Abstract no. 9091 / Poster no. 79 ASCO 2023

RET testing and treatment patterns among aNSCLC patients in US clinical practice

Eunice Kim,[1] Jesse Sussell,[1] Carmen Ng,[1] Justin Nedzesky,[1,2] Qing Zhang,[1] Celina Ngiam,[1] Aaron S. Mansfield[3]

BACKGROUND

- Targeting oncogenic driver alterations, such as ***RET***, has proven to be an effective clinical approach across various tumor types, including advanced non-small cell lung cancer (aNSCLC).[1,2]
- **Biomarker testing** is important and commonly recommended for patients with aNSCLC before commencing first-line treatment to ensure the most appropriate targeted therapy is selected.[3]
- This retrospective cohort study characterized *RET* testing and treatment patterns among aNSCLC patients in US clinical practice.

METHODS

- The **Flatiron Health electronic health record-derived database**, comprising de-identified patient-level structured and unstructured data, was used to select patients diagnosed with aNSCLC (stage ≥IIIB) in 2017–2022 (**Table 1**).
- Adult patients (≥18 years of age), with ≥90 days of follow-up and ≥2 visits within 90 days after advanced diagnosis were included.
- **Patients without a result date for a *RET* test were excluded**.
- Rates of *RET* testing ≤90 days after advanced diagnosis were recorded; testing rates before advanced diagnosis, and ≤30, ≤60, and ≥90 days after advanced diagnosis were also recorded as **sensitivity analyses**.
- Logistic regression was used to identify baseline characteristics predictive of testing ≤90 days after advanced diagnosis.
- Common treatments for patients with *RET*+ **aNSCLC before and after US approval of RET inhibitors** were described.

RESULTS

Table 1. Cohort attrition

Description	N (%)
Patients in the aNSCLC Flatiron Health database	79,942 (100.0)
aNSCLC diagnosis between January 2017 and March 2022	38,414 (48.1)
Age ≥18 years at advanced diagnosis	38,412 (48.1)
At least 2 visits after advanced diagnosis (once at diagnosis and once <90 days after diagnosis) to ensure patients are treated in the Flatiron Health network	33,464 (41.9)
At least 90 days of follow-up from advanced diagnosis to ensure sufficient follow-up	26,529 (33.2)
Patients with *RET* testing with at least one result date available	26,329 (32.9)

aNSCLC, advanced non-small cell lung cancer.

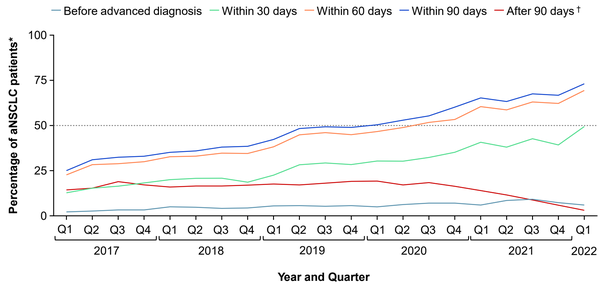
- A total of 26,329 patients with aNSCLC met inclusion criteria (**Table 2**).
- **Rates of *RET* testing ≤90 days after advanced diagnosis increased** from 25% among patients diagnosed in 2017 Q1 (n=1,398) to 73% among patients diagnosed in 2022 Q1 (n=810; **Figure 1**).

