RWD88

Real-World Treatment Patterns, Genetic Testing, and Clinical Outcomes among Patients with mCRPC Treated with Olaparib Monotherapy in US Urology Clinics

Neal Shore, MD[1], Chinelo Orji[2], Kumar Mukherjee[3], Lorraine O'Donnell[4], Audrey Himes[4], Lai Peng[4], Katie Grant[4], James Eller[4], Sameer R. Ghate[2]

1. Carolina Urologic Research Center 2. Merck & Co., Inc., Rahway, NJ, USA 3. AstraZeneca Pharmaceuticals LP, 4. Specialty Networks, a Cardinal Health Company

Background

- Olaparib is an approved PARP inhibitor (PARPi) for treating metastatic castration-resistant prostate cancer (mCRPC), in patients with HRR mutations (HRRm) following treatment with abiraterone acetate with prednisone or enzalutamide.[1,2]
- Despite its approval in 2020, there is limited real-world evidence on olaparib's effectiveness as monotherapy for mCRPC.
- In addition, the timing of genetic testing in anticipation of disease progression is vital to evaluate candidates for PARPi therapy to maximize patient outcomes.[3,4]

Objectives

The objective of the study was to describe baseline patient characteristics, treatment patterns, genetic testing patterns, and clinical outcomes among patients with mCRPC having positive HRRm status who were treated with olaparib monotherapy following prior treatment with enzalutamide and/or abiraterone.

Methods

Data Source

- Retrospective analysis using Specialty Networks Uro-oncology de-identified US-community based electronic medical record (EMR) database, PPS Analytics Patient Population Health Management Platform.
- Database contains structured data from EMR, practice management, dispensing, and imaging systems. Unstructured data were curated from medical charts (clinical progress notes, radiology, and genomic records) accessed by highly trained clinical analysts.

Patient eligibility

- Patients diagnosed with mCRPC who received olaparib monotherapy between June 2020 and December 2023.
- All patients received abiraterone or enzalutamide following initial prostate cancer diagnosis and prior to olaparib monotherapy.
- All patients had documentation of at least one positive HRRm (*BRCA1, BRCA2, ATM, BRIP1, BARDI1, CDK12, CHEK1, CHECK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, RAD54L*).

Study Period

- Pre-index period: 6 months before patient's index therapy
- Index date (olaparib therapy start date): 06/01/20-12/31/23
- Variable follow-up period: 06/01/20-03/31/24

Study endpoints

- Included treatment patterns, real-world time on treatment (rwToT), real world progression-free survival (rwPFS), and real-world overall survival (rwOS).
- Results were stratified by treatment regimen received pre-olaparib (chemotherapy pre-olaparib versus no chemotherapy received pre-olaparib), line of therapy (LOT) in which earliest olaparib monotherapy was received, and by non-*BRCA* HRRm/*BRCAm* status.

Results

Demographics

- 200 patients, median age 74.5 years
- 68.5% White, 18.4% African American, 13% Other/Unknown

Treatment Patterns

- Figure 1: Pre-mCRPC therapies included androgen receptor pathway inhibitors (ARPIs) (abiraterone, enzalutamide, apalutamide, and darolutamide) in 45% of the cohort.
- Table 1: Provides the most common treatment regimens and sequences pre- and post-olaparib.
- Median rwToT was 7 months.

Testing Patterns

- Table 2: 41.5% tested *BRCA*-positive (*BRCA1* 6%, *BRCA2* 27.5%, and co-mutation with *non-BRCA* HRRm 8%).
- Figures 2 & 3: 11% had somatic testing, 89% germline testing, and only 17% were tested prior to mCRPC diagnosis.

Clinical Outcomes

- Median rwOS in months: Overall 19.8 months
  - Received chemotherapy pre-olaparib, 15.9 months
  - Did not receive chemotherapy pre-olaparib, 20.5 months (Figure 4)
- Median rwPFS in months: Overall 12.9 months
  - Received chemotherapy pre-olaparib, 12.6 months
  - Did not receive chemotherapy pre-olaparib, 13.3 months (Figure 5)
- Figure 6: Olaparib monotherapy was used primarily in 2L+ mCRPC (92.5%)

Table 1. Immediate treatment regimen pre- and post-olaparib monotherapy (N=200)

Most Common Treatment Sequences	N (%)
enzalutamide -> olaparib -> no additional treatment[a]	8 (4%)
abiraterone -> olaparib -> no additional treatment	16 (8%)
enzalutamide/sipuleucel-T -> olaparib -> no additional treatment	13 (6.5%)
enzalutamide/olaparib -> olaparib -> no additional treatment	7 (3.5%)
enzalutamide -> olaparib -> docetaxel	6 (3%)
abiraterone/sipuleucel-T -> olaparib -> no additional treatment	5 (2.5%)
docetaxel -> olaparib -> no additional treatment	5 (2.5%)

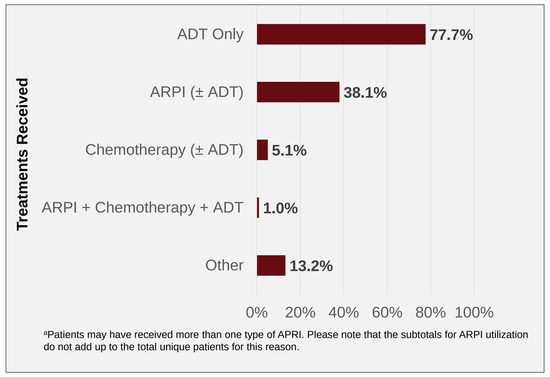
[a]Most common treatment regimen post-olaparib was no additional treatment (59%), which also included patients who died, were lost to follow-up, or who were still receiving olaparib monotherapy at the end of the study period.

