Poster 97

Treatment Discontinuation Among Patients with Stage IV HER2-Negative Breast Cancer: A Multisite Study in the United States

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Objective

- To describe treatment discontinuation among patients with stage IV HER2-negative breast cancer from 1st to 4th line of treatment (LOT) based on electronic medical records across three academic cancer centers in the United States

Conclusions

- The attrition rate of 20% to 30% of patients who discontinued treatment after each LOT without subsequent treatment was high among patients with stage IV HER2-negative breast cancer.
- The most effective treatment options should be used in earlier LOT in this patient population since patients may not receive subsequent LOT.

Plain language summary

Why did we perform this research?

Breast cancer that has spread beyond the breast and surrounding lymph nodes to other parts of the body is known as stage IV breast cancer. A protein called HER2 is used to determine treatment that is appropriate and effective in breast cancer and patients who have low levels or no HER2 are considered to have HER2-negative breast cancer.

Stage IV HER2-negative breast cancer can be treated but patients often need to stop and change treatments due to various reasons, such as failure to control the cancer growth and intolerable side effects. We performed this study to understand how and why patients with stage IV HER2-negative breast cancer stop treatment.

How did we perform this research?

We collected information about the treatment of patients with stage IV HER2-negative breast cancer at three different cancer centers. We described the percentage of patients who stopped treatment and the reasons of stopping treatment up to the fourth line of therapy, which refers to the order in which treatments are given.

What were the findings of this research?

More than three quarters of patients stop treatment at each line of therapy. Most patients stopped treatment because the cancer continued to grow. However, a substantial proportion of patients stopped treatment because of side effects that were intolerable. Among those who stopped treatment, around one-fifth to one-third do not receive a new treatment.

What are the implications of this research?

More effective treatment should be used as early as possible as some patients do not move on to a new treatment after stopping their previous therapy.

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Introduction

- Prior to the approval of trastuzumab deruxtecan in 2022, patients with stage IV HER2-negative breast cancer were ineligible for HER2-directed treatment but may require multiple LOTs.[1,2]
- At the time of study, treatment options for stage IV HER2-negative breast cancer typically include CDK4/6 inhibitors and endocrine therapy for hormone receptor-positive disease and systemic chemotherapy for hormone receptor-negative disease.[3,4]
- Patient attrition at different lines of treatment and reasons of treatment discontinuation can highlight potential treatment gaps but have not been well described in the literature.
- Using chart review of medical records, we were able to extract data on trends and reasons of treatment discontinuation that may not be available from claims databases.

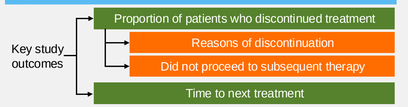
Methods

- Study design: Retrospective cohort study via chart review of electronic medical records
- Study period: 1 Jan 2017 to 31 Dec 2021. Patients were followed up from diagnosis of stage IV breast cancer until death, last follow up at the study site, or December 31, 2021, whichever occurred earlier
- Study sites: (i) Huntsman Cancer Institute, UT, (ii) H. Lee Moffitt Cancer Center, FL, and (iii) Winthrop P. Rockefeller Cancer Institute, AR contributed patient-level de-identified data
- Cohort identification: Based on International Classification of Disease codes and verified by review of clinical notes and pathology reports
- Ethics approval: This study was exempted from ethical review by the University of Utah Institutional Review Board

Table 1. Study eligibility criteria

Inclusion criteria
1. Diagnosis of stage IV breast cancer
2. Aged 18 years and older at diagnosis of stage IV breast cancer
3. Classified as HER2-negative, i.e.: • HER2 IHC 0: IHC 0 • HER2-low: IHC1+, IHC 2+/ISH-
4. Received at least one line of therapy for stage IV breast cancer between 1 Jan 2017 and 31 Dec 2020
5. ≥2 encounters on separate dates for breast cancer in study period
Exclusion criteria
1. Diagnosis of primary cancers other than breast cancer

Figure 1. Key study outcomes



- Treatment discontinuation was inferred from documentation in the clinical notes and verified based on pharmacy records.
- Time to next treatment was the interval between treatment start of consecutive lines of therapy and the median was estimated using Kaplan-Meier methods, with censoring at last follow-up or the end of study period, whichever earlier.

