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Attrition rates from first- to third-line therapy in HER2+ metastatic breast cancer in Europe

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Objectives

- To understand and characterize contemporary **attrition rates (percentage of patients who completed a line of therapy [LOT] but did not receive the subsequent LOT)** after first-line (1L) and second-line (2L) therapy among women with human epidermal growth factor receptor 2-positive (HER2+) metastatic breast cancer (mBC) receiving routine care at selected oncology centers in EU4 countries (France, Germany, Italy, and Spain) and the UK
- To highlight the potential lost opportunity for patients with HER2+ mBC to benefit from optimal targeted treatments at the earliest indicated LOT

Conclusions

- These data from routine clinical practice in EU4 countries and the UK indicate that 29.6% and 34.2% of patients with HER2+ mBC who completed 1L and 2L therapy, respectively, did not receive a subsequent LOT, which was primarily due to death, move to end-of-life palliative care, loss to follow up (FU), and 'other' reasons for attrition; this highlights the importance of using optimal HER2-directed treatments in the earliest indicated setting
- Further research is needed to understand the high variation in reasons for attrition, as this may reflect differences in patient fitness, clinician and patient attitudes to treatment, and access to treatments across centers
- Future analyses for this study will focus on characterizing treatment patterns and real-world outcomes

Plain language summary

Why did we perform this research?

In some people with human epidermal growth factor receptor 2 (HER2)-positive metastatic breast cancer (mBC) (cancer that has spread from its original site), the first (or first-line [1L]) treatment they are given either does not work or eventually stops working, and they need a different option (a second-line [2L] treatment). Some people who receive a 2L treatment may also need a third-line treatment. We performed this study to identify people in the real world who complete a 1L or 2L treatment but do not receive additional medication (the attrition rate) and the reasons why this can occur.

How did we perform this research?

We used an existing database of medical records to obtain information about treatments and outcomes of people in France, Germany, Italy, Spain, and the UK. We focused on women across Europe between 2017 and 2021 with HER2-positive mBC.

What were the findings of this research?

We found that some women with HER2-positive mBC completed 1L (29.6%) and 2L (34.2%) treatment but did not receive a subsequent treatment. This was primarily due to death, transfer to end-of-life medical care (eg hospice), loss to follow up, and 'other' reasons for attrition.

What are the implications of this research?

This study highlights the importance of choosing the most effective drugs as early as possible to treat people with HER2-positive mBC and systematically documenting the causes of attrition at each line of treatment to understand why some people are not offered the most effective drugs.

Poster

Supplementary material

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Introduction

- Women with HER2+ mBC who experience progression after 1L therapy (trastuzumab, pertuzumab, and a taxane) typically require a subsequent LOT[1]
- Trastuzumab emtansine (T-DM1) was standard of care in the 2L setting until the recent approval (July 2022 in the EU) of trastuzumab deruxtecan (T-DXd) after ≥1 anti-HER2 regimen[2]
- Receiving optimal targeted therapy in the earliest indicated setting is important to maximize the likelihood and durability of a clinical benefit[3]
- As new therapies become available, understanding treatment patterns by LOT may help guide treatment decision making and inform the optimal treatment paradigm for patients with HER2+ mBC

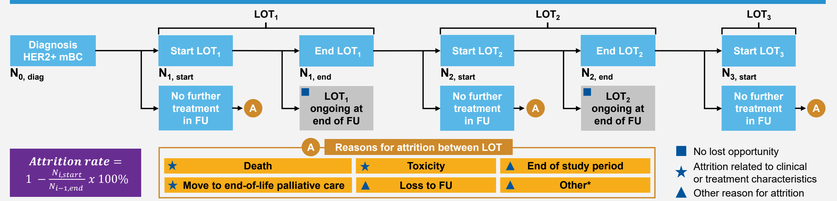
Methods

- In this ongoing multicenter observational study, electronic medical record (EMR) data were collected retrospectively from women ≥18 years old diagnosed with HER2+ mBC between 2017 and 2021, in EU4 countries and the UK
- Structured EMR data and manually abstracted unstructured data from oncology centers were curated. Patients had the opportunity to be followed up for ≥12 months from mBC diagnosis