Table 2. Most common genetic mutations identified among patients (N=200)

Positive Mutation[a]	N (%)
Any *BRCA*	83 (41.5%)
BRCA1 only	12 (6%)
BRCA2 only	55 (27.5%)
Co-mutation with *non-BRCA* HRRm	16 (8%)
Non-BRCA HRRm	133 (66.5%)
ATM only	54 (27%)

[a]Does not equal 100% because of co-mutations

Figure 1. Treatments received pre-mCRPC (N=197)



[a]Patients may have received more than one type of APRI. Please note that the subtotals for ARPI utilization do not add up to the total unique patients for this reason.

Figure 2. Type of genetic testing specimen

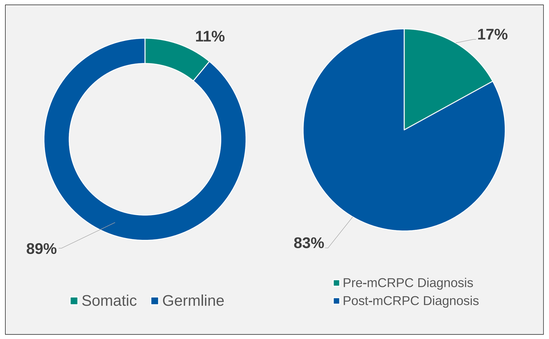


Figure 3. Timing of genetic testing relative to mCRPC diagnosis

Figure 4: Real-world Overall Survival KM Analysis by Chemotherapy Received before Olaparib

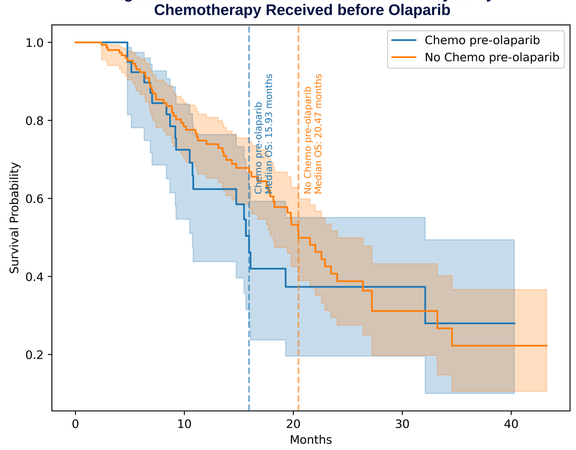


Figure 5: Real-world Progression Free Survival KM Analysis by Chemotherapy Received before Olaparib

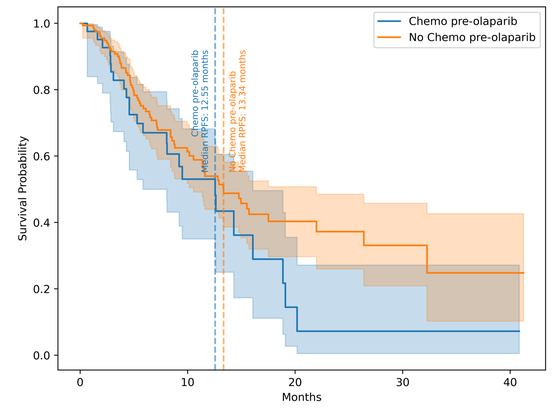
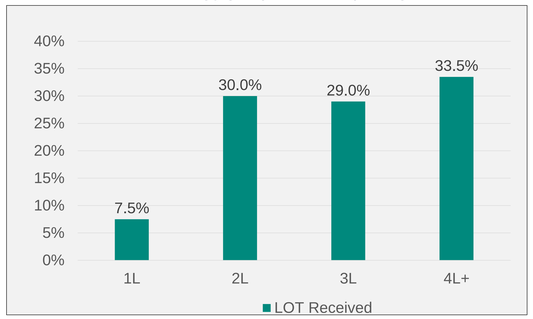


Figure 6. Earliest olaparib monotherapy received by Line of Therapy (LOT) in mCRPC (N=200)



Conclusions

This study highlights significant opportunities to improve treatment and genetic testing patterns for patients with mCRPC. According to this real-world data study, the majority of patients with HRRm mCRPC treated with olaparib monotherapy received ADT only as treatment pre-mCRPC. These data also demonstrate suboptimal genetic testing practices, and a delay in care with most patients receiving olaparib monotherapy in 2L or later.

Earlier treatment with olaparib monotherapy may improve rwOS in patients with mCRPC who have progressed after receiving an ARPI. Results from these real-world community urology data show that patients derived clinical benefit with olaparib, despite the delayed use of olaparib in later lines of therapy.

Study Limitations

rwOS and rwPFS may be understated due to the overall study period and the extended index period to ensure adequate sample size. This study also only included patients treated for mCRPC with olaparib monotherapy, and did not include combination therapy. Data from this study were obtained from a private practice urology network, where the clinical practice approach may be different. The findings may not be generalizable.

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Contact information

Chinelo Orji, PhD
Assoc. Dir., Outcomes Research
Merck & Co., Inc., Rahway, NJ, USA
chinelo.orji@merck.com

https://bit.ly/4cUJETq

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