Real-world analysis of biomarker testing and use of targeted therapies in metastatic non-small cell lung cancer (mNSCLC) in the US

Poster #2552

Michael J Dennis[1], Devin Abrahami[2], Maria Cecilia Vieira[2], Darrin Benjumea[3], Marley Boyd[3], Anran Shao[3], Kirsten Duncan[2], John Kelton[2], Sandip Pravin Patel[4]

[1]Dana Farber Cancer Institute, Boston, MA, USA; [2]Pfizer Inc., New York City, NY, USA; [3]Genesis Research Group, Hoboken, NJ, USA; [4]University of California San Diego, La Jolla, CA, USA

Objective

- To investigate real-world use of biomarker testing, testing characteristics, and associated use of biomarker-informed targeted therapies for EGFR, ALK, ROS1, MET, BRAF, RET, and PD-L1 mutations in US patients diagnosed with metastatic non-small cell lung cancer (mNSCLC).

Background

- Between 1998 and 2022, over 40% of new oncology drugs approved by the US FDA were precision therapies.[1]
- In mNSCLC, detecting biomarkers for targeted therapies (EGFR, ALK, ROS1, BRAF V600E variant, MET exon 14 skipping variant, RET and PD-L1) has become essential for adequate clinical care.[2]

Methods

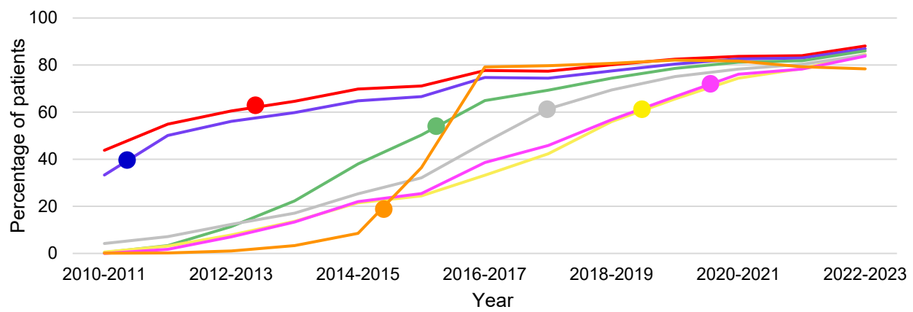
- Adults ≥18 years old with stage IV mNSCLC from the nationwide Flatiron Health electronic health record-derived de-identified database (01/2011 – 04/2023).
- Biomarker characteristics assessed included proportion of patients receiving biomarker tests, timing of test, characteristics of patients, test type (single, multiple or next-generation sequencing [NSG]) and sample type (blood or tissue).
- Proportion of patients receiving guideline recommended, biomarker-informed targeted therapies was assessed from study year of first FDA approval of targeted therapy (**Table 1**).

Table 1: Biomarker-informed therapy definitions

Biomarker	Therapies Included	Date of First FDA Approval
EGFR	**afatinib**, gefitinib, erlotinib, osimertinib, dacomitinib, mobocertinib, amivantamab-vmjw	July 2013
ALK	**crizotinib**, ceritinib, alectinib, brigatinib, lorlatinib	August 2011
ROS1	**crizotinib**, ceritinib, entrectinib	March 2016
MET	**cabmatinib**	May 2020
BRAF	**dabrafenib+trametinib**	July 2015
RET	**pralsetinib**, selpercatinib	September 2020
PD-L1	**pembrolizumab**, cemiplimab, atezolizumab, nivolumab+ipilimumab, tremelimumab+durvalumab	October 2015

Bold represents first FDA approved targeted therapy.

Figure 1: Percentage of patients receiving biomarker testing by year



	EGFR	ALK	ROS1	MET	BRAF	RET	PD-L1
Avg 2011-2023	74.9%	71.6%	54.2%	41.4%	48.8%	42.3%	49.3%
2023	88.7%	87.7%	86.9%	85.7%	85.2%	84.8%	78.7%

Circles represent date of the first FDA approved of a biomarker-informed therapy for each biomarker.

References: **[1]** Suehnholz et al. Cancer Discov, 2024. **[2]** Pennell et al. Am Soc Clin Oncol Educ Book, 2019.

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Table 2: Patient characteristics at metastatic diagnosis among all patients and patients who received ≥1 biomarker test

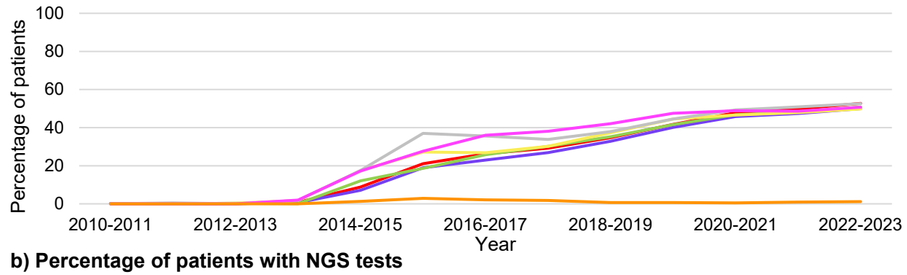
Characteristics	All patients (N=42,037)	Tested patients (N=34,510)
Age, years		
Mean (SD)	67.6 (10.4)	67.4 (10.5)
Sex, %		
Male	51.1	49.4
Female	48.9	50.6
Race, %		
White	66.7	66.8
Black or African American	9.5	9.4
Asian	3.2	3.6
Hispanic / Latino	<0.1	<0.1
Other Race	9.5	9.6
Unknown	10.9	10.5
Practice Type, %		
Academic	20.3	20.2
Community	77.8	77.7
Unknown	1.8	2.1
Insurance Type, %		
Commercial	31.7	33.6
Medicaid	1.9	1.8
Medicare	28.3	28.2
Other / Unknown	38.1	36.4
Smoking Status, %		
History of smoking	83.1	81.7
No history of smoking	16.1	17.9
Unknown	0.8	0.4
Histology, %		
Squamous	19.0	14.2
Non-squamous	76.2	81.7
Not otherwise specified	4.8	4.1

