Real-World Outcomes among Advanced EGFRm NSCLC Patients after Osimertinib and Platinum-Based Chemotherapy: An Update to a Natural History Study with an Extended Dataset

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PURPOSE

- This study utilizes an extended, real-world electronic health record dataset to expand upon a previous natural history study evaluating clinical outcomes among mNSCLC patients who received prior treatment with osimertinib and PBC.[6]

DISCUSSION

- Sample size in this study increased by 42% compared to the previous analysis (from 126 to 179 patients included; baseline characteristics were consistent) and follow-up was extended by 2 months. [5,6]
- Progression-free survival and overall survival, and response to treatment were poor in this study of patients with EGFRm mNSCLC after failure of osimertinib and PBC, as observed in prior findings. [5,6]
- In the PS-weighted cohort, median rwPFS was 3.5 months (95% CI: 2.7, 4.6), compared to 4.2 (95% CI: 2.8, 5.2) in the previous study, and median rwOS was 9.1 months (95% CI: 7.3, 11.3), consistent with the previous study (9.1; 95% CI: 7.4, 11.4).
- Response to index LOTs was poor in the PS-weighted exploratory matched cohort with an rwORR of 12.7% (95% CI: 4.8%, 25.7%) compared to 14.1% (95% CI: 3.7%, 33.1%) previously.
- This study complements previous real-world findings with better statistical precision, which help support the contextualization HER3-DXd investigational treatment trial findings.

CONCLUSION

- Leveraging an extended dataset with increased sample size, the findings from this study further confirm the limited clinical benefit of currently available therapies for patients with EGFRm mNSCLC after failing osimertinib and PBC. Suboptimal outcomes in this patient population demonstrate a need for effective treatment options.

BACKGROUND

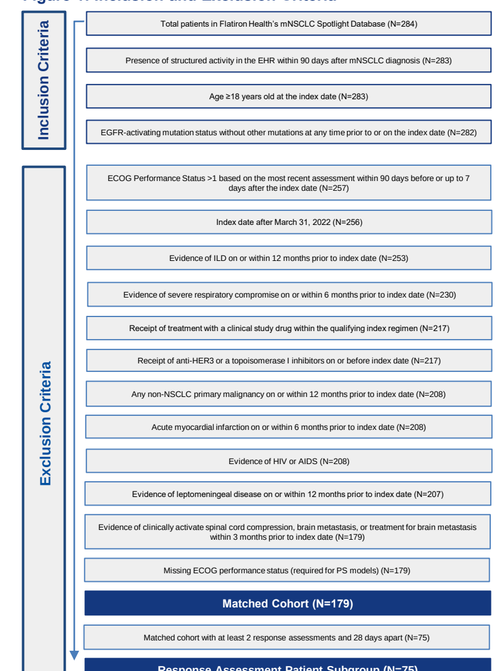
- Osimertinib, a third generation EGFR tyrosine kinase inhibitor, has emerged as standard of care for the treatment of EGFR-mutated (EGFRm) metastatic non-small cell lung cancer (mNSCLC).[1] When disease progresses, treatment options beyond osimertinib and platinum-based chemotherapy (PBC) are limited.[2]
- Ongoing clinical trials are assessing novel treatment options in this setting, including HERTHENA-Lung01 (HL-01) a multinational single-arm phase II trial evaluating the safety and efficacy of patritumab deruxtecan (HER3-DXd).[3,4]
- Data on clinical outcomes has been limited for patients with EGFRm mNSCLC after failure of osimertinib and PBC. A recent natural history study (NHS) was conducted to fill this gap. The study demonstrated poor clinical outcomes among this patient population.[5,6] The present study is an update from this prior NHS using an expanded real-world dataset with a later data cutoff of July 2023.

METHODS

- This study used the nationwide Flatiron Health electronic health record (EHR)-derived de-identified database from approximately 280 US cancer clinics (~800 sites of care).[7]
- The index date was defined as the date of initiation of a new line of therapy (LOT) after osimertinib and PBC, on or prior to 31 July 2022. Selection criteria were adapted from the HL-01 study.[3,4]
- Two cohorts of interest were defined: 1) the matched cohort and 2) the response assessment patient subgroup, using the same definitions as in the previous NHS.[6] (**Figure 1**)
- Propensity score (PS) weighting was used to ensure a similar distribution of baseline characteristics for both cohorts, as compared to HL-01 patients. Nine prespecified covariates (age, sex, race, smoking, ECOG score, prior LOTs, prior immunotherapy, liver metastases, and history of brain metastases) were used for PS weighting. Effective sample size (ESS) was estimated and reported.
- Outcomes included: 1) real-world overall survival (rwOS; the time from index date to death); 2) real-world progression-free survival (rwPFS; defined as the time from index date to disease progression or death); and 3) confirmed real-world objective response rate (confirmed rwORR, defined as the proportion with confirmed partial or complete response among those with ≥2 response assessments ≥28 days apart) and assessed in the response assessment subgroup.
- Kaplan-Meier methods were used to evaluate time-to-event outcomes (rwPFS, rwOS). Confirmed rwORR was estimated as proportions with Clopper-Pearson exact 95% confidence intervals (CIs).