Results

Table 2. Patient characteristics

Characteristic/Variable	Overall (N = 232)	Hormone receptor-positive (N = 199)	Hormone receptor-negative (N = 33)
Age in years, median (IQR)	56.6 (47.8, 67.5)	56.6 (48.1, 67.1)	56.1 (45.2, 68.8)
HER2 expression, n (%)			
HER2 IHC 0	59 (25.4%)	45 (22.6%)	14 (42.4%)
HER2-low	173 (74.6%)	154 (77.4%)	19 (57.6%)
Histology type, n (%)			
Lobular	35 (15.1%)	33 (16.6%)	2 (6.1%)
Ductal	168 (72.4%)	144 (72.4%)	24 (72.7%)
Other	16 (6.9%)	11 (5.5%)	5 (15.2%)
Unknown	13 (5.6%)	11 (5.5%)	2 (6.1%)
Histology grade, n (%)			
Grade 1	15 (6.5%)	15 (7.5%)	0 (0.0%)
Grade 2	109 (47.0%)	104 (52.3%)	5 (15.2%)
Grade 3	87 (37.5%)	61 (30.7%)	26 (78.8%)
Unknown	21 (9.1%)	19 (9.5%)	2 (6.1%)
ECOG status, n (%)			
Grade 0 and 1	161 (69.3%)	137 (68.8%)	24 (72.7%)
Grade 2 and above	25 (10.7%)	22 (11.0%)	3 (9.1%)
Unknown	46 (19.8%)	40 (20.1%)	6 (18.2%)
Metastasis site(s)†, n (%)			
Brain	9 (3.9%)	7 (3.5%)	2 (6.1%)
Lung	45 (19.4%)	35 (17.6%)	10 (30.3%)
Liver	52 (22.4%)	42 (21.1%)	10 (30.3%)
Bone	176 (75.9%)	161 (80.9%)	15 (45.5%)
Others	52 (22.4%)	39 (19.6%)	13 (39.4%)

† Patients may have more than one site of metastasis

Table 3. Treatment regimens received from first to fourth line of therapy

Treatment regimens, n (%)	Line of therapy†			
	1st line	2nd line	3rd line	4th line
Hormone receptor-positive disease	**N = 199**	**N = 122**	**N = 70**	**N = 43**
Endocrine therapy and/or CDK4/6 inhibitors	112 (56.3%)	38 (31.1%)	13 (18.5%)	4 (9.3%)
Other combinations with endocrine therapy	12 (6.0%)	18 (14.8%)	8 (11.4%)	6 (14.0%)
Endocrine therapy alone	32 (16.1%)	28 (23.0%)	10 (14.3%)	4 (9.3%)
Chemotherapy alone	38 (19.1%)	28 (23.0%)	35 (50.0%)	22 (51.2%)
Others‡	5 (2.5%)	10 (8.2%)	4 (5.7%)	7 (16.3%)
Hormone receptor-negative disease	**N = 33**	**N = 22**	**N = 13**	**N = 7**
Chemotherapy alone	22 (66.7%)	17 (77.3%)	7 (53.8%)	4 (57.1%)
Combinations with chemotherapy	9 (27.3%)	2 (9.1%)	4 (30.8%)	1 (14.3%)
Others‡	2 (6.0%)	3 (13.6%)	2 (15.4%)	2 (28.6%)

† A new line of therapy is defined as a distinct change in the treatment regimen due to disease progression, adverse effects and/or patient preferences
‡ Others include immunotherapy and/or targeted therapy without endocrine therapy or chemotherapy

