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Patient characteristics, treatment patterns, and real-world outcomes among patients in the US with human epidermal growth factor receptor 2-expressing solid tumors

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Objective

- To describe demographic and clinical characteristics, and treatment patterns and real-world response rates (rwRRs), by human epidermal growth factor receptor 2 (HER2) immunohistochemistry (IHC) status among patients in the US with HER2 IHC 3+/2+ solid tumors

Conclusions

- These data provide valuable insights into the treatment patterns and rwRRs for patients with HER2 IHC 3+/2+ solid tumors diagnosed between 2016 and 2023
- In the overall population, chemotherapy-based regimens were the predominant treatments across all lines of therapy; however, some variation was observed between patients with HER2 IHC 3+ and IHC 2+ tumors and across tumor types
- Given the poor response rates observed in this patient population, particularly with later lines of therapy, and the limited availability of HER2-directed treatments in the second-line or later setting at the time of the study (2016–2023), these findings highlight the need for effective HER2-directed treatment options in these patients
- Results should be interpreted with caution owing to the selective patient population who underwent HER2 IHC testing at a time when it was not routinely performed

Plain language summary

Why did we perform this research?

Human epidermal growth factor receptor 2 (HER2) is a protein found on the surface of cancer cells in a wide range of tumor types.[1,2] Trastuzumab deruxtecan (T-DXd) is an antibody-drug conjugate, which is a chemotherapy with a linker (together called deruxtecan) joined to an antibody (trastuzumab). T-DXd binds to HER2 on the surface of cancer cells. Once inside the cell, T-DXd releases the chemotherapy to kill these cells.[3,4] T-DXd is approved in multiple countries worldwide, including the US, for people with solid tumors that have high levels of the HER2 protein (known as HER2-positive immunohistochemistry [IHC] 3+) and have spread (advanced) or cannot be completely removed with surgery, and who have received prior systemic treatment and/or have no satisfactory treatment options available.[5–7] Prior to these approvals, testing for HER2 expression using IHC methods was not routinely performed for people with solid tumors beyond breast and gastric cancers. We performed this study to understand the characteristics of people with HER2 IHC 3+/2+ solid tumors, how they are treated, and how well their tumors respond to these treatments.

How did we perform this research?

We collected information about the treatments and responses of people with HER2 IHC 3+/2+ advanced solid tumors (excluding breast and gastric cancers) diagnosed between January 2016 and December 2023, using a database of electronic health records and other data sources (Tempus® multi-modal database).

What were the findings of this research?

Among the 392 participants identified, the most common treatments received across all lines of therapy were chemotherapy-based regimens. There was some variation observed in the types of treatments received between participants with HER2 IHC 3+ and IHC 2+ tumors, and among those with different tumor types. Of the participants who received treatment, 39% had a decrease in the size or number of tumors, or all signs of cancer had disappeared (known as a complete or partial response) with first-line treatment, 15% had a response with second-line treatment, and 21% of participants had a response with third-line treatment. A similar trend in response rates with each line of therapy was observed across participants with endometrial, colorectal, and non-small cell lung cancer.

What are the implications of this research?

This study provides valuable insights into the treatment patterns and responses of people with HER2 IHC 3+/2+ solid tumors between 2016 and 2023, highlighting the need for more effective treatment options that target specific tumor characteristics in these people.

Where can I access more information?

For more information, please reach out to Anuj Shah at anuj.shah@astrazeneca.com.

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Introduction

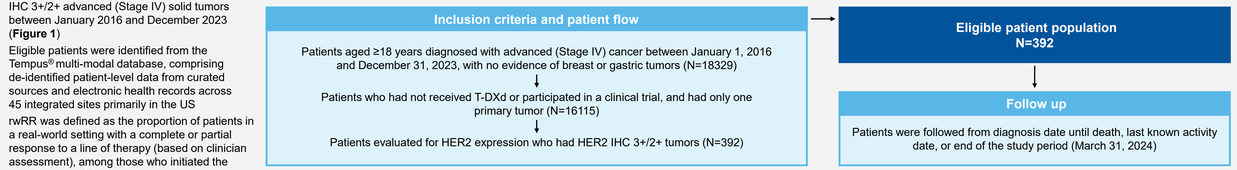
- HER2 expression has been reported in a wide range of solid tumors,[1,2] and has been associated with poor prognosis[3,4]
- Historically, there have been limited HER2-targeted therapies available for patients with solid tumors other than breast and gastric cancers
- Trastuzumab deruxtecan (T-DXd) is now approved in multiple countries worldwide, including the US,* for patients with unresectable or metastatic HER2-positive (IHC 3+) solid tumors that have progressed after prior treatment and/or have no satisfactory alternative treatment options[5–7]
  - Prior to the US approval* of T-DXd in 2024, HER2 IHC testing was not routinely performed for patients with solid tumors beyond breast and gastric cancers, and thus, real-world data for these patients are limited
- Here, we report real-world treatment patterns and response rates for patients in the US with HER2 IHC 3+/2+ solid tumors