Table 2. Baseline characteristics

Characteristic	Overall (N=26,329)	Not tested within 90 days* (n=14,054)	Tested within 90 days* (n=12,275)
Median age at diagnosis, years (IQR)	70 (63–77)	70 (63–77)	70 (62–77)
Female, n (%)	12,889 (49.0)	6,721 (48.0)	6,168 (50.0)
Race/ethnicity, n (%)			
White	17,249 (66.0)	9,149 (65.0)	8,100 (66.0)
Black	2,434 (9.2)	1,412 (10.0)	1,022 (8.3)
Hispanic or Latino	897 (3.4)	519 (3.7)	378 (3.1)
Asian	705 (2.7)	346 (2.5)	359 (2.9)
Other	2,248 (8.5)	1,164 (8.3)	1,084 (8.8)
Unknown	2,796 (11.0)	1,464 (10.0)	1,332 (11.0)
Socioeconomic status, n (%)			
5 – Highest	3,165 (12.0)	1,520 (11.0)	1,645 (13.0)
4	4,373 (17.0)	2,173 (15.0)	2,200 (18.0)
3	4,571 (17.0)	2,387 (17.0)	2,184 (18.0)
2	4,534 (17.0)	2,482 (18.0)	2,052 (17.0)
1 – Lowest	4,047 (15.0)	2,360 (17.0)	1,687 (14.0)
Unknown	5,639 (21.0)	3,132 (22.0)	2,507 (20.0)
Insurance within 30 days of advanced diagnosis, n (%)			
Commercial	13,927 (53.0)	7,050 (50.0)	6,877 (56.0)
Medicare	3,598 (14.0)	2,079 (15.0)	1,519 (12.0)
Medicaid	1,129 (4.3)	633 (4.5)	496 (4.0)
Other	3,533 (13.0)	1,861 (13.0)	1,672 (14.0)
Unknown	4,142 (16.0)	2,431 (17.0)	1,711 (14.0)
Smoking status, n (%)			
History of smoking	22,926 (87.0)	12,531 (89.0)	10,395 (85.0)
***De novo* disease,** n (%)	19,318 (73.0)	9,403 (67.0)	9,915 (81.0)
ECOG PS, n (%)			
0	7,891 (30.0)	4,124 (29.0)	3,767 (31.0)
1	10,434 (40.0)	5,482 (39.0)	4,952 (40.0)
2–4	4,290 (16.0)	2,379 (17.0)	1,911 (16.0)
Unknown	3,714 (14.0)	2,069 (15.0)	1,645 (13.0)
Median follow-up, months (IQR)	12 (6–24)	13 (7–25)	11 (6–22)

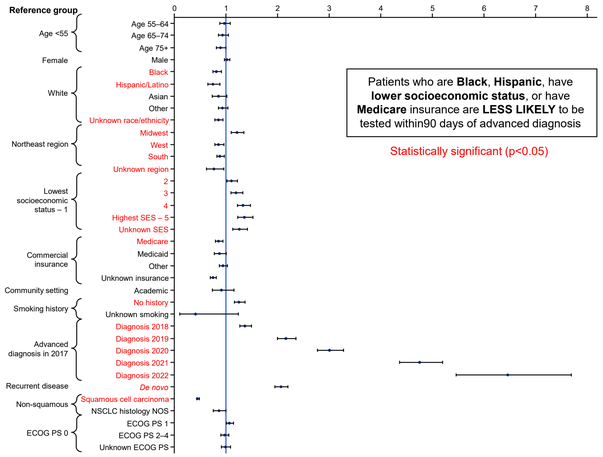
*p<0.001 between patients not tested and patients tested within 90 days of diagnosis.
ECOG PS, Eastern Cooperative Oncology Group performance status; IQR, interquartile range.

Figure 1. Timing of testing among tested patients



*During quarter of advanced diagnosis; 26,329 advanced NSCLC patients over the entire study period; †Data analysis began 2022 Q3, so the proportion of patients who were diagnosed in 2022 Q1 and tested after 90 days is likely underestimated. NSCLC, non-small cell lung cancer.

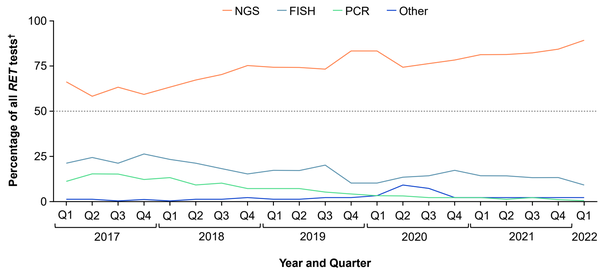
Figure 2. Predictors of *RET* testing ≤90 days after aNSCLC diagnosis



Error bars indicate 95% CIs. aNSCLC, advanced non-small cell lung cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; NOS, not otherwise specified; NSCLC, non-small cell lung cancer; SES, socioeconomic status.

- Patients were **less likely to receive *RET* testing** within 90 days if they were **Black** (multivariate odds ratio [OR] 0.8) or **Hispanic** (OR 0.8) than patients who were White, if they had **Medicare** (OR 0.9; all p<0.001) compared to commercial insurance, or if they lived in the West or South regions (OR 0.9; p≤0.006) compared to the Northeast region (**Table 2; Figure 2**).
- Patients were **more likely to receive *RET* testing** within 90 days if they were in the **highest socioeconomic quintile** (OR 1.4), had ***de novo* disease** (OR 2.1), or **no history of smoking** (OR 1.3; all p<0.001) (**Table 2; Figure 2**).

Figure 3. *RET* test type* usage over time



*Reflects the first *RET* test within the 90 days after advanced NSCLC diagnosis; the sample size over the entire study period (n=12,275) reflects the number of patients *RET*-tested within the 90-day window. For each of these patients, only one test is included, even if multiple happen within 90 days; †During quarter of patient's advanced diagnosis. FISH, fluorescence in situ hybridization; NGS, next-generation sequencing; NSCLC, non-small cell lung cancer.