RESULTS

Figure 1: Inclusion and Exclusion Criteria



- Of 284 total patients with EGFRm mNSCLC previously treated with osimertinib and PBC in the real-world database, 179 patients met the inclusion criteria for the matched cohort. (**Figure 1**)
- Of these 179 patients, 75 had evidence of at least 2 response assessments spaced at least 28 days. (**Figure 1**)
- The reference and response assessment groups had a median follow-up of 9.0 and 13.5 months, respectively, compared to 7.3 and 9.2 months in the prior NHS.
- In the matched cohort before weighting, the median (IQR) age was 68 (60, 74) years compared to 67 (59,73) in the previous study. The majority of patients were female (65.9%, same as prior study) and White (59.2% compared to 55.6% compared to prior study). More than half (54.8%) had at least 3 previous lines of therapy, compared to 65.1% in the prior study. (**Table 1**)
- In the response assessment cohort before weighting, more than half (61.4%) had at least 3 previous lines of therapy, compared to 59.7% in the prior study. (**Table 1**)

Table 1: Baseline Demographics and Clinical Characteristics

Characteristic	HL-01 Trial (N=225)	Matched Cohort		Response Assessment Patient Subgroup	
		Before PS Weighting (N=179)	After PS Weighting (ESS=97)	Before PS Weighting (N=75)	After PS Weighting (ESS=41)
Demographic Characteristics					
Mean age at start of index LOT, years (SD)	63 (--)	66.4 (9.8)	62.5 (11.5)	66.1 (9.8)	61.4 (17.4)
Gender, %					
Female	58.9	65.9	61.6	65.3	67.2
Male	41.1	34.1	38.4	34.7	32.8
Race, %					
Asian	45.9	19.0	33.2	28.0	49.5
Black or African American	1.4	8.9	13.6	4.0	4.9
White	41.1	59.2	37.9	58.7	37.2
Other	11.5	5.6	8.0	5.3	5.2
Unknown	–	7.3	7.3	4.0	3.2
Ethnicity, %					
Hispanic or Latino	–	5.6	6.9	1.3	0.8
Not Hispanic or Latino	–	78.2	76.2	88.0	85.6
Unknown	–	16.2	17.0	10.7	13.6
Practice Type, %					
Academic	–	14.5	23.1	14.7	27.8
Community	–	82.1	75.1	77.3	67.9
Academic, Community	–	3.4	1.8	8.0	4.3
Clinical Characteristics					
Median BMI, kg/m2 (IQR)	–	24.4 (21.1, 28.4)	24.1 (20.5, 28.3)	24.8 (21.5, 28.3)	24.1 (21.4, 27.3)
Mean Charlson Comorbidity Index, mean (SD)	–	1.0 (1.3)	0.9 (1.3)	0.9 (1.1)	0.8 (1.8)
Charlson Comorbidity Index Group, %					
0	–	49.7	51.0	49.3	56.9
1-2	–	36.9	37.2	36.0	30.5
3+	–	13.4	11.8	14.7	12.6
ECOG at index, %					
0	32.1	38.5	32.0	41.3	33.1
1	66.5	61.5	68.0	58.7	66.9
Median number of prior lines of therapy, n (IQR)	3 (1, 11)	3 (2, 4)	3 (2, 4)	3 (2, 4)	3 (2, 4)
Number of prior lines of therapy, %					
≤2	25.4	45.3	29.2	38.7	30.4
3	–	28.5	28.2	30.7	25.9
4+	–	26.3	42.6	30.7	43.6
Median time from aNSCLC diagnosis to index date, months (IQR)	–	28.8 (17.8, 42.6)	35.6 (24.5, 47.6)	30.8 (15.2, 42.8)	35.6 (25.6, 52.4)

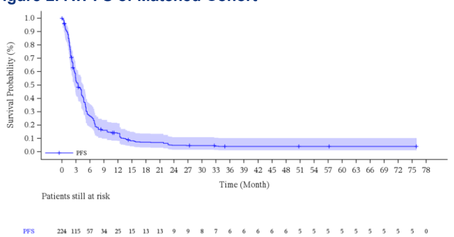
- Following PS weighting the 9 covariates in the matched cohort were balanced (standardized mean differences for each of 9 variables <0.2). For the response assessment subgroup, sex was removed from the PS model to optimize covariate balance.