*Under accelerated approval based on objective response rate and duration of response; continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial

Methods

- This was a retrospective cohort study of patients in the US diagnosed with HER2 IHC 3+/2+ advanced (Stage IV) solid tumors between January 2016 and December 2023 (**Figure 1**)
- Eligible patients were identified from the Tempus® multi-modal database, comprising de-identified patient-level data from curated sources and electronic health records across 45 integrated sites primarily in the US
- rwRR was defined as the proportion of patients in a real-world setting with a complete or partial response to a line of therapy (based on clinician assessment), among those who initiated the specified line of therapy

Figure 1. Study design



HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; T-DXd, trastuzumab deruxtecan

Results

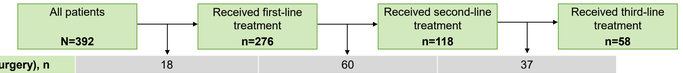
- A total of 392 patients were identified and included in the analysis; of these, 127 patients had HER2 IHC 3+ tumors, and 265 patients had IHC 2+ tumors
- Patient demographics and clinical characteristics are shown in **Table 1**

Table 1. Patient demographics and clinical characteristics

	Overall (N=392)	HER2 IHC 3+ (n=127)	HER2 IHC 2+ (n=265)
Median age, years (Q1–Q3)	66 (57–72)	66 (55–72)	65 (57–72)
Female, n (%)	261 (67)	72 (57)	189 (71)
Race, n (%)			
White	177 (45)	59 (46)	118 (45)
African American	45 (11)	16 (13)	29 (11)
Asian	17 (4)	4 (3)	13 (5)
Other	20 (5)	9 (7)	11 (4)
Unknown / not available	133 (34)	39 (31)	94 (35)
Smoking status, n (%)			
Non-smoker	166 (42)	54 (43)	112 (42)
Previously smoked	103 (26)	36 (28)	67 (25)
Current smoker	36 (9)	12 (9)	24 (9)
Missing	87 (22)	25 (20)	62 (23)
Tumor type, n (%)			
Endometrial	104 (27)	21 (17)	83 (31)
Colorectal	100 (26)	38 (30)	62 (23)
NSCLC	74 (19)	23 (18)	51 (19)
Other*	114 (29)	45 (35)	69 (26)
Year of advanced diagnosis, n (%)			
2016	4 (1)	0	4 (2)
2017	15 (4)	7 (6)	8 (3)
2018	30 (8)	15 (12)	15 (6)
2019	41 (10)	20 (16)	21 (8)
2020	62 (16)	17 (13)	45 (17)
2021	90 (23)	25 (20)	65 (25)
2022	87 (22)	24 (19)	63 (24)
2023	63 (16)	19 (15)	44 (17)
ECOG performance status, n (%)			
0	100 (26)	36 (28)	64 (24)
1	109 (28)	36 (28)	73 (28)
2+	39 (10)	10 (8)	29 (11)
Missing	144 (37)	45 (35)	99 (37)

*<15 patients per tumor type: anus; appendix; biliary tract; bladder; cervix uteri; duodenum; ethmoid sinus; extrahepatic bile duct; fallopian tube; female genital tract; gallbladder; head, face or neck; ileum; intrahepatic bile duct; jejunum; kidney; liver; ovarian; parotid gland; pancreatic; pharynx; renal pelvis; salivary gland; small intestine; submandibular gland; testicular; urinary system; and uterine
ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; NSCLC non-small cell lung cancer; Q, quartile

Figure 2. Treatment flow chart

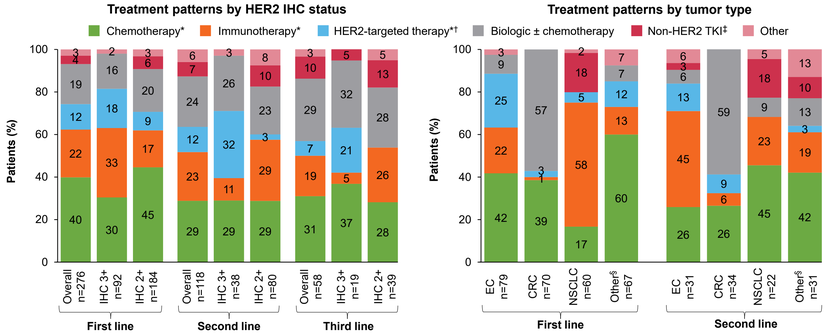


Local therapy only (RT/surgery), n	18	60	37
End of data, n	59	64	8
Death, n	39	34	15

