MP01-10

Homologous recombination repair mutations, next-generation sequencing testing, and time-to-next-treatment by race among patients with metastatic castration-sensitive prostate cancer

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Key Takeaways

- NGS testing rates for deleterious HRR mutations, including *BRCA*, among patients treated for mCSPC have increased from 8.8% in 2018 to 29.0% in 2023. Similarly, of those receiving a test, the proportion receiving the first NGS test while castration-sensitive has increased from 35% to 87% during this same period
- Although NGS testing has become more prevalent and has occurred during earlier stages among those tested, testing rates remain suboptimal in identifying patients who could benefit from PARP inhibitor therapy

Conclusions

- *BRCA* mutations were the most common HRR mutation observed, and regardless of race, patients with mCSPC harboring *BRCA* mutations progressed to subsequent treatment more rapidly, suggesting an unmet need for these patients
- NGS testing rates have increased in recent years with less racial disparity, but remain suboptimal for patients with mCSPC, overall, and across race groups, reducing the opportunity to benefit from newly available PARP inhibitors

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Poster

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Acknowledgements
This study was sponsored by Johnson & Johnson.

Disclosures
M.A. Bilen, B. Lowentritt, and G. Brown received consulting fees from Johnson & Johnson. S. Burbage and I. Khilfeh are employees and stockholders of Johnson & Johnson. C. Rossi, L. Diaz, G. Wong, Y. Wang, and D. Pilon are employees of Analysis Group, Inc., a consulting company that has provided paid consulting services to Johnson & Johnson.

Background

- Homologous recombination repair (HRR) gene mutations, particularly *BRCA1* or *BRCA2* (hereafter "*BRCA+*") are associated with more adverse clinical outcomes among patients with advanced prostate cancer (PC)[1,2]
- Novel therapies such as poly ADP-ribose polymerase (PARP) inhibitors (i.e., niraparib, olaparib, talazoparib, and rucaparib) have been approved for patients with metastatic castration-resistant prostate cancer (mCRPC) in the US, with clinical trials ongoing for their use in metastatic castration-sensitive prostate cancer (mCSPC)[3,4]
- Targeted treatment is optimal when genetic mutations are detected early in the disease course before progression, but widespread, timely testing remains a challenge
- While the existence of racial and socioeconomic disparities in PC care and survival is well known, there is limited evidence evaluating race-stratified treatment patterns and testing in the mCSPC setting[5]

Objective

- This study describes time-to-next-treatment (TTNT) and next-generation sequencing (NGS) testing rates for HRR gene mutations among patients with mCSPC, overall, and by race

Methods

Data source

- Data from oncology centers included in the nationwide (US-based) Flatiron Health-Foundation Medicine, Inc. (FMI) Metastatic PC Clinico-Genomic Database (CGDB; 1 January 2011 to 31 December 2022) and Core Registry (1 January 2013 to 31 December 2023) were evaluated
- Data were de-identified and Health Insurance Portability and Accountability Act (HIPAA) compliant
- Flatiron Health, Inc. and FMI did not participate in data analyses

Study design

- A retrospective longitudinal cohort study design was used
- Patients receiving their first treatment for mCSPC were included if they had results from ≥1 HRR mutation test and:
  1. The start date of an advanced PC treatment (e.g., androgen receptor pathway inhibitors [ARPIs], chemotherapy) after the date of metastasis detection was on or after 1 January 2018 (index date)
  2. The start date of ADT monotherapy was on or after 1 January 2018, with the index date defined as the latter of ADT initiation or the date of metastasis detection
- Patients were classified as HRR+ based on testing results for both germline and somatic mutations, observed prior to the index date as well as those post-index until castration resistance progression, if observed
  - The following HRR mutations were assessed: *BRCA1, BRCA2, BRIP1, CHEK2, FANCA, PALB2, RAD51B, RAD54L*
- Annual NGS testing rates were assessed among patients with mCSPC in the Core Registry from 2018 to 2023

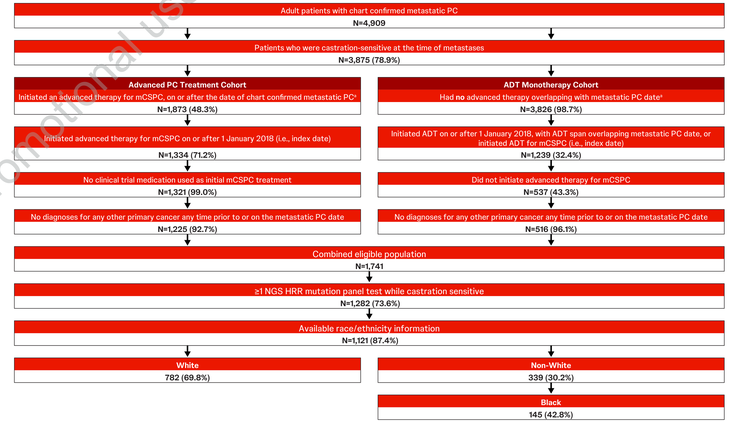
Patient selection criteria

- The inclusion and exclusion criteria used to select patients with mCSPC from the CGDB are shown in **Figure 1**