Table 2. Confirmed rwORR of Response Assessment Cohort

	N/ESS*	Confirmed rwORR (95% CI)
Before PS weighting	75	18.7% (10.6%, 29.3%)
After PS weighting	41	12.7% (4.8%, 25.7%)

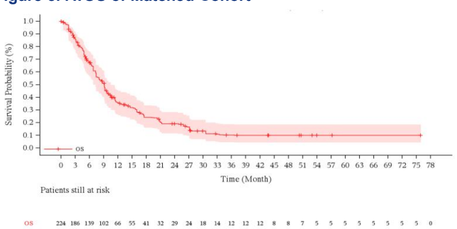
* N refers to the number of patients before PS weighting. ESS refers to the equivalent number of patients after applying PS weighting (the number of independent unweighted observations that achieve the same precision (or variance) as the weighted sample)

Figure 2. rwPFS of Matched Cohort



	N/ESS*	Median rwPFS in months (95% CI)
Before PS weighting	179	3.4 (2.9, 4.4)
After PS weighting	97	3.5 (2.7, 4.6)

Figure 3. rwOS of Matched Cohort



	N/ESS*	Median rwOS in months (95% CI)
Before PS weighting	179	9.9 (8.5, 12.1)
After PS weighting	97	9.1 (7.3, 11.3)

- Among the 75 eligible patients in the response assessment matched cohort, the confirmed rwORR after PS weighting was 12.7% (95% CI: 4.8%, 25.7%). (**Table 2**)
- Among the 179 eligible patients in the matched cohort, the median rwPFS and rwOS were 3.5 (95% CI: 2.7, 4.6) and 9.1 (95% CI: 7.3, 11.3) months, respectively, after PS weighting (**Figure 2 & 3**). The probability of surviving without progression or death, and without death at 12 months was 13.9% and 35.9%, respectively.

References

1. Wu L, Ke L, Zhang Z, Yu J, Meng X. Development of EGFR TKIs and Options to Manage Resistance of Third-Generation EGFR TKI Osimertinib: Conventional Ways and Immune Checkpoint Inhibitors. Front Oncol. 2020;10:602762. doi:10.3389/fonc.2020.602762
2. NCCN. Non-Small Cell Lung Cancer (Version 3.2023). 2023https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf
3. NCT04619004. HERTHENA-Lung01: Patritumab Deruxtecan in Subjects With Metastatic or Locally Advanced EGFR-mutated Non-Small Cell Lung Cancer. 2020. https://clinicaltrials.gov/ct2/show/NCT04619004
4. Helena A. Yu et al.,HERTHENA-Lung01, a Phase II Trial of Patritumab Deruxtecan (HER3-DXd) in Epidermal Growth Factor Receptor–Mutated Non–Small-Cell Lung Cancer After Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor Therapy and Platinum-Based Chemotherapy. JCO. 2023;41:5363-5375. doi:10.1200/JCO.23.01476
5. Patel JD, Meng J, Phani S, et al. Abstract 6754: Clinical characteristics, real-world treatment patterns, and clinical outcomes among patients with previously treated metastatic or unresectable EGFR-mutated non-small cell lung cancer in the United States. Cancer Research. 2023;83(7_Supplement):6754-6754. doi:10.1158/1538-7445.Am2023-6754
6. Patel, J., Meng, J., Le, H. *et al.* Real-World Treatment Patterns and Clinical Outcomes Among Patients with Metastatic or Unresectable *EGFR*-Mutated Non-Small Cell Lung Cancer Previously Treated with Osimertinib and Platinum-Based Chemotherapy. Adv Ther. 2024;41:3299-33115; doi:10.1007/s12325-024-02936-4
7. Ma X, Long L, Moon S, Adamson BJS, Baxi SS. Comparison of Population Characteristics in Real-World Clinical Oncology Databases in the US: Flatiron Health, SEER, and NPCR. medRxiv. 2023:2020.03.16.20037143. doi:10.1101/2020.03.16.20037143

Acknowledgements and Disclosures

This study was funded by Daiichi Sankyo Inc. Medical writing assistance was provided by Kate Gilpin, an employee of Aetion.