Real-world clinical outcomes among patients with EGFR-mutated (Ex19del/L858R) metastatic NSCLC treated at City of Hope with osimertinib monotherapy by TP53 alteration status

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Key Takeaway

Among patients with EGFRm (Ex19del/L858R) metastatic NSCLC receiving osimertinib monotherapy as their first observed treatment, patients with *TP53* alterations had numerically higher discontinuation due to progression or death, and shorter OS relative to those without *TP53* alterations; median OS in the subgroup of *TP53* alterations (26.2 months) was consistent with other real world studies (25.7 months)[13]

Conclusions

Median OS in the overall cohort of patients with EGFRm (Ex19del/L858R) metastatic NSCLC receiving osimertinib monotherapy as their first observed treatment was numerically shorter than that found in clinical trial data (FLAURA: 38.6 months),[14] but in line with other real-world studies (Spira et al: 29.8 months; Sabari et al: 28.6 months)[13,15]

Overall, median TTD (15.1 months) was descriptively shorter than TTD reported in clinical trial data (FLAURA: 20.8 months)[5] but similar to that observed in real-world studies (Spira et al, 15.9 months)[15]. Median TTNT was 16.2 months, and was similar to median TTNT observed in real-world studies (Spira et al, 17.6 months)[15]

Median TTD and TTNT were similar across *TP53* alteration status; however, patients with TP53 alterations relative to those without had numerically higher rates of discontinuation due to progression or death, highlighting the need for more effective therapies in patients with *TP53* co-alterations

Due to data availability at the time of this study, this study focused on patients receiving osimertinib monotherapy as their first observed therapy; however, newer first-line combination regimens have since demonstrated improved outcomes over osimertinib monotherapy, including in high-risk subgroups such as patients with *TP53* co-mutations,[6,7,11] warranting future real-world studies

Acknowledgements

This study was sponsored by Johnson & Johnson.

Disclosures

P. Vadagam is an employee of Johnson & Johnson. L. Morrison and B. Emond are employees of Analysis Group, Inc., a consulting company that has provided paid consulting services to Johnson & Johnson, which funded the development and conduct of this study. S. Gruber and C.M. Lovly are employees of City of Hope. S. Gruber has served in a consulting or advisory role for Genetech and reports research funding from AbbVie. Over the past 24 months, C.M. Lovly has been a consultant for and received honoraria from: AbbVie, Amgen, AriHeart, Astra Zeneca, Black Diamond, BMS, Boehringer Ingelheim, Daiichi Sankyo, Exact, Foresight, Foundation Medicine, Guardant, Genentech, Gilead, Guardant, Immunity Bio, Jazz, JNJ, Merck, Nuvalent, Nuvation, Onviv, Pfizer, Regeneron, Summit, Takeda, Taiho, Tempus.

Background

- Approximately ~15% of patients with non-small cell lung cancer (NSCLC) are reported to have epidermal growth factor receptor mutations (EGFRm),[1] with exon 19 deletions (Ex19del) and exon 21 L858R substitutions (L858R) comprising 85-90%[2]
- For patients with advanced NSCLC and EGFR mutations treated with tyrosine kinase inhibitors (TKIs), the 5-year survival rate is below 20%[3,4]
- Osimertinib monotherapy is one of the first-line (1L) treatment options,[5] while more effective combination regimens are recently approved based on Phase 3 trials confirming superior efficacy[6,7]
- *TP53* co-alterations occur in ~50% of EGFRm NSCLC[8] and have been associated with more aggressive disease and less favorable outcomes with EGFR TKI therapy;[9,10] in a meta-analysis of 24 studies, concurrent *TP53* mutations were associated with shorter progression free survival (hazard ratio [HR], 1.51) and overall survival (HR, 1.64) versus *TP53* wild-type[9]
- Further real-world studies are needed to evaluate clinical outcomes among patients with EGFRm (Ex19del/L858R) metastatic NSCLC receiving osimertinib monotherapy, particularly those with *TP53* co-alterations