RT, radiotherapy

- Of the 392 patients, 70% (276/392) received first-line treatment, 43% (118/276) of those received second-line treatment, and 49% (58/118) of those received third-line treatment (**Figure 2**)

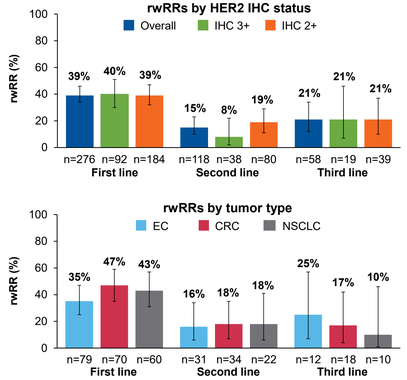
Figure 3. Percentage of patients who received a treatment class by HER2 IHC status and tumor type



Percentages may not sum to 100 owing to rounding. *Alone or in combination with other agents, except where specific combinations are listed as distinct categories; †Included ado-trastuzumab emtansine, lapatinib, neratinib, pertuzumab, trastuzumab, and tucatinib; ‡Included afatinib; ‖<15 patients per tumor type: anus; appendix; biliary tract; bladder; cervix uteri; duodenum; ethmoid sinus; extrahepatic bile duct; fallopian tube; female genital tract; gallbladder; head, face or neck; ileum; intrahepatic bile duct; jejunum; kidney; liver; ovarian; parotid gland; pancreatic; pharynx; renal pelvis; salivary gland; small intestine; submandibular gland; testicular; urinary system; and uterine
CRC, colorectal cancer; EC, endometrial cancer; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor

- In the overall study population, chemotherapy-based regimens were the most common treatment class across all lines of therapy (**Figure 3**)
  - Trastuzumab, either as a monotherapy or as part of a combination regimen, was the most common HER2-targeted agent used at each line of therapy (11%, 9%, and 5% at first, second, and third line, respectively)
  - Some variation in treatment patterns was observed between patients with HER2 IHC 3+ and IHC 2+ tumors; for example, HER2-targeted therapy was received by a higher proportion of patients with IHC 3+ tumors compared with those with IHC 2+ tumors across all lines of therapy
- Treatment patterns also varied across the different tumor types:
  - The use of immunotherapy-based regimens was common in patients with non-small cell lung cancer as a first-line treatment (58%) and in those with endometrial tumors as a second-line treatment (45%)
  - In patients with colorectal cancers, bevacizumab + chemotherapy (± other agents) was the most common treatment regimen received at first (47%) and second line (41%)
  - Notably, HER2-targeted therapies were received at first line by 25% of patients with endometrial tumors

Figure 4. rwRRs by HER2 IHC status and tumor type*



*Selected tumor types; rwRRs are based on aforementioned treatments. Error bars represent 95% CIs
CI, confidence interval; CRC, colorectal cancer; EC, endometrial cancer; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; NSCLC, non-small cell lung cancer; rwRR, real-world response rate

- Overall, rwRRs were ≤40% across all lines of therapy and were generally lower in the second- and third-line settings compared with the first-line setting (**Figure 4**)
- Notably, the rwRRs with second-line treatment were numerically lower in patients with IHC 3+ tumors (8%) compared with those with IHC 2+ tumors (19%); rwRRs with third-line treatment were consistent across the HER2 IHC subgroups
- Across the different tumor types, rwRRs were generally consistent with those observed in the overall study population

Limitations

- Patients included in this analysis represent a selective population who underwent HER2 IHC testing at a time when it was not routinely performed, and as such, may not reflect the general real-world patient population
- In the absence of standardized guidelines for these tumor types, the timing of HER2 testing was variable
- rwRRs were not adjusted for treatment heterogeneity and are a subjective measure; however, they are representative of real-world clinical practice
- The small sample sizes across HER2 IHC and tumor type subgroups, particularly in the second- and third-line settings, limit interpretation
- Information regarding the IHC assay and scoring guidelines used for HER2 testing was not available in the Tempus® multi-modal database

Acknowledgments

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Disclosures

Anuj Shah reports employment with AstraZeneca.

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