1182P - US real-world (RW) patient characteristics with *MET*ex14 skipping advanced non-small cell lung cancer (aNSCLC)

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CONCLUSIONS

- **Real-world patient demographics and clinical characteristics of the Flatiron cohort confirm patients with *MET*ex14 skipping as a distinct population compared to patients with unselected aNSCLC; older, independent of smoking history, with predominantly non-squamous histology, exclusive of *KRAS*, *ROS-1* or *BRAF* mutations, and low TMB**
- **Analyses indicate a need for routine testing practices to identify patients prior to treatment with systemic therapy, since targeted MET-TKIs are now available for use**
  - ***MET*ex14 skipping should be included in standard molecular genetic diagnostic testing in aNSCLC**

LIMITATIONS

- The analyses did not include any statistical comparisons between groups, so no results regarding significant differences have been reported
- The data source used to analyze real-world patient outcomes was a convenience sample drawn from cancer centers in the Flatiron network and cannot be assumed to be representative of the population of patients with aNSCLC who have *MET*ex14 skipping in the US
  - It should be noted that the real-world setting observed in this study may not be applicable to other countries
- Baseline characteristics, such as BMI, may be outdated at the index date
  - The Flatiron data extract used for this study included patients who started their aNSCLC treatment before meeting other study inclusion criteria; hence, the analyses are subject to immortal time bias
- Other limitations include low frequency of testing for *MET*ex14 skipping in early patient data from 2011 onwards, and multiple changes in the standard of care treatment of aNSCLC during the period that data for this study were collected

INTRODUCTION

- Lung cancer is a leading cause of cancer-related death in the US, accounting for an estimated 21.4% of all cancer deaths in 2022;[1] NSCLC accounts for approximately 80–85% of all lung cancers[2,3]
- Approximately 3-4% of patients with NSCLC harbor *MET*ex14 skipping, which has been recognized as an oncogenic driver[4]
- Results from Phase II clinical studies indicate that the MET-TKIs capmatinib (GEOMETRY mono−1; NCT02414139) and tepotinib (VISION; NCT02864992) have confirmed efficacy in lung cancer patients whose tumors harbor *MET*ex14 skipping;[5,6] both drugs have been approved by the US FDA
- Understanding the real-world testing, patient demographics and clinical characteristics is necessary to assess the unmet need in patients with aNSCLC and *MET*ex14 skipping; this study used real-world clinical data to address this research gap
- Here, we evaluated the characteristics of adult patients with *MET*ex14 skipping aNSCLC using real-world data predating the FDA approval of the two TKIs, capmatinib and tepotinib

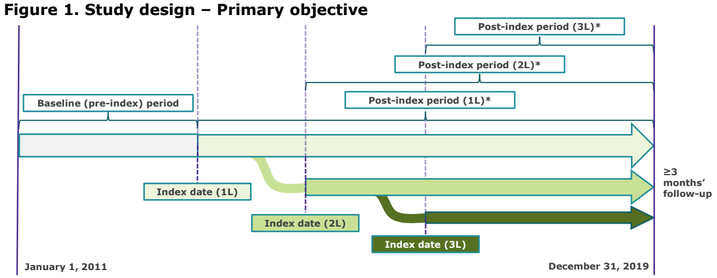
METHODS

- This retrospective cohort study used the electronic health records from de-identified Flatiron Clinical-Genomic Database (CGDB) for patients who were diagnosed with aNSCLC harboring *MET*ex14 skipping and who initiated 1L treatment from Jan 1, 2011 to Sep 30, 2019 with ≥3 months' follow-up (**Figure 1**)
- Exclusion criteria included documentation of *EGFR* mutations or *ALK* rearrangements
- For the 1L cohort, the index date was the start date of the first LOT
  - For the analysis of the 2L subgroup, the index date was the start of the 2L treatment
  - For the brain metastasis subgroup, the index date was the start date of the first LOT initiated after the patient met the inclusion criteria (i.e., received a diagnosis of brain metastasis)

METHODS (CONTINUED)

- The baseline period was defined as any time prior to the index date
  - Patients were followed from the index date to the end of follow-up (the date of last confirmed activity, defined as the latest recorded visit prior to data cut-off for those still living at the end of the study or the date of death)
  - Treatment patterns and clinical outcomes were assessed during this follow-up window
- Descriptive analyses assessed the distribution of sample demographics and clinical characteristics
  - The number and percentage of patients with each of the genomic alterations and the number and percentage of patients who received different treatments by treatment line were reported
- Patient characteristics were categorized by LOT, with 2L as a subset of 1L, and 3L as a subset of 2L
  - Characteristics of patients with brain metastases at index were also analyzed

Figure 1. Study design – Primary objective



*Index-specific post-index periods end at the earliest of the event of interest (defined based on the outcome being analyzed), loss to follow up, death, and data cut-off date (December 31, 2019).