- Between 2017 and 2022:
  - There were **increases** in the use of **next-generation sequencing** (**Figure 3**; 66% to 89%)
  - Blood samples for **biomarker testing increased** (25% to 49%)
  - Among those who had testing within 90 days, there was a **decrease** in **the mean days from diagnosis to test result** (33 to 28 days) for the first *RET* test.

- Among all patients with aNSCLC tested within 90 days during 2017–2022 (n=12,275), **80 were *RET*+**, and **73** of these *RET*+ patients **received first-line treatment ≤90 days after advanced diagnosis** (**Table 3**).
- The **most common first-line treatments** before (n=35) and after (n=38) RET inhibitor approval were **chemotherapy (40%)** and **RET inhibitor (42%)**, respectively (**Table 3**).
- Among *RET*+ patients who initiated first-line treatment after approval of the first RET inhibitor (n=38), **22 patients (58%) did not receive a RET inhibitor** (three [14%] of whom were PD-L1 positive).

Table 3. Treatment patterns of *RET*+ patients

Treatment type, n (%)	Patients who initiated 1L before approval* of first RET inhibitor (n=35/73)	Patients who initiated 1L on or after approval* of first RET inhibitor (n=38/73)
Chemotherapy only	14 (40.0)	4 (11.0)
Chemotherapy and checkpoint inhibitor	10 (29.0)	7 (18.0)
Checkpoint inhibitor only	5 (14.0)	4 (11.0)
RET inhibitor	—	16 (42.0)
Other targeted therapy	2 (6.0)	3 (8.0)
Clinical trial drug	4 (11.0)	1 (3.0)
Other†	0 (0.0)	3 (8.0)

*Approval of first RET inhibitor was May 8, 2020; †Patients may have received treatments for another malignancy as patients with advanced NSCLC and ≥1 malignancy were not excluded. 1L, first-line; NSCLC, non-small cell lung cancer

Limitations

- Patients who may have had another cancer were not excluded; patients may have been treated (e.g., chemotherapy) for a non-lung cancer.
- These data may not be applicable to all care settings in the US, as most patients in the database originate from community oncology settings.
- Missing data is a limitation with real-world (RW) analyses: we may not have captured all *RET*+ patients who were tested and received first-line treatment within 90 days of diagnosis (i.e., this number may be higher in RW practice).
- RNA-based NGS is the optimum method for detecting *RET* fusions in patients with NSCLC. This analysis included all test types (NGS, FISH, PCR, and other): RW optimized, gold-standard *RET* testing rates are likely lower than reported.

CONCLUSIONS

In patients with aNSCLC, *RET* testing has increased over time, but certain patient subgroups are less likely to undergo *RET* testing (Figure 2). This limits patient access to appropriate targeted therapy.

After RET inhibitor approval, only 42% of patients with *RET*+ aNSCLC were treated with a RET inhibitor in the first-line setting.

These findings suggest a disparity in patient access to *RET* testing, and an unmet medical need among patients with *RET*+ aNSCLC.

SUMMARY

The proportion of patients tested for *RET*+ aNSCLC has increased from 2017 to 2022

Access to *RET* testing varies between **patient subgroups**; this limits the use of optimal treatment pathways

Affiliations
[1]Genentech, Inc., South San Francisco, CA, USA;
[2]CHOICE Institute, University of Washington, Seattle, WA, USA. Genentech, Inc., South San Francisco, CA, USA; [3]Mayo Clinic, Rochester, MN, USA.

Disclosures
E. K. is an employee of Genentech, Inc. and reports owning stocks or shares in Genentech, Inc. Co-authors' full disclosures can be accessed at: https://coi.asco.org/

Acknowledgments
This study was sponsored by Genentech, Inc. Third party medical writing assistance, under the direction of the authors, was provided by Emily Hollebon, MSc, of Ashfield MedComms, an Inizio Company, and was funded by F. Hoffmann-La Roche Ltd/Genentech, Inc. The **Flatiron Health database** is a longitudinal database, comprising de-identified patient-level structured and unstructured data, curated via technology-enabled abstraction: https://www.medrxiv.org/content/10.1101/2020.03.16.20037143v2 and https://arxiv.org/abs/2001.09765. During the study period, the de-identified data originated from approximately 280 US cancer clinics (~800 sites of care). The majority of patients in the database originate from community oncology settings; relative community/academic proportions may vary depending on study cohort. Refer to the Flatiron Health Knowledge Center for additional information.

References
1. Nokin, et al. Trends Cancer 2021
2. Tan, et al. Clin Oncol 2022
3. Ionescu, et al. Curr Oncol 2022