Poster 1016P

Patient characteristics, HER2 testing, and treatment patterns in advanced *HER2* (*ERBB2*)-mutant NSCLC in real-world clinical practice

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Objective

- To describe the clinical and human epidermal growth factor receptor 2 (*HER2*) testing characteristics and treatment patterns in a real-world population of patients with advanced *HER2* (*ERBB2*)-mutant (HER2m) non-small cell lung cancer (NSCLC)

Conclusions

- The median time from advanced NSCLC diagnosis to receipt of a *HER2* test result decreased between 2019 and 2022, suggesting that HER2 testing practices improved over time
- Although the most common treatment received across all lines of therapy was chemotherapy only, the use of targeted treatment regimens, including HER2-directed therapies such as trastuzumab deruxtecan (T-DXd; a HER2-directed antibody-drug conjugate), increased in later lines of therapy, possibly reflecting changes in evidence and treatment availability during the study period
- These data provide valuable insights into the *HER2* testing and treatment patterns for patients with advanced HER2m NSCLC

Plain language summary

Why did we perform this research?

Some people with non-small cell lung cancer (NSCLC) have a mutation in a gene called human epidermal growth factor receptor 2 (*HER2*; also known as *ERBB2*),[1–4] which is known as *HER2*-mutant (HER2m) NSCLC. Trastuzumab deruxtecan (T-DXd) is an antibody-drug conjugate, which is a chemotherapy with a linker (together called deruxtecan) joined to an antibody (trastuzumab). Trastuzumab binds to HER2 on the surface of cancer cells; once inside the cell, T-DXd releases the chemotherapy to kill these cells.[5,6] T-DXd is recommended in multiple countries worldwide for people with HER2m NSCLC that has spread from the original site to other parts of the body (advanced or metastatic) or cannot be completely removed by surgery (unresectable) and who have received prior treatment.[7] Despite the availability of HER2-directed treatment, such as T-DXd, for people with HER2m NSCLC, testing for the presence of *HER2* mutations is not uniformly performed globally.[8] We carried out this study to understand the clinical and HER2 testing characteristics for people with HER2m NSCLC and evaluate the treatments these people receive.

How did we perform this research?

We collected information from health records on the clinical and *HER2* testing characteristics and treatment patterns for people diagnosed with advanced HER2m NSCLC between January 2019 and December 2022.

What were the findings of this research?

Health records were completed for 430 participants. Bone was the most common site to where the cancer had spread, observed in 53% of participants. The time from advanced NSCLC diagnosis to receipt of *HER2* test result decreased between 2019 and 2022. The most common treatment used across all lines of therapy was chemotherapy only. Use of targeted treatments was common in later treatment settings. Of those who received targeted therapy as a second-line (n=59) and/or third-line (n=20) treatment, most received a HER2-directed therapy (64% and 90%, respectively).

What are the implications of this research?

This study provides valuable insights into the clinical and *HER2* testing characteristics and treatment patterns for people with advanced HER2m NSCLC.

Where can I access more information?

For more information, please reach out to Dr. Timothy Clay at tim@drtimclay.com.au or Sabra Zaraa at sabra.zaraa@astrazeneca.com.

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Introduction

- *HER2* mutations have been identified in approximately 3–5% of NSCLC cases and are associated with a poor prognosis[1,2]
- T-DXd was approved in the EU in 2023 as the first HER2-directed therapy for patients with unresectable or metastatic HER2m NSCLC who have received prior systemic therapy,[3] and has since been approved in multiple other countries worldwide[4]
  - Currently, there are no HER2-directed therapies approved in the first-line setting for HER2m NSCLC
- Despite the availability of HER2-directed therapy, routine *HER2* testing in clinical practice is not uniformly performed globally,[5] and therefore, real-world data for patients with HER2m NSCLC are limited
- Here we report the clinical and *HER2* testing characteristics and treatment patterns for patients with HER2m NSCLC in real-world clinical practice across eight countries

