Poster P3-08-10

Real-world treatment patterns and clinical outcomes for patients with metastatic triple-negative breast cancer in the United States: an electronic health records observational study

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Objective

- To describe real-world treatment patterns and clinical outcomes for patients with metastatic TNBC in the United States.

Conclusions

- Clinical outcomes in patients with metastatic TNBC remain poor, particularly in patients who are ineligible for immunotherapy, including patients with PD-L1-negative disease.
- In patients with confirmed PD-L1-positive disease, around a third of patients did not receive 1L immunotherapy.
- Median OS in both the PD-L1-positive and PD-L1-negative populations was lower than that reported in clinical studies.[1,2]
- More than 40% of patients did not receive treatment beyond 1L, highlighting an unmet need to provide more effective, 1L targeted treatments, especially in those with PD-L1-negative metastatic TNBC.

Plain language summary

Why did we perform this research?

- Triple-negative breast cancer (TNBC), a type of breast cancer where cells do not have the HER2, estrogen, or progesterone receptors on the surface of their cells, has the worst outcomes of all types of breast cancer.
- Standard treatment for metastatic TNBC (TNBC that has spread from its original site) where the tumor cells have a protein called PD-L1 on their surface is pembrolizumab (a type of drug called immunotherapy, which makes cancer cells more susceptible to being killed by the immune system) plus chemotherapy.
- However, chemotherapy is the only option for people who are not eligible for or cannot tolerate pembrolizumab, and the outlook for these people is poor.
- In this analysis, we investigated the treatments being used in day-to-day clinical practice and the clinical outcomes for people with metastatic TNBC in the United States.

How did we perform this research?

- Researchers looked at anonymized health records of patients in a database, called the Flatiron Enhanced Datamart, for people diagnosed with metastatic TNBC between January 01, 2018 and June 30, 2023, who were treated for metastatic disease.
- The research continued until the people died, information stopped being added to the database or the analysis ended (November 30, 2023).
- The analysis captured information from 1044 people about their disease and the treatments they received.
- The length of time people lived from the date they were included in the analysis (real-world overall survival, rwOS), and the length of time people lived without their cancer getting worse (real-world progression-free survival, rwPFS) were also assessed.

What were the findings of this research?

- The most common type of treatment used was chemotherapy, given alone or in combination with immunotherapy.
- People who received immunotherapy had a longer time before their disease got worse and lived longer than people who did not receive immunotherapy.

What are the implications of this research?

- There is a need for new treatments for metastatic TNBC that are more effective compared with conventional chemotherapy.

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Poster presented at San Antonio Breast Cancer Symposium (SABCS) 2024; San Antonio, TX, USA; 10–13 December 2024

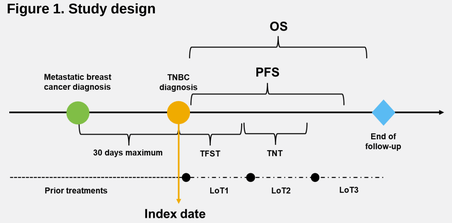
Introduction

- Survival outcomes for patients with metastatic TNBC whose tumors are PD-L1-positive have improved with the approval of immunotherapy in 2020.[1–3]
- In the phase 3 KEYNOTE-355 study, pembrolizumab + chemotherapy significantly improved median OS vs chemotherapy in patients with a PD-L1 CPS of ≥10.[1]
- However, there was no difference in median OS in patients with CPS <10,[1] and chemotherapy remains the standard of care for patients who have PD-L1-negative disease and for those who cannot receive immunotherapy.
- This study assessed real-world treatment patterns and clinical outcomes for patients with metastatic TNBC in the United States.

Methods

- This was a retrospective, observational study utilizing de-identified electronic health record data from the Flatiron Enhanced Datamart (**Figure 1**), which collates data from ~800 community and academic oncology centers across the US.
- Patients (≥18 years) diagnosed with metastatic TNBC between January 01, 2018 and June 30, 2023, who received at least one LoT were included.
  - Patients diagnosed with other primary cancers (except non-melanoma skin cancer) ≤3 years prior to metastatic TNBC diagnosis and patients enrolled in clinical trials were excluded.
- Patients were followed until date of death, last recorded activity in the Flatiron database, or data cutoff (November 30, 2023).
- Baseline and clinical characteristics, and treatments received were captured. rwOS (time from index date to date of death) and rwPFS (time from index date to date of the earliest progression event or death due to any cause) after diagnosis of metastatic TNBC and from the start of each LoT were calculated using the Kaplan–Meier method.

Figure 1. Study design



Primary endpoint:
- Type of drug given in LoT1

Secondary endpoints:
- Treatment patterns for LoT1–5
- Clinical outcomes by LoT

Results and interpretation

- The cohort comprised 1044 patients with metastatic TNBC.
- Median follow up from metastatic breast cancer diagnosis was 40.1 months (IQR 25.7–54.8).
- Median patient age was 61 years; approximately one-third of patients were diagnosed with de novo stage IV disease (**Table 1**).