RESULTS

- A total of 108 patients from the Flatiron database who had at least 3 months of follow-up, were *MET*ex14 skipping positive, and initiated 1L treatment, were included in this study
  - 57 were recorded as having proceeded to 2L therapy; 26 patients proceeded to 3L therapy
- The median age at 1L index was 75 years (range 46–85), 54.6% were female, 63.0% patients had a history of smoking, and most had Stage IIIB–IV cancer at initial diagnosis (73.1%); 7.4% had squamous cell carcinoma (**Table 1, S1; Figure S1, 2**)
  - 75.9% had an index date of 2016–2019 (**Figure S1; Table S1**)
- Baseline characteristics of patients who received treatment in 2L were similar to the overall population

Table 1. Baseline demographic characteristics, overall Flatiron cohort, by LOT

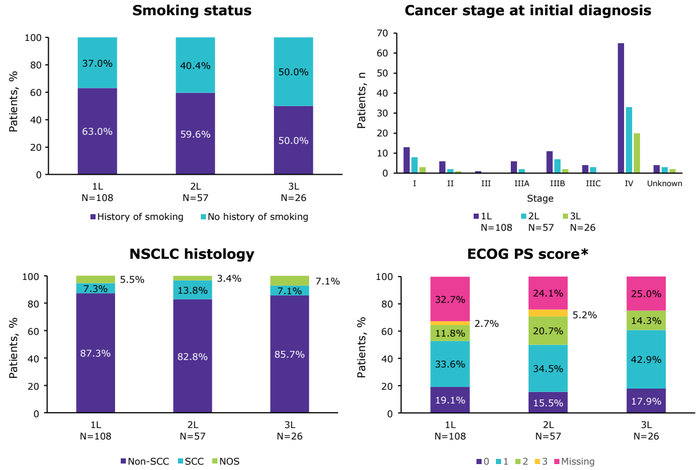
Baseline characteristics		1L (N=108)	2L (N=57)	1L Brain metastasis subgroup (N=23)
Age, years	Median (range)	75 (46–85)	73 (46–85)	72 (48–85)
	Mean (SD)	73.1 (8.3)	72.2 (8.8)	72.4 (8.5)
Sex, n (%)	Male	49 (45.4)	23 (40.4)	10 (43.5)
	Female	59 (54.6)	34 (59.6)	13 (56.5)
Race, n (%)	Asian	3 (2.8)	4 (7.0)	1 (4.3)
	Black	5 (4.6)	2 (3.5)	1 (4.3)
	White	77 (71.3)	39 (68.4)	14 (60.9)
	Other	14 (13.0)	7 (12.3)	3 (13.0)
	Missing	9 (8.3)	5 (8.8)	4 (17.4)
ECOG PS*, n (%)	0	21 (19.4)	9 (15.8)	3 (13.0)
	1	37 (34.3)	20 (35.1)	8 (34.8)
	2	13 (12.0)	11 (19.3)	3 (13.0)
	3	3 (2.8)	3 (5.3)	1 (4.3)
	Missing	34 (31.5)	14 (24.6)	8 (34.8)
Smoking history, n (%)	Yes	68 (63.0)	34 (59.6)	17 (73.9)
	No	40 (37.0)	23 (40.4)	6 (26.1)
Histology, n (%)	Non-squamous cell carcinoma	94 (87.0)	47 (82.5)	22 (95.7)
	SCC	8 (7.4)	8 (14.0)	0
	NOS	6 (5.6)	2 (3.5)	1 (4.3)

*At or within 60 days before the treatment.

RESULTS (CONTINUED)

- 34 patients (31.5%) did not have a recorded ECOG PS at or within 60 days before the index date (**Table 1**)
- Of 89/108 patients with genomic testing prior to 1L, no patients were reported to have *KRAS*, *ROS-1* or *BRAF* mutations (**Table 2**)
  - Of 31 patients with available PD-L1 expression data, 13 (41.9%) had high PD-L1 (≥50%)
  - TMB, assessed in 61 patients, was low (mean [SD]: 6.6 [4.7])
- Of 23 patients with brain metastasis at index (21.3%), median age was 72 years (range 48–85), 56.5% were female, 73.9% had a history of smoking, and 91.3% had Stage IIIB–IV NSCLC at initial diagnosis (**Table 1, S1**)

Figure 2. Baseline clinical characteristics, overall Flatiron cohort, by LOT



*At or within 60 days before index date.

Table 2. Genomic test results prior to start of LOT

Alterations	1L Cohort (N=108)
***KRAS**, n (%)**	
Mutant	0
Wild type	89 (82.4)
Missing	19 (17.6)
***ROS-1**, n (%)**	
Fusion	0
Wild type	89 (82.4)
Missing	19 (17.6)
***BRAF**, n (%)**	
Mutant	0
Wild type	89 (82.4)
Missing	19 (17.6)
PD-L1, n (%)	
Negative (0%)	9 (8.3)
Low positive (1% to 49%)	9 (8.3)
High positive (50% to 100%)	13 (12.0)
Missing	77 (71.3)
TMB status reported	
N	61
Mean (SD)	6.56 (4.66)
Median (range)	5 (1–31)
Interquartile range	4–8

*All patients who received a genomic test who did not have a recorded alteration were categorized as wild type; all patients who did not receive a test were categorized as missing.

Abbreviations: 1L, first line; 2L, second line; 3L, third line; ALK, anaplastic lymphoma kinase; aNSCLC, advanced non-small cell lung cancer; BMI, body mass index; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group Performance tatus; EGFR, epidermal growth factor receptor; LOT, line of therapy; *MET*ex14, *MET* exon 14; NOS, not otherwise specified; NSCLC, non-small cell lung cancer; PD-L1, programmed death-ligand; SCC, squamous cell carcinoma; SD; standard deviation; TMB, tumor mutation burden; TKI, tyrosine kinase inhibitor.

References: 1. National Cancer Institute. 2021. https://seer.cancer.gov/statfacts/html/lungb.html. Accessed 25 July 2022; 2. Travis WD, et al. *J Thorac Oncol*. 2016;11(8):1204–1223; 3. Travis WD, et al. *J Thorac Oncol*. 2015;10(9):1243–1260; 4. Drilon A, et al. *J Thorac Oncol*. 2017;12(1):15–26; 5. Wolf J, et al. *New Engl J Med*. 2020;383(10):944–957; 6. Paik PK, et al. *New Engl J Med*. 2020;383(10):931–943.

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Supplementary materials

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