The primary endpoint was attrition rate (percentage of patients who completed an LOT but did not receive the subsequent LOT) after 1L and 2L therapy

- An overview of how attrition rates were calculated and reasons for attrition are shown in **Figure 1**
- Documented reasons for attrition included death or move to end-of-life palliative care (within 30 days of end of LOT), discontinuation due to toxicity, end of study period, loss to FU, or 'other' if reasons did not meet these criteria, or if death or move to end-of-life palliative care occurred >30 days after treatment discontinuation

Figure 1. Attrition rates algorithm



*Includes site-reported end of treatment reasons of 'progression', 'other known', 'unknown', and 'missing'
A, attrition; FU, follow up; HER2+, human epidermal growth factor receptor 2-positive; LOT, line of therapy; mBC, metastatic breast cancer; N, number of patients

Results and interpretation

- This analysis included data from 496 women across seven sites in five countries: one in France, two in Germany, one in Italy, one in Spain, and two in the UK
- Data here are shown for all patients with HER2+ disease. Pooled data split according to hormone receptor status are available in supplementary material (**Supplementary figure 1 and 2**)
- Overall median duration of FU was 41.1 months (95% confidence interval [CI] 22.4, 52.8). A total of 59.1% of patients were postmenopausal, 60.9% had de-novo disease, 60.9% had Stage IV disease, and 27.4% had ≥4 metastatic sites. Overall, 41.9%, 26.4%, and 12.3% received a total number of one, two, and three LOTs per patient, respectively

Table 1. Patient demographics and clinical characteristics

	France (N=115)	Germany (N=84)	Italy (N=105)	Spain (N=56)	UK (N=136)
Median age at mBC diagnosis, years (Q1–Q3)	56.0 (46.0–71.0)	67.5 (57.0–76.0)	56.0 (47.0–63.0)	55.5 (49.0–68.0)	61.5 (49.0–73.0)
Median duration of FU, months (Q1–Q3)	38.8 (21.3–51.4)	24.4 (12.1–44.5)	45.4 (29.4–56.3)	40.9 (20.2–56.5)	44.0 (27.8–54.0)
Median BMI, kg/m² (Q1–Q3)	24.7 (22.0–28.6)	26.0 (23.0–29.1)	24.2 (22.1–28.8)	26.3 (23.6–30.1)	28.6 (24.3–31.9)
Postmenopausal status, n (%)	52 (45.2)	57 (67.9)	45 (42.9)	40 (71.4)	99 (72.8)
Metastatic sites, n (%)					
<4	83 (72.2)	61 (72.6)	76 (72.4)	48 (85.7)	92 (67.7)
≥4	32 (27.8)	23 (27.4)	29 (27.6)	8 (14.3)	44 (32.4)
Metastatic location, n (%)*					
Brain	19 (16.5)	22 (26.2)	47 (44.8)	19 (33.9)	44 (32.4)
Bone	69 (60.0)	54 (64.3)	58 (55.2)	35 (62.5)	69 (50.7)
Lung	40 (34.8)	36 (42.9)	41 (39.1)	14 (25.0)	62 (45.6)
Liver	48 (41.7)	44 (52.4)	47 (44.8)	20 (35.7)	70 (51.5)
Lymph nodes	71 (61.7)	39 (46.4)	55 (52.4)	22 (39.3)	71 (52.2)
De-novo disease, n (%)	76 (66.1)	48 (57.1)	58 (55.2)	30 (53.6)	90 (66.2)
Stage, n (%)†					
0/I/II/III	35 (30.4)	30 (35.7)	34 (32.4)	26 (46.4)	44 (32.4)
IV	76 (66.1)	48 (57.1)	58 (55.2)	30 (53.6)	90 (66.2)
Total number of LOTs per patient, n (%)‡					
0	0	5 (6.0)	5 (4.8)	1 (1.8)	23 (16.9)
1	44 (38.3)	44 (52.4)	47 (44.8)	26 (46.4)	47 (34.6)
2	37 (32.2)	20 (23.8)	33 (31.4)	11 (19.6)	30 (22.1)
3	17 (14.8)	6 (7.1)	11 (10.5)	11 (19.6)	16 (11.8)