Methods

- This was a retrospective chart review of patients diagnosed with advanced (Stage IIIb, IIIc, or IV) HER2m NSCLC (**Figure 1**)
- Data were obtained from patient health records completed by 130 physicians across eight countries (Australia, Canada, France, Germany, Italy, Republic of Korea, Taiwan, and the UK)
  - Participating physicians were recruited across a range of settings, including academic facilities, and cancer and community centers
- To minimize the risk of selection bias, patients were identified sequentially from the start of the index period (January 1, 2019); an equal number of patients were selected per year until the end of the index period (December 31, 2022)

Figure 1. Study design

Inclusion and exclusion criteria

- Adult patients diagnosed with advanced (Stage IIIb, IIIc, or IV) NSCLC between January 1, 2019, and December 31, 2022
- Positive test for *HER2* mutation(s) at any timepoint after diagnosis of advanced NSCLC disease
- Received at least one line of active anticancer therapy after advanced NSCLC diagnosis
- No history of clinical trial enrollment for NSCLC
- Complete medical record from time of initial diagnosis to date of data extraction (if alive), or date of death

→ **Patient population N=430**

↓

Follow up

Patients were followed from diagnosis date until death or end of the study period (December 31, 2024)

HER2, human epidermal growth factor receptor 2; NSCLC, non-small cell lung cancer

Results

Patient characteristics

- Health records were completed for 430 patients (Australia, n=41; Canada, n=49; France, n=87; Germany, n=61; Italy, n=45; Republic of Korea, n=34; Taiwan, n=40; UK, n=73)
- Patient demographics and clinical characteristics are shown in **Table 1**; adenocarcinoma was the most common histological subtype, reported in 84% of patients; squamous cell carcinoma was observed in 12% of patients
  - Bone was the most common metastatic site at advanced NSCLC diagnosis (53% of patients)

HER2 testing

- Median (quartile [Q]1–Q3) time from advanced NSCLC diagnosis date to *HER2* mutation test request was 13 (2–66) days; next-generation sequencing was the most common testing method (61%), followed by single-gene polymerase chain reaction (23%)
- Median (Q1–Q3) time from diagnosis of advanced NSCLC date to *HER2* test result was 36 (15–215) days in 2019, which decreased to 29 (18–55) days in 2022
- In total, 272 patients (63%) had a *HER2* mutation in a known location (**Table 2**); 27% had a *HER2* mutation within a known exon location, with the majority of these mutations observed in exons 19 and 20
  - Notably, 9% of all patients had co-occurring epidermal growth factor receptor mutations

Table 1. Baseline demographics and clinical characteristics

	N=430
Age, median (range), years	66 (22–89)
Male, n (%)	241 (56)
Disease stage at advanced NSCLC diagnosis, n (%)	
IIIb	29 (7)
IIIc	48 (11)
IV	353 (82)
ECOG PS score at advanced NSCLC diagnosis, n (%)	
0	102 (24)
1	237 (55)
≥2	86 (20)
Unknown	5 (1)
Histology, n (%)	
Adenocarcinoma	361 (84)
Squamous cell carcinoma	51 (12)
Large cell carcinoma	15 (3)
Unknown	3 (1)

	N=430
Metastatic sites at advanced NSCLC diagnosis, n (%)*	
n†	353
Bone	186 (53)
Contralateral lung	138 (39)
Liver	136 (39)
Lymphatic system / lymph nodes	121 (34)
Pleura	89 (25)
Adrenal glands	84 (24)
Brain‡	57 (16)
PD-L1 status at advanced NSCLC diagnosis, n (%)	
n§	323
<1%	99 (31)
1–49%	151 (47)
≥50%	69 (21)
Unknown	4 (1)

*Sites in >10% of patients shown; †data not available for 77 patients; ‡central nervous system imaging was not mandatory or systematically performed for all patients at diagnosis; §patients with tumors tested for PD-L1 status with a conclusive result (high/low expression)
ECOG PS, Eastern Cooperative Oncology Group performance status; NSCLC, non-small cell lung cancer; PD-L1, programmed cell death ligand 1