Objective

- To describe clinical outcomes among patients with EGFRm (Ex19del/L858R) metastatic NSCLC receiving osimertinib monotherapy as their first treatment at City of Hope, stratified by *TP53* alteration status

Methods

Data source

- Electronic medical records (EMR) data from City of Hope were used (1/1/2018–12/31/2025).
- City of Hope is a National Cancer Institute-designated Comprehensive Cancer Center comprised of a national system of hospitals and treatment centers
- EMR data captures patient demographic and clinical characteristics, genomic profiling data, diagnoses, physician orders and drug administrations, and laboratory results
- Data were de-identified and complied with the patient health information requirements of the Health Insurance Portability and Accountability Act (HIPAA)

Study design and study population

- A descriptive retrospective cohort study design was used
- Adults with EGFRm (Ex19del/L858R) metastatic NSCLC initiating osimertinib monotherapy as their first observed treatment at City of Hope were descriptively analyzed
- The index date was defined as the date of initiation of osimertinib monotherapy for EGFRm (Ex19del/L858R) NSCLC
- Patient demographic and clinical characteristics, including biomarker status, prior and up to the index date (baseline period) were described
- The follow-up period was defined as the time from the index date until the earliest of patient's last visit or death

Study measures and statistical analysis

- Time to discontinuation (TTD), time to next treatment (TTNT), and overall survival (OS), as provided by City of Hope, were evaluated from osimertinib monotherapy initiation using Kaplan-Meier analyses, stratified by *TP53* alteration status
  - TTD was defined as the time from the initiation of the line of therapy to the end of the line of therapy; TTNT was defined as the time from the initiation of the line of therapy to the initiation of the next line of therapy; OS was defined as the time from the initiation of the line of therapy to the date of death
  - Patients without discontinuation, a subsequent line of therapy, or date of death were censored at the end of the follow-up period

Results

Study sample and baseline characteristics

- Among 108 patients initiating osimertinib monotherapy as their first treatment at City of Hope, the median age was 65.5 years, 63.9% (n=69) were female, 55.6% (n=60) were Asian and the median follow-up was 27.5 months (**Table 1**)
- Overall, 52.8% (n=57) had bone metastases, and 36.1% (n=39) had central nervous system metastases before the initiation of osimertinib monotherapy
- The median time from diagnosis of NSCLC to initiation of 1L therapy was 1.3 months
- Of 59 patients (54.6%) with co-alteration testing prior to initiation of osimertinib monotherapy, *TP53* alterations (of any type) were detected in 66.1% (n=39); patients with *TP53* alterations (n=39) relative to patients without *TP53* alterations (n=69) were slightly older (median age: 68.0 years; 63.0 years) and a higher proportion were female (71.8%; 59.4%), respectively