Study outcomes

- TTNT was defined as the time from first mCSPC treatment (index date) to the start of a subsequent therapy, including the use of clinical trial medication, with follow-up censored at the earliest of end of clinical activity or data availability (31 December 2022)
  - TTNT was assessed using Kaplan-Meier analyses and stratified among White, non-White (i.e., Black, Asian, Hispanic, other) and Black subgroups
  - TTNT was only assessed among patients with advanced PC treatment (i.e., excluded ADT monotherapy patients)
- Annual NGS testing rates were also stratified by race-specific subgroups

Figure 1: Sample Selection



ADT: androgen deprivation therapy; HRR: homologous recombination repair; mCSPC: metastatic castration-sensitive prostate cancer; NGS: next-generation sequencing; PC: prostate cancer.
Note: a. Not mutually exclusive.

Results

Patient characteristics

- A total of 1,121 patients with mCSPC were included, of whom 782 (69.8%) were White, 339 (30.2%) Non-White, and 145 (12.9%) were Black (**Table 1**)
- The prevalence of HRR mutations, including *BRCA*, was highest for White patients (17.4%), followed by non-White (16.5%) and Black patients (15.2%)

Table 1: Patient Characteristics

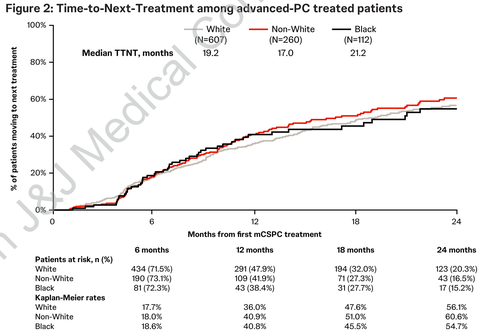
	White patients N = 782	Non-White patients N = 339	Black patients N = 145
***Patient characteristics*[a]**			
Age, years, mean ± SD [median]	70 ± 9 [70]	68 ± 9 [68]	66 ± 9 [66]
Insurance plan type, n (%)			
Commercial	289 (37.0)	142 (41.9)	68 (46.9)
Medicare	316 (40.4)	100 (29.5)	35 (24.1)
Medicaid	11 (1.4)	20 (5.9)	13 (9.0)
Dual coverage	3 (0.4)	6 (1.8)	4 (2.8)
Unknown	163 (20.8)	71 (20.9)	25 (17.2)
Practice type, n (%)			
Community only	570 (72.9)	287 (84.7)	125 (86.2)
Academic only	177 (22.6)	26 (7.7)	16 (11.0)
Both academic and community	35 (4.5)	26 (7.7)	4 (2.8)
Time from metastatic diagnosis to index date,[b] days, mean ± SD [median]	148.5 ± 266.3 [56.0]	182.7 ± 379.3 [63.0]	182.5 ± 383.7 [61.0]
Year of index date, n (%)			
2018	129 (16.5)	47 (13.9)	20 (13.8)
2019	181 (23.1)	80 (23.6)	30 (20.7)
2020	182 (23.3)	77 (22.7)	26 (17.9)
2021	183 (23.4)	85 (25.1)	42 (29.0)
2022	107 (13.7)	50 (14.7)	27 (18.6)
***HRR mutation testing*[c]**			
Metastatic disease at first test, n (%)	760 (97.2)	333 (98.2)	143 (98.6)
Time from metastatic date to first test (days), mean ± SD [median]	324 ± 394 [141]	340 ± 414 [173]	350 ± 454 [173]
HRR positive	136 (17.4)	56 (16.5)	22 (15.2)
BRCA1/2 positive	99 (12.7)	37 (10.9)	14 (9.7)
Type of mutation[d], n (%)			
Somatic	54 (39.7)	21 (37.5)	10 (45.5)
Germline	42 (30.9)	9 (16.1)	3 (13.6)
Unknown	13 (9.6)	9 (16.1)	2 (9.1)
Missing	47 (34.6)	20 (35.7)	8 (36.4)

BRCA1/2: *BRCA1* or *BRCA2*; HRR: homologous recombination repair; SD: standard deviation.
Notes: a. Patient characteristics were evaluated on the index date, with the exception of time from metastatic diagnosis to index date, which was evaluated based on the first observed metastatic diagnosis in the data. b. Only calculated among patients treated with an advanced PC therapy. c. Mutation testing was assessed any time prior to castration-resistance, if observed. d. Mutation types were assessed among HRR positive patients. Mutation types are not mutually exclusive as patients could have multiple mutation tests. Mutation types were classified as unknown if explicitly stated, and as missing if they were unavailable.

