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Homologous recombination repair mutation testing patterns in metastatic castration-resistant prostate cancer: analysis of real-world data in the United States

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Background

- Approximately 25% of patients with metastatic castration-resistant prostate cancer (mCRPC) harbor homologous recombination repair mutations (HRRm)[1, 2].
- HRRm have been associated with an increased risk of death[3].
- Clinical trials of poly-ADP polymerase inhibitors (PARPi) alone or in combination with androgen receptor pathway inhibitors have demonstrated superior outcomes when treating HRRm mCRPC[4-6].
- Despite multiple clinical practice guidelines that detail the importance of broad HRRm testing in mCRPC[7, 8], real-world data on HRRm testing in the United States of America (US) remains limited, thereby making it difficult to assess its utility in the real world.

Objective

- To assess real-world HRRm testing patterns in the US among patients with mCRPC.

Materials and Methods

DATA SOURCE

- Data were drawn from the Adelphi Real World Metastatic Prostate Cancer (mPC) Disease Specific Programme (DSP)™, an independent cross-sectional survey, including chart reviews and elements of retrospective data collection, of physicians and their consulting patients with mCSPC and mCRPC in the US between November 2022 – July 2023.
- The DSP methodology has been previously published[9, 10], validated[11] and proven to be representative over time[12].
- Inclusion criteria for physicians in the DSP included: a specialty in medical oncology or urology; saw ≥ four patients with mPC per month; and personally responsible for prescribing decisions.
- Inclusion criteria for patients in the DSP included: ≥ 18 years old at diagnosis; received active drug treatment for their mPC at data collection; and had never participated in a clinical trial.
- Physicians first completed an attitudinal survey reporting their specialty and clinical trials experience.
- Physicians then completed electronic patient record forms for their next eight consecutive patients with mCRPC; reporting patient demographics/clinical characteristics, patient insurance status and whether the patient was tested for mutations in at least one of ten HRR genes of interest (ATM, ATR, BRCA1, BRCA2, CDK12, CHEK2, FANCA, NBN, PALB2, RAD51C).
- Patient insurance was grouped into two types: public insurance included Medicaid/Medicare/Tricare and private insurance included any privately arranged/commercial insurance.

ANALYSIS

- Variables were analyzed both descriptively and stratified by their HRRm testing status at the point of data collection: HRRm tested and not HRRm tested.
- A logistic regression was also used to assess the impact of these variables on the likelihood of the patient receiving an HRRm test.

Conclusion:

Despite guideline recommendations and the therapeutic and prognostic value of HRRm testing, nearly half of the patients with mCRPC in the US were not tested. Statistically significant testing disparities were noted across several clinical and demographic characteristics. These findings highlight a continuing need to increase HRRm testing in the US.

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Presenting author: Dr. Pedro Barata

Results

- Data on 448 patients with mCRPC was provided by 70 physicians (49 medical oncologists and 21 urologists).
- HRRm testing was received by 53% (236/448) of patients (**Figure 1**).
- 'At mPC diagnosis' was the most commonly reported timepoint of testing, recorded for 23% of all patients (**Figure 2**).
- Logistic regression found that patients with metastatic disease at initial diagnosis (odds ratio [OR] 0.41), no known family history of HRRm-related cancer (OR 0.40) or a Gleason score <8 at initial diagnosis (OR 0.51) had statistically significantly lower odds of receiving a HRRm test (all p<0.05; **Figure 3**).
- Rates of HRRm testing varied by specialty of treating physician (57% [193/337], medical oncologists 39% [43/111] urologist; **Table 1**), however this was not found to be statistically significant using logistic regression (**Figure 3**).
- Sixty-one percent (102/166) of patients who presented with localized disease at their initial diagnosis received a HRRm test vs 48% (57/120) of patients who initially presented with regional disease, and 47% (71/150) of patients who had metastatic disease at initial diagnosis (**Table 1**).
- HRRm testing rates were similar between patients with and without visceral metastases present at data collection at 53% (79/148) and 52% (157/300), respectively (**Table 1**).
- Despite 63% (75/120) of patients with private insurance receiving HRRm testing compared to 48% (151/313) of patients with public insurance (**Table 1**), insurance status was not a statistically significantly factor associated with whether a patient received HRRm testing in the logistic regression (**Figure 3**).