Table 1. Patient baseline characteristics and demographics

Characteristic/demographic	Overall (N=1044)	Confirmed PD-L1+ (n=109)	Confirmed PD-L1− (n=258)
Median age, years (IQR)	61 (52–71)	59 (50–68)	60 (51–69)
Age group, n (%)			
<40 years	68 (6.5)	4 (3.7)	13 (5.0)
40–60 years	395 (37.8)	51 (46.8)	115 (44.6)
>60 years	581 (55.7)	54 (49.5)	130 (50.4)
Sex, n (%)			
Female	1036 (99.2)	108 (99.1)	256 (99.2)
Male	8 (0.8)	1 (0.9)	2 (0.8)
Race, n (%)			
White	544 (52.1)	57 (52.3)	137 (53.1)
Black or African American	226 (21.7)	24 (22.0)	57 (22.1)
Not reported	134 (12.8)	18 (16.5)	33 (12.8)
Other	116 (11.1)	8 (7.3)	24 (9.3)
Asian	21 (2.0)	2 (1.8)	7 (2.7)
Hispanic	3 (0.3)	0 (0)	0 (0)
Stage at initial breast cancer diagnosis, n (%)			
I	106 (10.2)	9 (8.3)	22 (8.5)
II	254 (24.3)	28 (25.7)	69 (26.7)
III	240 (23.0)	18 (16.5)	64 (24.8)
IV	369 (35.3)	46 (42.2)	82 (31.8)
Not reported	75 (7.2)	8 (7.3)	21 (8.1)

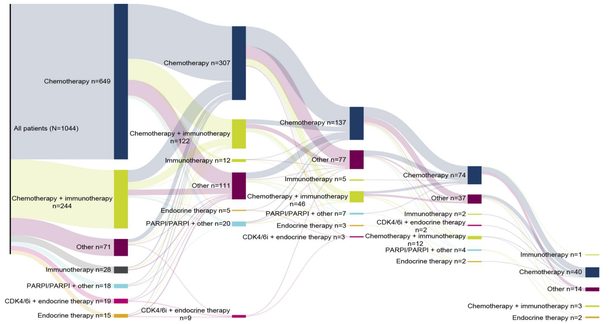
- Of the 1044 patients, 586 (56.1%) received 2L, 278 (26.6%) 3L, 133 (12.7%) 4L, and 60 (5.7%) 5L therapy.
- The most common drug class in all LoTs was chemotherapy given as monotherapy or in combination with immunotherapy: LoT1 85.5%, LoT2 73.2%, LoT3 65.8%, LoT4 64.7%, and LoT5 71.70% (**Table 2** and **Figure 2**).

Table 2. Treatment by LoT

Treatment, n	LoT1	LoT2	LoT3	LoT4	LoT5
Chemotherapy	649	307	137	74	40
Chemotherapy + immunotherapy	244	122	46	12	3
Targeted therapy, including ADCs[a]	47	82	61	27	11
Immunotherapy	28	12	5	2	1
ET +/- CDK4/6 inhibitor	34	14	6	4	2
PARPi mono or combination[b]	18	23	8	4	0
Other[c]	24	26	15	10	3

[a]Including sacituzumab govitecan: LoT1, n=45; Lot2, n=78; LoT3, n=60; LoT 4, n=27; LoT5, n=11.
[b]PARPi monotherapy or in combination with ET, chemotherapy, targeted therapy, immunotherapy, chemotherapy and immunotherapy, or CDK4/6 inhibitor and ET.
[c]Includes chemotherapy + targeted therapy, chemotherapy + ET, CDK4/6 inhibitor monotherapy, mTOR inhibitor monotherapy, chemotherapy + other cytoprotective, chemotherapy + ET + CDK4/6 inhibitor, ET + immunotherapy + targeted therapy, chemotherapy + CDK4/6 inhibitor, chemotherapy + ET + targeted therapy, ET + mTOR inhibitor, immunotherapy + targeted therapy, ET + PI3K inhibitor, chemotherapy + other agent, not reported, PI3K inhibitor, chemotherapy + ET + immunotherapy, and chemotherapy + immunotherapy + targeted therapy.

Figure 2. Treatment patterns over LoT[a]



[a]Patients who did not receive the next LoT because they were still receiving the prior LoT at the end of the study: 1L 10/1044 (0.96%), 2L 15/586 (2.6%), 3L 5/278 (1.8%), 4L 2/133 (1.5%), 5L 4/60 (6.7%).