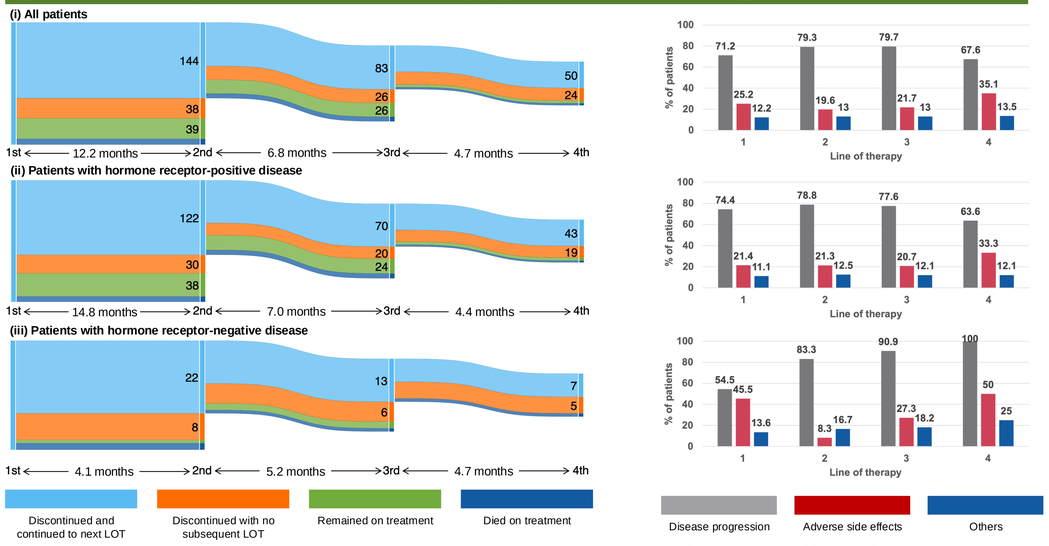
- A total of 232 pts were included in the analysis with 85.8% (n=199) presenting with hormone receptor-positive breast cancer (**Table 2**). Treatment regimens are shown in **Table 3**.
- At each line of therapy, more than 75% of patients discontinued treatment (**Table 4**), of which 20-30% did not receive subsequent therapy (1st LOT: 21%; 2nd LOT: 24%; 3rd LOT: 32%) (**Figure 2**).
- Among pts with documented reasons for discontinuation, disease progression was the most common reason, followed by adverse drug events between 19.6% and 35.1% (**Table 4, Figure 2**).
- TTNT decreased with LOT for pts with HR-positive BC from 14.8 months at 1st LOT to 7.0 and 4.4 months at 2nd and 3rd LOT, respectively and ranged between 4.1 to 5.2 months for those with HR-negative BC across LOT.

Table 4. Trends of treatment discontinuation from first to fourth line of therapy

Line of therapy	1st N = 232	2nd N = 144	3rd N = 83	4th N = 50
Median follow up from treatment start in months	27.2	13.9	8.1	5.1
Remained on treatment, n (%)	39 (16.8%)	26 (18.1%)	5 (6.0%)	6 (12.0%)
Died while on treatment, n (%)	11 (4.7%)	9 (6.3%)	4 (4.8%)	6 (12.0%)
Discontinued treatment, n (%)	**182 (78.4%)**	**109 (75.7%)**	**74 (89.2%)**	**38 (76.0%)**
With explicit reasons for discontinuation†, n (%)	139 (59.9%)	92 (63.9%)	69 (83.1%)	37 (74.0%)
Progression	99 (71.2%)	73 (79.3%)	55 (79.7%)	25 (67.6%)
Adverse drug events	35 (25.2%)	18 (19.6%)	15 (21.7%)	13 (35.1%)
Others‡	17 (12.2%)	12 (13.0%)	9 (13%)	5 (13.5%)

† Patients may have more than one reason for discontinuation
‡ Others include transition to supportive care, loss to follow-up, lack of insurance coverage and cessation of patient assistance program

Figure 2. Patient attrition (left) and reasons of discontinuation (right) from first to fourth line of therapy



Note: Bar width and labels indicate number of patients for each category while arrows beneath bars represent median time to next treatment

Note: Patients may have >1 reason of discontinuation. Others include transition to supportive care, loss to follow-up, lack of insurance coverage and cessation of patient assistance program

Abbreviations

CDK: Cyclin-dependent kinase
ECOG: Eastern Cooperative Oncology Group
HER2: Human epidermal growth factor receptor 2
IHC: Immunohistochemistry
IQR: Interquartile range
ISH: In-situ hybridization
LOT: line of therapy

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References

1. Vidal et al. 2022 Future Oncol; 18(7):849-858.
2. Kimura et al. 2024 Breast Cancer Res Treat;206(1):91-103.
3. Gradishar et al. 2020 J Natl Compr Canc Netw;18(4):452-478.
4. Gennari et al. 2021 Ann Oncol;32(12):1475-1495.