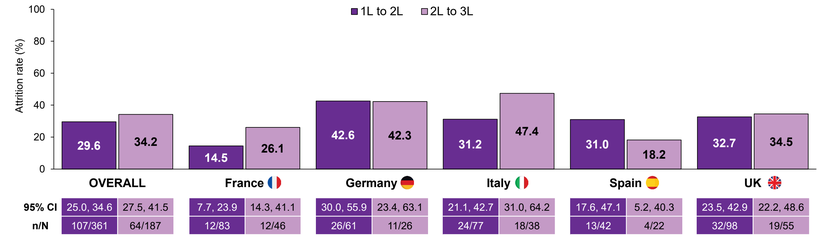
*Patients may belong to >1 category; †n=25 patients had 'unknown' or 'missing' staging information; ‡n=62 patients received ≥4 LOTs per patient
BMI, body mass index; FU, follow up; LOT, line of therapy; mBC, metastatic breast cancer; Q, quartile

Table 2. Number of patients starting 1L and 2L therapy

	OVERALL (N=496)	France (N=115)	Germany (N=84)	Italy (N=105)	Spain (N=56)	UK (N=136)
1L, n (%)	462 (93.1)	115 (100)	79 (94.0)	100 (95.2)	55 (98.2)	113 (83.1)
2L, n (%)	254 (51.2)	71 (61.7)	35 (41.7)	53 (50.5)	29 (51.8)	66 (48.5)

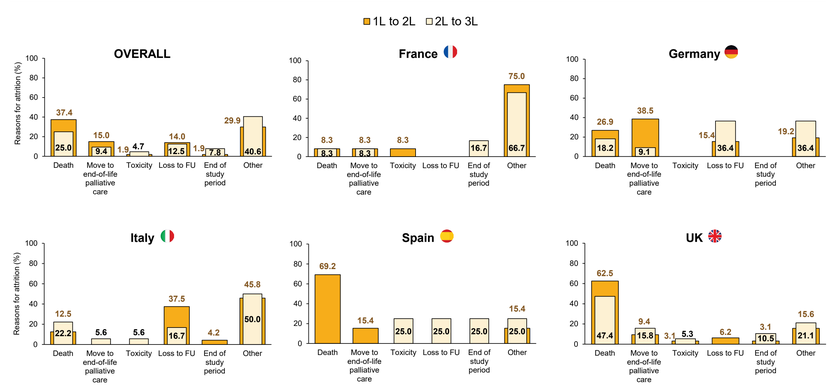
1L, first line; 2L, second line

Figure 2. Attrition rates between LOT



1L, first line; 2L, second line; 3L, third line; CI, confidence interval; LOT, line of therapy

Figure 3. Reasons for attrition between LOT*



*Main drivers behind the 'other' reasons for attrition category will be reported in the manuscript
1L, first line; 2L, second line; 3L, third line; FU, follow up; LOT, line of therapy

- Overall reasons for attrition were death (1L to 2L, 37.4% [n=40]; 2L to 3L, 25.0% [n=16]), move to end-of-life palliative care (1L to 2L, 15.0% [n=16]; 2L to 3L, 9.4% [n=6]), toxicity (1L to 2L, 1.9% [n=2]; 2L to 3L, 4.7% [n=3]), loss to FU (1L to 2L, 14.0% [n=15]; 2L to 3L, 12.5% [n=8]), end of study period (1L to 2L, 1.9% [n=2]; 2L to 3L, 7.8% [n=5]), and 'other' (1L to 2L, 29.9% [n=32]; 2L to 3L, 40.6% [n=26]) (**Figure 3**)
- Further details on 'other' reasons for attrition can be found in supplementary material (**Supplementary figure 3**)

References

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Disclosures

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