Time-to-Next-Treatment

- Non-White patients had the shortest median TTNT (17.0 months), followed by White (19.2 months) and Black patients (21.2 months) (**Figure 2**)
- Among all patients, those with *BRCA* mutations had numerically shorter TTNT (White: 13.4 months, Non-White: 9.9 months, Black: 15.7 months) relative to those without HRR mutations (White: 19.4 months, Non-White: 18.4 months, Black: 19.2 months)

Figure 2: Time-to-Next-Treatment among advanced-PC treated patients



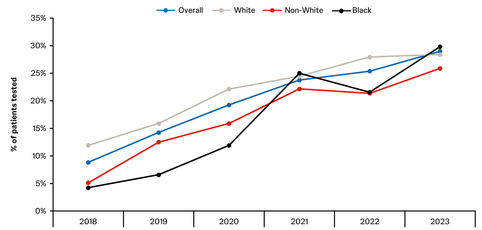
	6 months	12 months	18 months	24 months
Patients at risk, n (%)				
White	434 (71.5%)	291 (47.9%)	194 (32.0%)	123 (20.3%)
Non-White	190 (73.1%)	109 (41.9%)	71 (27.3%)	43 (16.5%)
Black	81 (72.3%)	43 (38.4%)	31 (27.7%)	17 (15.2%)
Kaplan-Meier rates				
White	17.7%	36.0%	47.6%	56.1%
Non-White	18.0%	40.9%	51.0%	60.6%
Black	18.6%	40.8%	45.5%	54.7%

mCSPC: metastatic castration-sensitive prostate cancer; TTNT: time-to-next-treatment.
Note: a. TTNT was censored at the end of the observation period (i.e., end of clinical activity or data availability).

NGS testing rates

- Annual NGS testing rates among treated patients with mCSPC increased between 2018 and 2023, but were higher among White (11.9% to 28.4%) relative to non-White patients (5.1% to 25.9%) (**Figure 3**)

Figure 3: Annual NGS Testing Rates[a]

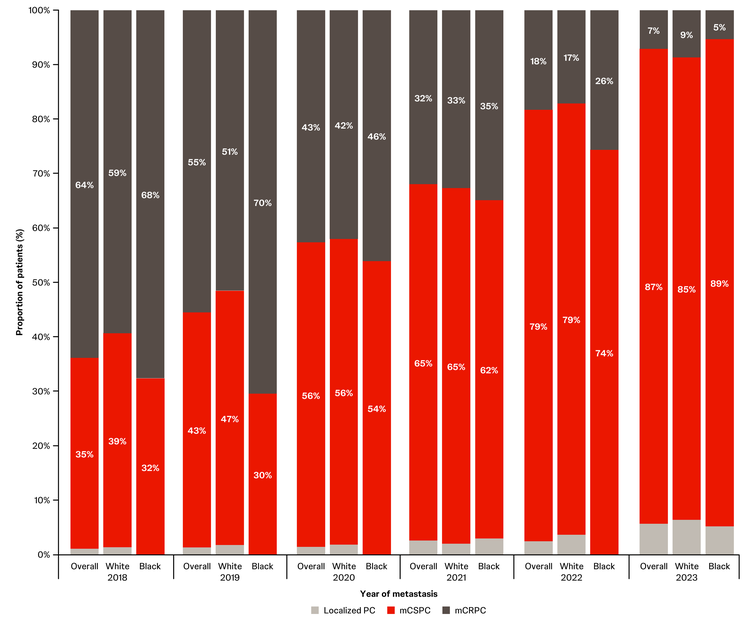


	2018	2019	2020	2021	2022	2023
Overall	8.8%	14.2%	19.2%	23.7%	25.4%	29.0%
White	11.9%	15.9%	22.1%	24.4%	27.9%	28.4%
Non-White	5.1%	12.5%	15.9%	22.2%	21.4%	25.9%
Black	4.2%	6.6%	11.9%	25.0%	21.5%	29.8%

CGDB: Clinico-Genomic Database; HRR: homologous recombination repair; NGS: next-generation sequencing.
Note: a. To evaluate NGS testing rates, untested patients were selected from the Core Registry using the same criteria used to select tested patients from the CGDB. However, patients were required to have no evidence of an NGS HRR mutation test prior to or on the index date.

- Overall, the proportion of patients initially tested with NGS while castration-sensitive has increased from 35% in 2018 to 87% in 2023 (**Figure 4**)

Figure 4: Disease Stage at Time of First NGS Test, by Calendar Year of Metastasis



mCSPC: metastatic castration-sensitive prostate cancer; mCRPC: metastatic castration-resistant prostate cancer; NGS: next-generation sequencing; PC: prostate cancer.

Limitations

- This study relied upon clinical data, which, like other real-world data sources, may contain inaccuracies or omissions (e.g., specimen collection dates, HRR mutation positivity rates, treatment start dates) and does not capture any diagnoses, testing services, or prescription fills obtained outside of the oncology network
- HRR mutation testing performed outside of Foundation Medicine testing will not be captured in the CGDB, thus potentially underestimating or overestimating the percentage of HRR positive patients with mCSPC

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Prostate Cancer

Presented at the American Urological Association (AUA) Annual Meeting 2025; April 26–29, 2025; Las Vegas, Nevada