Table 1: Patient characteristics

	All patients N=108	TP53-altered N=39	Non TP53-altered N=69
Demographic characteristics			
Age at index date (years), mean ± SD [median]	**64.2 ± 11.7 [65.5]**	**66.8 ± 11.4 [68.0]**	**62.7 ± 11.6 [63.0]**
>30 to ≤60	36 (33.3)	9 (23.1)	27 (39.1)
>60 to ≤70, n (%)	36 (33.3)	13 (33.3)	23 (33.3)
>70 to ≤85, n (%)	35 (32.4)	17 (43.6)	18 (26.1)
>85, n (%)	1 (0.9)	0 (0.0)	1 (1.4)
Female, n (%)	**69 (63.9)**	**28 (71.8)**	**41 (59.4)**
Race, n (%)			
Asian	60 (55.6)	20 (51.3)	40 (58.0)
White	42 (38.9)	16 (41.0)	26 (37.7)
Unknown	6 (5.6)	3 (7.7)	3 (4.3)
Ethnicity, n (%)			
Hispanic or Latino	93 (86.1)	33 (84.6)	60 (87.0)
Not Hispanic or Latino	14 (13.0)	5 (12.8)	9 (13.0)
Unknown	1 (0.9)	1 (2.6)	0 (0.0)
Clinical characteristics			
EGFR variant type[1]			
Exon 19 deletion	55 (50.9)	20 (51.3)	35 (50.7)
L858R mutation	54 (50.0)	20 (51.3)	34 (49.3)
ECOG score, n (%)			
0	33 (30.6)	13 (33.3)	20 (29.0)
1	32 (29.6)	9 (23.1)	23 (33.3)
2	5 (4.6)	1 (2.6)	4 (5.8)
3	1 (0.9)	1 (2.6)	0 (0.0)
4	0 (0.0)	0 (0.0)	0 (0.0)
Missing	37 (34.3)	15 (38.5)	22 (31.9)
Quan-CCI, mean ± SD [median]	**8.7 ± 1.9 [8.0]**	**8.6 ± 2.0 [8.0]**	**8.7 ± 1.9 [8.0]**
Cancer stage at initial diagnosis of NSCLC, n (%)			
Localized NSCLC (Stage 0–IIB)	1 (0.9)	0 (0.0)	1 (1.4)
Locally advanced NSCLC (Stage IIIA–IIIC)	2 (1.9)	2 (5.1)	0 (0.0)
Metastatic NSCLC (Stage IV–IVB)	102 (94.4)	34 (87.2)	68 (98.6)
Unknown	3 (2.8)	3 (7.7)	0 (0.0)
LC-related characteristics			
Time from metastatic NSCLC diagnosis to initiation of first observed therapy (months), mean ± SD [median]	**2.1 ± 2.7 [1.3]**	**2.1 ± 2.5 [1.4]**	**2.0 ± 2.9 [1.3]**
Metastatic sites[1], n (%)	**108 (100.0)**	**39 (100.0)**	**69 (100.0)**
Bone	57 (52.8)	19 (48.7)	38 (55.1)
Central nervous system	39 (36.1)	9 (23.1)	30 (43.5)
Liver	18 (16.7)	7 (17.9)	11 (15.9)
Other	72 (66.7)	27 (69.2)	45 (65.2)

Abbreviations: CCI: Charlson Comorbidity Index; ECOG: Eastern Cooperative Oncology Group; EGFR: epidermal growth factor receptor; LC: lung cancer; NSCLC: non-small cell lung cancer; SD: standard deviation.
Notes:
1. Categories were not mutually exclusive.

Treatment patterns

- Among patients receiving osimertinib monotherapy as their first treatment, 94.4% (n=102) discontinued osimertinib, primarily due to progression (70.6%; n=72) (**Table 2**)
- Patients with *TP53* alterations relative to those without *TP53* alterations had numerically higher rates of discontinuation due to progression (76.3%; 67.2%) and death (7.9%; 4.7%), respectively

Table 2: Treatment patterns

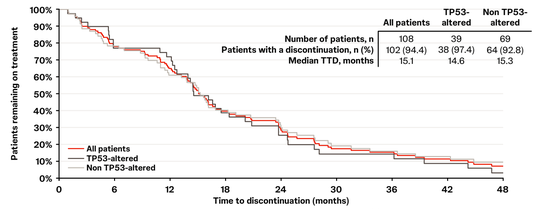
	All patients N=108	TP53-altered N=39	Non TP53-altered N=69
Length of observation period (months)[1], mean ± SD [median]	31.2 ± 17.6 [27.5]	28.9 ± 14.6 [25.8]	32.6 ± 19.0 [28.4]
Patients with treatment discontinuation, n (%)	102 (94.4)	38 (97.4)	64 (92.8)
Duration of line of therapy[2] (months)	**19.8 ± 16.6 [15.5]**	**18.8 ± 14.2 [16.2]**	**20.4 ± 17.9 [15.3]**
≥ 0 to ≤ 12	38 (35.2)	11 (28.2)	27 (39.1)
> 12 to ≤ 24	39 (36.1)	18 (46.2)	21 (30.4)
>24	25 (24.5)	9 (23.7)	16 (25.0)
Duration of treatment-free interval[3] (months)	**0.7 ± 2.6 [0.0]**	**0.8 ± 3.5 [0.0]**	**0.6 ± 1.8 [0.0]**
> 0 to ≤ 1	88 (81.5)	35 (89.7)	53 (76.8)
> 1 to ≤ 3	8 (7.4)	2 (5.1)	6 (8.7)
>3	6 (5.6)	1 (2.6)	5 (7.2)
Reason for discontinuation			
Progression	72 (70.6)	29 (76.3)	43 (67.2)
Death	6 (5.9)	3 (7.9)	3 (4.7)
Toxicity	7 (6.9)	2 (5.3)	5 (7.8)
Completed treatment	3 (2.9)	1 (2.6)	2 (3.1)
Other[4]	14 (13.7)	3 (7.9)	11 (17.2)
Patients without treatment discontinuation	6 (5.6)	1 (2.6)	5 (7.2)
Patients with a next line of therapy	91 (84.3)	33 (84.6)	58 (84.1)