- During the study period, more than 40% of patients did not receive 2L treatment. Of the 586 patients who did receive 2L, most received chemotherapy (n=307, 52.4%) or chemotherapy plus immunotherapy (n=122, 20.8%) (**Table 2** and **Figure 2**).
- From date of metastatic TNBC diagnosis, rwOS for the overall cohort was 14.0 months (95% CI 12.9–16.0); rwPFS was 5.8 months (95% CI 5.4–6.3) (**Figure 3** and **4**).
- Median rwOS (12.7 months) and rwPFS (4.9 months) were shorter for patients who had PD-L1-negative disease than for those who had PD-L1-positive disease (18.6 months and 7.1 months, respectively) (**Figure 3** and **4**).
- Among patients with confirmed PD-L1 status (n=367), 109 (29.7%) were PD-L1-positive and 258 (70.3%) were PD-L1-negative.
- From January 01, 2021 onwards, immunotherapy was received by 33/39 (84.6%) patients with PD-L1-positive tumors, of whom 21/33 (63.6%) received immunotherapy in LoT1 (**Table 3**).

Table 3. Immunotherapy by LoT and rwOS for confirmed PD-L1 status patients (on or after Jan 2021)

	PD-L1+	PD-L1−
Patients with confirmed PD-L1 status, n	39	119
Number of patients who received immunotherapy, n (%)	33 (84.6)	19 (16.0)
Immunotherapy received in		
LoT1	21 (63.6)	16 (84.2)
LoT2	9 (27.3)	1 (5.3)
LoT3	3 (9.1)	2 (10.5)

- Median rwOS was longer for patients with PD-L1-positive tumors who received immunotherapy (18.6 months [95% CI 15.2–26.3]) than for those who did not (15.5 months [95% CI 8.3–not estimable]).

Limitations

- The database does not capture reasons for treatment discontinuation in a LoT other than progression or death.
- rwPFS is based on physician assessment rather than RECIST criteria.

Figure 3. rwOS for the overall cohort and by PD-L1 status

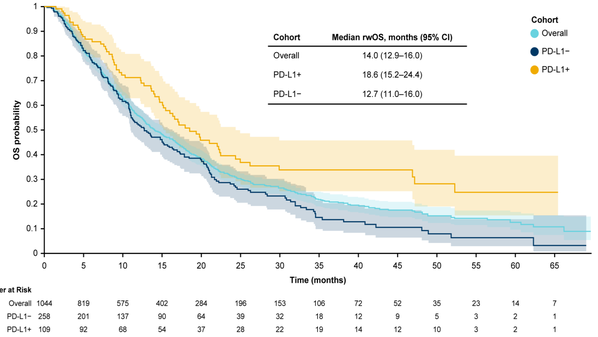
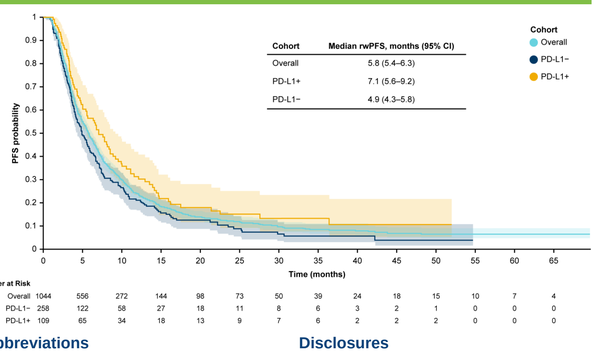


Figure 4. rwPFS for the overall cohort and by PD-L1 status



Abbreviations

1L, first-line; 2L, second-line; 3L, third-line; 4L, fourth-line; 5L, fifth-line; ADC, antibody-drug conjugate; CDK4/6, cyclin dependent kinase 4/6; CPS, combined positive score; HER2, human epidermal growth factor receptor 2; ET, endocrine therapy; IQR, interquartile range; LoT, line of therapy; mTOR, mammalian target of rapamycin; OS, overall survival; PARPi, PARP inhibitor; PD-L1, programmed death-ligand 1; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; rwOS, real-world overall survival; rwPFS, real-world progression-free survival; TFST, time to first subsequent therapy; TNBC, triple-negative breast cancer; TNT, time to next therapy.

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Disclosures

Dr Traina has acted as a consultant or advisor for AstraZeneca, Daiichi Sankyo, Exact Sciences, G1 Therapeutics, Genentech/Roche, Gilead Sciences, GlaxoSmithKline, Hengrui Pharmaceutical, Merck, Pfizer, Stemline Therapeutics, and TerSera; has received research funding (to institution) from Astellas Pharma, AstraZeneca, Ayala Pharmaceuticals, Daiichi Sankyo, Genentech/Roche, and Pfizer. Please refer to the associated abstract for co-author disclosures.

Acknowledgments

The study was funded by AstraZeneca. Medical writing support for the development of this poster, under the direction of the authors, was provided by Mark Holland of Ashfield MedComms (Macclesfield, UK), an Inizio company, and funded by AstraZeneca.