Table 2. Location of *HER2* mutations

n (%)	N=430
Known exon location*	116 (27)
19	30 (26)
20	76 (66)
Other	9 (8)

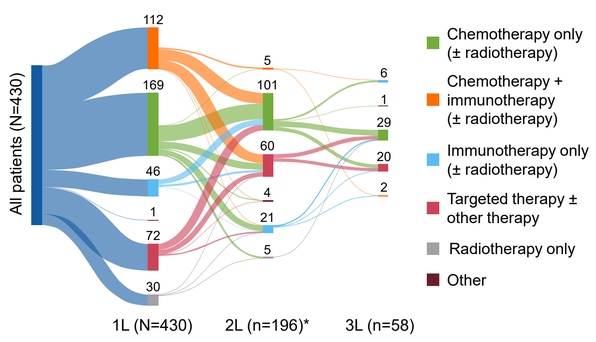
n (%)	N=430
Extracellular	106 (25)
Transmembrane	47 (11)
Other	3 (1)
Unknown / not reported	158 (37)

*One patient (1%) had a *HER2* mutation in an unknown exon location
HER2, human epidermal growth factor receptor 2

Treatment patterns

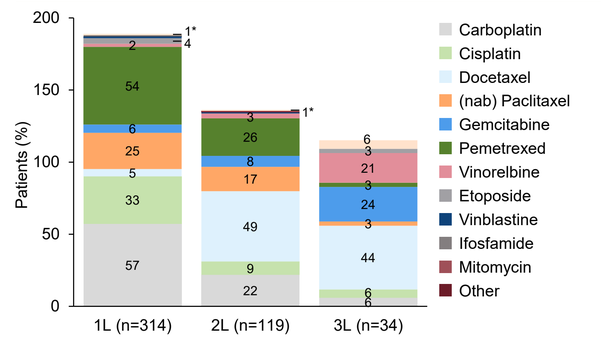
- Median (Q1–Q3) time from advanced NSCLC diagnosis date to initiation of first-line treatment was 27 (10–42) days; *HER2* test results were received prior to initiating first-line treatment for 47% of patients
- Overall, patients received between one and seven lines of therapy for advanced NSCLC; 54% of patients received one line of therapy only, 33% received two lines of therapy, 13% received three lines of therapy, and 1% received four or more lines of therapy
- Across all settings, the most common treatment received was chemotherapy only (**Figure 2**)
  - Use of any targeted therapy was more common in the second- and third-line settings (31% and 34%, respectively), compared with the first-line setting (17%)
- In the first-line setting, carboplatin was received by 57% of patients, and pemetrexed by 54% of patients; docetaxel was the most common chemotherapy agent received in the second-line (49%) and third-line (44%) settings (**Figure 3**)

Figure 2. Overall treatment patterns by line of therapy in advanced HER2m NSCLC



Data shown are patients, n. *The type of treatment received was not reported for two patients
1/2/3L, first/second/third line; HER2(m), human epidermal growth factor receptor 2 (mutant); NSCLC, non-small cell lung cancer

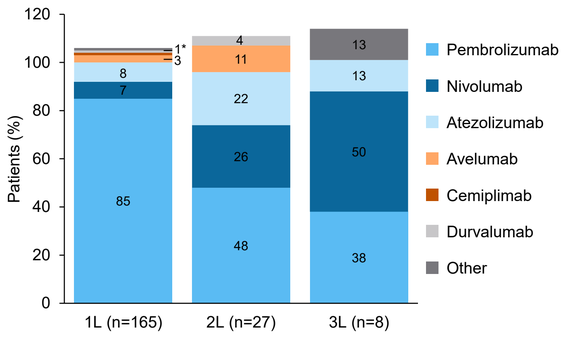
Figure 3. Chemotherapy agents received by line of therapy in advanced HER2m NSCLC