Abbreviations: SD: standard deviation.
Notes:
1. The length of observation period was evaluated from the start of the current line of therapy until death or last date of visit, whichever occurred first.
2. The duration of the line of therapy was defined as the time from the start of the line of therapy to the day before the initiation of the next line (or the end of the observation period for patients without a subsequent line).
3. Duration of treatment-free interval was defined as the time between the end of the current line of therapy (or the end of the observation period for patients with an ongoing line of therapy) and the start of the subsequent line of therapy (or the end of the observation period for patients without a subsequent line).
4. Other reason for discontinuation included molecular findings, patient preference, financial/insurance reasons, held for surgery, and other.

TTD, TTNT, and OS

- Median TTD was 15.1 months, TTNT was 16.1 months, and OS was 29.1 months among patients receiving osimertinib monotherapy as first observed treatment (**Figure 1A, 1B, 1C**)
- Patients with *TP53* alterations had similar median TTD relative to patients without *TP53* alterations (14.6 months; 15.3 months); median TTNT was also comparable (16.8 months; 15.9 months), respectively
- Median OS was descriptively shorter for patients with *TP53* alterations compared to those without *TP53* alterations (26.2 months; 30.4 months), respectively

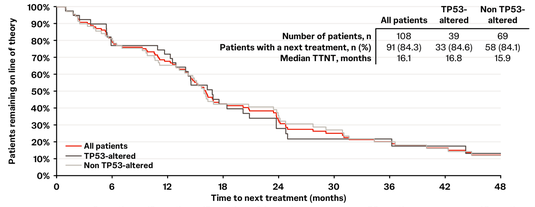
Figure 1A: Kaplan-Meier curves for time to treatment discontinuation



Patients at risk, n (%)	6 months	12 months	18 months	24 months	36 months	48 months
All patients	84 (77.8)	70 (64.8)	42 (38.9)	30 (27.8)	15 (13.9)	6 (5.6)
TP53-altered	30 (76.9)	28 (71.8)	15 (38.5)	9 (23.1)	5 (12.8)	1 (2.6)
Non TP53-altered	54 (78.3)	42 (60.9)	27 (39.1)	21 (30.4)	10 (14.5)	5 (7.3)
Kaplan-Meier rates (%)						
All patients	77.8	64.8	39.5	28.0	15.1	6.8
TP53-altered	76.9	71.8	38.5	25.2	14.0	2.8
Non TP53-altered	78.3	60.9	40.1	29.7	15.7	9.2

Abbreviations: TTD: time to discontinuation.

