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Olaparib Use and gBRCA Testing among selected HER2-Negative Early-Stage Breast Cancer Patients in the United States Community Oncology Setting

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Background

- Breast cancer (BC) is the most common form of cancer in the US.[1]
- Overall, women have a 2% likelihood of inheriting a pathogenic mutations in breast cancer susceptibility gene 1 (BRCA1) or breast cancer susceptibility gene 2 (BRCA2) gene(s), 10% among women with breast cancer prior to age 40.[2]
- BRCA mutations are associated with a >60% lifetime risk of developing BC, compared to approximately 13% for women in the general population.[3]
- Current guidelines recommend germline BRCA (gBRCA) testing for all newly-diagnosed patients with breast cancer ≤ 65 years and select patients >65 years based on personal history, family history, and/or ancestry, or eligibility for poly (ADP-ribose) polymerase inhibitor (PARPi) therapy [4]
- Olaparib, approved in 2022, is a PARP indicated for the adjuvant treatment of patients with deleterious or suspected deleterious germline BRCA genetic mutations (gBRCAm), HER2-negative, high-risk early breast cancer (eBC) who have been treated with neoadjuvant or adjuvant chemotherapy.[5-6]

Objective

- This retrospective to describe the contemporary real-world landscape among HER2-negative eBC patients who were either olaparib treated, gBRCA mutated+geneomic risk tested, or had high genomic risk in the community oncology setting with regard to biomarker testing (including gBRCA), treatment patterns, and olaparib uptake.

Methods

- Data were sourced from structured and unstructured fields in the iKnowMed™ (iKM) oncology-focused electronic health record system, implemented across The US Oncology Network, which includes 1.4 million patients treated annually.[7]
- Retrospective observational study among adult HER2-negative eBC (stage I-III) patients who initiated systemic adjuvant treatment between 01 Jan 2020 – 31 Oct 2024 (adjuvant treatment initiation date as index date).
- Patient selection was conducted in a stepwise method, prioritizing patients who:
  - initiated olaparib, followed by
  - non-olaparib patients who received BRCA and genomic risk testing (Oncotype DX [ODX] or Mammaprint), followed by
  - non-olaparib patients with a high genomic risk score (defined as ODX≥25 or High Mammaprint result).
- Exclusion criteria: hormone therapy only adjuvant treatment, evidence of metastatic BC on or prior to index date, post-index date clinical trial enrollment, treatment of other primary cancers in the 3-year period prior to eBC diagnosis, HER2+ result within 90 days of first eBC-related treatment
- Patient and treatment characteristics, including biomarker and testing patterns, were assessed descriptively, overall and by gBRCA status and olaparib receipt.

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Results

Table 1. Selected demographic and clinical characteristics among olaparib users or non-olaparib users with gBRCAm+genomic risk testing or high genomic risk

	Overall N=251	Olaparib N=34	Non-olaparib N=217
Age at baseline (years), mean (SD)	55.3 (12.4)	46.7 (12.1)	56.6 (12.0)
Race, N (%)			
White	155 (61.8)	21 (61.8)	134 (61.8)
Black/Asian/Other	61 (24.3)	8 (23.5)	53 (24.4)
Not documented	35 (13.9)	5 (14.7)	30 (13.8)
Stage at initial BC diagnosis, N (%)			
I	22 (8.8)	8 (23.5)	14 (6.5)
II	210 (83.7)	23 (67.7)	187 (86.2)
III	19 (7.6)	3 (8.8)	16 (7.4)
Family history (yes), N (%)	205 (81.7)	31 (91.2)	174 (80.2)
HR status, N(%) *			
TNBC	27 (10.8)	16 (47.1)	11 (5.1)
HR+	222 (89.2)	18 (52.9)	204 (94.9)
Duration of follow-up from index date (months), mean (SD)	32.5 (12.9)	25.7(15.2)	33.6 (12.2)
Index Year, N (%)			
2020-2021	159 (63.3)	14 (41.2)	145 (66.8)
2022-2024	92 (36.7)	20 (58.9)	72 (33.2)

Table 2. gBRCA testing among HER2-negative eBC patients among olaparib users or non-olaparib users with gBRCAm+genomic risk testing or high genomic risk

	gBRCA tested (N=166)	gBRCA mutation (n=42)	gBRCA not tested (N=85)
HR status, N (%) *			
HR+	143 (86.1)	24 (57.1)	79 (95.2)
TNBC	23 (13.9)	18 (42.9)	4 (4.8)
gBRCA testing after adjuvant therapy initiation, N (%)	19 (11.4)	1 (2.4)	--
Olaparib initiation, N (%)	34 (20.5)	32 (76.2)	0 (0)

- A total of 251 patients met the eligibility criteria (222 HR+, 27 TNBC, 2 HR untested).The majority of patients (n=216, 97.3%) were high genomic risk (ODX or Mammaprint)
  - 206 HR+ patients were categorized as high genomic risk
- Compared to the overall cohort, olaparib users were younger (46.7 vs. 55.3 years), were more likely to have a family history of cancer (91.2% vs. 81.7%) and had a higher proportion of TNBC patients (41.7% vs. 10.8%).

Disclosures

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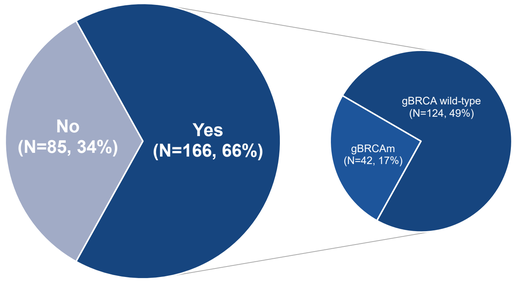
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Figure 1. gBRCA testing among HER2-negative eBC patients among olaparib users or non-olaparib users with gBRCAm+genomic risk testing or high genomic risk



- Among olaparib users or non-olaparib users with gBRCAm+genomic risk testing or high genomic risk, approximately one-third (34%) of patients did not receive BRCA testing.
- 12% (n=19) of patients received testing after adjuvant therapy initiation
  - 1 of the 19 (5.3%) patients with delayed gBRCA testing had a record of gBRCA mutation.
- All patients who received olaparib (n=34) received gBRCA testing.
  - 2 patients with gBRCAwt received olaparib
- The median (Q1,Q3) time from gBRCA result date to olaparib initiation date was 8.8 (6.7, 12.6) months.
  - Pre-approval [n=10]:10.7 (9.1, 16.3) months
  - Post-approval (March 11, 2022) [n=21]: 8.0 (6.5, 9.6) months

Conclusions

- Despite utilizing patient selection methods that prioritized olaparib users as well as patients tested for BRCA and genomic risk, olaparib uptake in the real-world is limited among HER2-negative eBC patients.
- Eligibility for olaparib is dependent upon having a BRCA mutation, but findings show that one-third of patients, especially HR+ patients, did not receive gBRCA testing among selected patients who initiated systemic adjuvant treatment for HER2-negative eBC.
  - Other studies among HER2-negative eBC patients from US community practices demonstrated gBRCA testing rates of 46% [8]
- Current guidelines recommend gBRCA testing for all patients with BC, and as a result, there is an opportunity to improve gBRCA testing rates and timing to identify additional patients who may be eligible for and benefit from targeted treatment such as olaparib.

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