Percentages do not sum to 100 as some patients received more than one agent; includes all patients who received chemotherapy as part of a treatment regimen. *1% of patients each received ifosfamide (1L), mitomycin (2L), and vinblastine (1L and 2L); other chemotherapy agents were received by <1% of patients at 1L and 1% of patients at 2L
1/2/3L, first/second/third line; HER2(m), human epidermal growth factor receptor 2 (mutant); NSCLC, non-small cell lung cancer

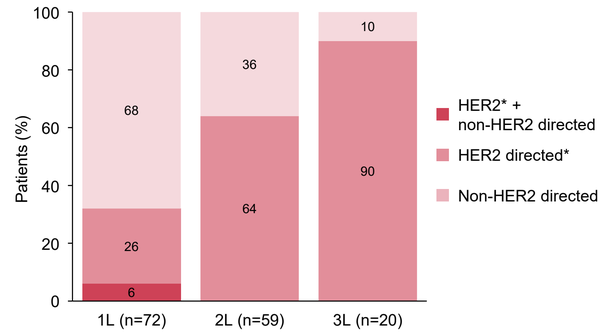
- In the first-line setting, pembrolizumab was the most frequently used immunotherapy, received by 85% of patients (**Figure 4**)
- There was variation in the type of immunotherapy received in later treatment settings, potentially reflective of regional differences
  - For example, nivolumab was the predominant immunotherapy used at second line across patients in European countries, whereas pembrolizumab was more commonly used in Australia, Canada, Republic of Korea, and Taiwan
- Among patients who received targeted therapy (with or without other agents), non-HER2-directed treatment was commonly received in the first-line setting, with 68% of patients receiving such regimens (**Figure 5**)
- Bevacizumab was the most common targeted therapy received in the first-line setting (38%), followed by trastuzumab (18%) and osimertinib (14%)
- HER2-directed therapy was more frequently used in the second- and third-line settings (64% and 90%, respectively) compared with the first-line setting (32%)
  - T-DXd was the most common targeted therapy used at second and third line, received by 35% and 40% of patients, respectively; trastuzumab and trastuzumab emtansine were also commonly used, each received by 15% of patients at second line and 25% of patients at third line

Figure 4. Immunotherapy agents received by line of therapy in advanced HER2m NSCLC



Percentages do not sum to 100 as some patients received more than one agent; includes all patients who received immunotherapy as part of a treatment regimen. *1% of patients each received cemiplimab, durvalumab, and other immunotherapy agents
1/2/3L, first/second/third line; HER2(m), human epidermal growth factor receptor 2 (mutant); NSCLC, non-small cell lung cancer

Figure 5. Types of targeted treatment received by line of therapy in advanced HER2m NSCLC



Includes all patients who received targeted therapy as part of a treatment regimen. *HER2-directed agents included lapatinib, pertuzumab, T-DXd, trastuzumab, and trastuzumab emtansine
1/2/3L, first/second/third line; HER2(m), human epidermal growth factor receptor 2 (mutant); NSCLC, non-small cell lung cancer; T-DXd, trastuzumab deruxtecan

Limitations

- Central nervous system imaging was not mandatory or systematically performed for all patients at diagnosis, limiting estimation of the true prevalence of brain metastases
- Patients were eligible for study entry following a positive *HER2* mutation test result at any timepoint after advanced NSCLC diagnosis, which may have influenced treatment patterns depending on when the *HER2* test result was received
- The exon location of *HER2* mutations was unknown for a large proportion of patients (73%), limiting estimation of the true prevalence
- The small number of patients who received third-line treatment limits interpretation of these data because they may not be representative of the broader real-world patient population
- Analyses were limited to patients with complete follow-up data, which may have introduced attrition bias
- Data obtained from real-world settings are subject to biases and confounding factors not observed in controlled trial settings, particularly for chart review studies that rely on accurate, complete patient record data

Poster

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