Table 1. Patient demographics/disease characteristics of patients with mCRPC in the US, stratified by HRRm testing status

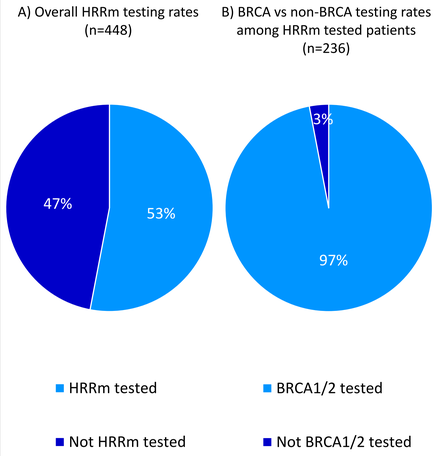
	All patients (n=448)	HRRm tested (n=236)	Not HRRm tested (n=212)
Physician specialty, n (%)			
Medical oncologist	337 (75)	193 (82)	144 (68)
Urologist	111 (25)	43 (18)	68 (32)
Patient age, years			
Mean (SD)	69.9 (8.3)	69.2 (8.2)	70.6 (8.3)
< 65, n (%)	99 (22)	63 (27)	36 (17)
≥ 65, n (%)	349 (78)	173 (73)	176 (83)
***Known family history of HRRm-related cancer, n (%)**			
Known history	48 (11)	35 (15)	13 (6)
No known history	400 (89)	201 (85)	199 (94)
Presence of visceral metastases, n (%)			
Yes	148 (33)	79 (33)	69 (33)
No	300 (67)	157 (67)	143 (67)
Disease state at initial diagnosis, n (%)			
Localized	166 (37)	102 (43)	64 (30)
Regional	120 (27)	57 (24)	63 (30)
Metastatic	150 (33)	71 (30)	79 (37)
Not assessed	12 (3)	6 (3)	6 (3)
Gleason score at initial diagnosis, n (%)			
< 8	140 (31)	60 (25)	80 (38)
≥ 8	186 (42)	105 (45)	81 (38)
Score not known	122 (27)	71 (30)	51 (24)
Insurance status, n (%)			
Public	313 (70)	151 (64)	162 (76)
Private	120 (27)	75 (32)	45 (21)
Unknown	15 (3)	10 (4)	5 (3)
Patient ethnicity, n (%)**			
White	273 (61)	144 (61)	129 (61)
Non-white	177 (39)	93 (39)	84 (39)

HRRm: homologous recombination repair mutations; mCRPC: metastatic castration-resistant prostate cancer; SD: standard deviation; US: United States of America

*HRRm-related cancers include those of the prostate, breast, ovaries and pancreas.

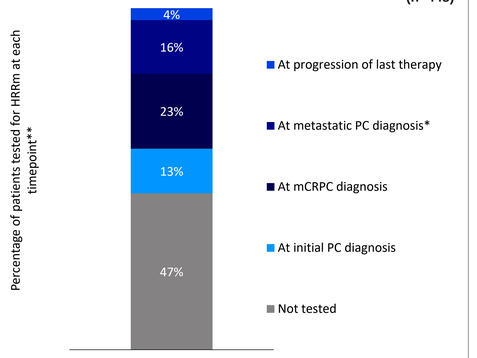
**Ethnicity was multiple-choice; patients with mixed-ethnic backgrounds appear in both categories.

Figure 1. Overall HRRm testing rates and BRCA1/2 testing rates specifically among HRRm tested patients with mCRPC in the US



HRRm: homologous recombinant repair mutation; mCRPC: metastatic castration-resistant prostate cancer; US: United States

Figure 2. The timepoints when HRRm tests were received by patients with mCRPC

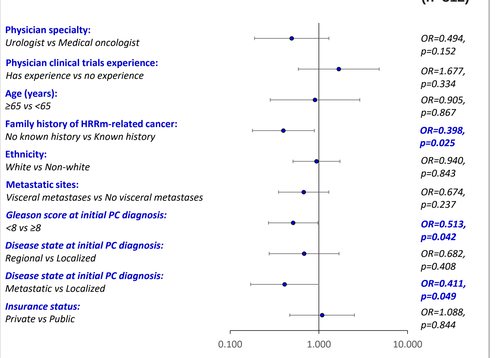


HRRm: homologous recombination repair mutation; mCRPC: metastatic castration-resistant prostate cancer; PC: prostate cancer

*Refers to patients who were previously treated for non-metastatic PC prior to metastatic PC.

**Patients fall into more than one timepoint if they were re-tested for HRRm.

Figure 3. Factors associated with patients with mCRPC receiving a HRRm test



HRRm: homologous recombination repair mutation; mCRPC: metastatic castration-resistant prostate cancer; OR: odds ratio; PC: prostate cancer

*Patients with missing data for any of the listed covariates were excluded from regression model.

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