Results

- In 42,037 patients with mNSCLC, 34,510 received ≥1 biomarker test, with proportions varying by biomarker by year (**Figure 1**).
  - Testing rates increased from 2011 through 2023 for each biomarker, with the highest rates in 2023 (**Figure 1**).
- Patients were on average 67.6 years old, evenly split between male and females, with the majority (83.1%) having a history of smoking and non-squamous histology (76.2%) (**Table 2**).
- Median (Q1, Q3) time from mNSCLC diagnosis to first biomarker result was 21 (12, 37) days.
- Tissue was the more common sample type for biomarker testing, although sampling by blood increased in recent years and varied by biomarker (**Figure 2a**).
  - On average, across the entire time period, tissue sampling was the most common form of biomarker testing for the PD-L1 biomarker (98.5%) and was least common for the RET biomarker (60.4%); EGFR: 76.4%, ALK: 73.9%, ROS1: 67.0%, MET: 63.9%, BRAF: 61.0%.
- Multiple testing methods were more common in ALK and PD-L1 (48.1% and 50.3%, respectively) and NGS was more common in the other biomarkers (EGFR: 57.1%, ROS1: 54.0%, MET: 74.1%, BRAF: 77.7%, and RET: 70.7%).
  - NGS testing frequency increased by year **(Figure 2b).**
- Single biomarker tests were common for PD-L1 (49.7%).
- Receipt of biomarker-informed therapies varied by biomarker, in order of increasing frequency: RET+ (23.0%), MET+ (34.0%), BRAF+ (42.7%), PDL1+ (56.3%), ROS1+ (59.8%), EGFR+ (70.6%), and ALK+ (89.0%) and generally increased in recent years (**Figure 3**).

Figure 2: Biomarker testing characteristics by year

a) Percentage of patients with blood sample test



b) Percentage of patients with NGS tests

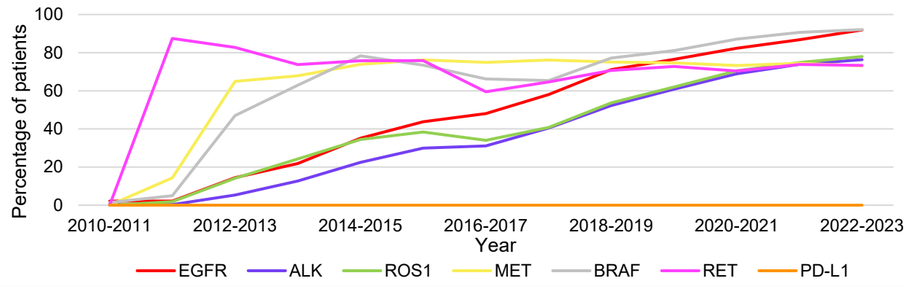
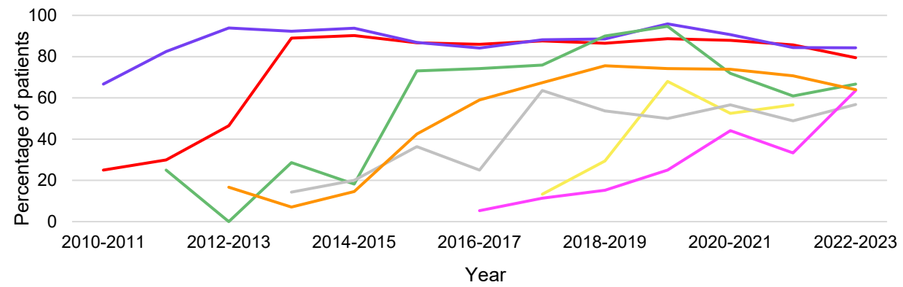


Figure 3: Percentage of patients receiving biomarker-informed therapy in any line by year, starting at year of first FDA approval of targeted therapy



	EGFR	ALK	ROS1	MET	BRAF	RET	PD-L1
Avg 2011-2023	70.6%	89.0%	59.8%	34.0%	42.7%	23.0%	56.3%
2023	79.5%	84.3%	66.7%	56.6%	56.8%	63.6%	64.0%

Conclusions

- Current real-world increasing biomarker testing rates and use of biomarker-informed therapies may be in response to clinical guideline recommendations.
- Despite increased testing, use of biomarker-informed therapy remains low for some biomarkers.
- Further follow through from implementation of robust biomarker testing to use of appropriate therapies is needed to lead to better patient outcomes.

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