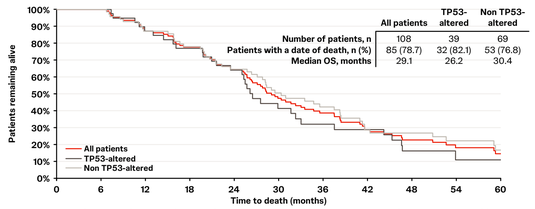
Figure 1B: Kaplan-Meier curves for time to next treatment



Patients at risk, n (%)	6 months	12 months	18 months	24 months	36 months	48 months
All patients	86 (79.6)	72 (66.7)	42 (38.9)	30 (27.8)	16 (14.8)	7 (6.5)
TP53-altered	30 (76.9)	28 (71.8)	15 (38.5)	9 (23.1)	5 (12.8)	2 (5.1)
Non TP53-altered	56 (81.2)	44 (63.8)	27 (39.1)	21 (30.4)	10 (15.9)	5 (7.3)
Kaplan-Meier rates (%)						
All patients	79.6	67.6	42.2	32.6	19.8	11.9
TP53-altered	76.9	71.8	42.2	27.6	21.5	12.9
Non TP53-altered	81.2	65.2	42.1	35.4	19.6	11.6

Abbreviations: TTNT: time to next treatment.

Figure 1C: Kaplan-Meier curves for overall survival



Patients at risk, n (%)	6 months	12 months	18 months	24 months	36 months	48 months	60 months
All patients	108 (100.0)	94 (87.0)	82 (75.9)	66 (61.1)	35 (32.4)	17 (15.7)	7 (6.5)
TP53-altered	39 (100.0)	34 (87.2)	30 (76.9)	23 (59.0)	10 (25.6)	4 (10.3)	1 (2.6)
Non TP53-altered	69 (100.0)	60 (87.0)	52 (75.4)	43 (62.3)	25 (36.2)	13 (18.8)	6 (8.7)
Kaplan-Meier rates (%)							
All patients	100.0	87.0	77.6	64.3	38.5	22.5	14.3
TP53-altered	100.0	87.2	76.9	64.0	31.8	15.9	10.6
Non TP53-altered	100.0	87.0	78.0	64.5	42.1	26.5	16.4

Abbreviations: OS: overall survival.

Limitations

- Since the data were limited to data collected by City of Hope, the first observed regimen used for treatment of EGFRm (Ex19del/L858R) NSCLC may not reflect actual 1L therapy if patients received prior treatment outside the practice
- The TP53-altered subgroup included patients with any *TP53* alteration and was not restricted to loss-of-function mutations (for which there was limited information available), which may be associated with a poorer prognosis[12]
- Furthermore, the subgroup of patients without *TP53* alterations included both patients who were tested and confirmed to not have *TP53* alterations (n=20) and those who were not tested (n=49)
- Due to the descriptive nature of the study, results were not adjusted for potential confounders, such as age, sex, race, ECOG score, and Quan-CCI
- Given the nature of structured EMR data, inaccuracies and misclassification may arise due to coding errors and missing data

References

1. Melosky B, et al. *Mol Diagn Ther*. 2022;26(1):7-18. 2. Vyse S, et al. *Signal transduction and targeted therapy*. 2019;4(1):5. 3. Lin JJ, et al. *J Thorac Oncol*. 2016;11(4):556-565. 4. SEER Cancer Statistics Review, 1975-2016. National Cancer Institute 2018. 5. Soria J-C, et al. *New England Journal of Medicine*. 2018;378(2):113-125. 6. Planchard D, et al. *New England Journal of Medicine*. 2023;389(21):1935-1948. 7. Cho BC, et al. *New England Journal of Medicine*. 2024;391(16):1486-1498. 8. Sun F, et al. *Lung Cancer*. 2025;208:108747. 9. Lan B, et al. *Oncol Lett*. 2022;24(5):384. 10. Le X, et al. *Cancers*. December 12, 2022;14(24):6127. 11. Felip E, et al. *Annals of Oncology*. 2024;35(9):805-816. 12. Zhang Z, et al. *MedComm*. 2024;5(6):e588. 13. Sabari JK, et al. *Journal of Thoracic Oncology*. 2025;20(9):1268-1278. 14. Ramalingam SS, et al. *New England Journal of Medicine*. 2020;382(1):41-50. 15. Spira AI, et al. *Advances in Therapy*. 2025:1-15.

Lung Cancer

Presented at the 2026 ASCO Quality Care Symposium, Boston, MA, USA, October 16-17, 2026

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