2:05pm
(MA12.08; Lopes)

EGFR esisters

Development of a **patient-friendly lung cancer lexicon**:
Sunday, Sep 8 6:15-7:45pm
(P2.16F.03; Feldman)

Poster tour: Monday, Sep 9 6:45-6:53pm

Additional posters:

- **COCOON TiP:** Enhanced vs standard dermatologic management with amivantamab + lazertinib in advanced NSCLC**:**
  Monday, Sep 9 12:00-2:00pm (P3.12D.04; Cho)
- **PolyDamas TiP:** Amivantamab + cetrelimab in advanced NSCLC:
  Virtual ePoster (EP.12H.02; Voon)

Disclosures

JK Sabari: served in a consulting or advisory role for AstraZeneca, Genentech, Janssen, Pfizer, Regeneron, Sanofi Genzyme, Takeda, and Mirati Therapeutics. **HA Yu:** served in a consulting or advisory role for AbbVie, Amgen, AstraZeneca, Black Diamond, Blueprint Medicines, Cullinan, Daiichi Sankyo, Janssen, Takeda, and Taiho. **P Mahadevia, Y Liu, L Demirdjian, YH Chen,** and **X Wang:** are employees of Janssen and may hold stock in Johnson & Johnson. **A Passaro:** served in a consulting or advisory role for AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo Europe GmbH, Johnson & Johnson/Janssen, MSD Oncology, Novartis, Pfizer, and Roche/Genentech; and participated in speakers bureaus for AstraZeneca, Boehringer Ingelheim, Daiichi Sankyo Europe GmbH, Johnson & Johnson/Janssen, and MSD Oncology.

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