Precision Medicine for Prostate Cancer

Discover guideline-recommended actionable and emerging biomarkers in prostate cancer.

Reading time: **8 min**

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Biomarker Testing is Transforming the Management of Prostate Cancer

Prostate cancer is the **2nd most frequent cancer** in men.[1]

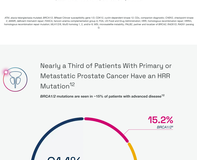
and the **5th leading cause of death** worldwide.[1]

Nearly **9 in 10 patients** with metastatic castration-resistant have potentially actionable biomarkers that can help to guide clinical management.[2,3]

Test All Patients With Metastatic Prostate Cancer for Homologous Recombination Repair Mutations (HRRm), Including *BRCA1/2*[4]

Homologous recombination repair gene mutations (HRRm), such as mutations in *BRCA1* or *BRCA2*, and ESS, may play a role in the progression from localized disease to metastatic castration-resistant prostate cancer.[5] Testing specifically for HRRm may have familial, prognostic, and therapeutic implications for patients with prostate cancer.[5,6]

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer recommend tumor testing for all patients with metastatic prostate cancer[4,5]



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Footnotes

Prostate cancer risk mutations: *BRCA1*, *BRCA2*, *ATM*, *PALB2*, *CHEK2*, *BRIP1*, *RAD51C*, and *RAD51D*.[5] Germline testing is recommended for patients with prostate cancer and a positive family history or a strongly cancer-prone family, or a personal history of breast cancer.[5] Germline testing can be considered for regional prostate cancer patients with personal history of cancer, and known germline variants of other diagnosis.[5] Germline testing is recommended for patients with metastatic disease or regional node positive, high-risk/very high-risk localized prostate cancer.[5] Germline testing can be considered for patients with regional prostate cancer.[5] Germline testing can be considered for patients with metastatic castration-resistant prostate cancer.[5] HRR genes: *ATM*, *BRCA1*, *BRCA2*, *CDK12*, *CHEK2*, *HDAC2*, *PALB2*, *RAD21*, *RAD51B*, *RAD51C*, *RAD51D*, *RAD54L*, and *TP53*.[5]

[a] Somatic testing is recommended for patients with metastatic castration-resistant prostate cancer and a positive family history, or a strongly cancer-prone family.[5] Somatic testing can be considered for patients with regional or localized prostate cancer.[5] Somatic testing can be considered for patients with metastatic castration-resistant prostate cancer.[5] HRR genes: *ATM*, *BRCA1*, *BRCA2*, *CDK12*, *CHEK2*, *HDAC2*, *PALB2*, *RAD21*, *RAD51B*, *RAD51C*, *RAD51D*, *RAD54L*, and *TP53*.[5]

[b] Germline testing is HRR genes: *BRCA1*, *BRCA2*, *ATM*, *PALB2*, *CHEK2*, and *BRIP1*.[5]

[c] Tissue-based testing is recommended for patients with metastatic castration-resistant prostate cancer.[5] Tissue-based testing can be considered for patients with regional or localized prostate cancer.[5]

[d] Tissue-based testing is HRR genes: *BRCA1*, *BRCA2*, *ATM*, *PALB2*, *CHEK2*, *BRIP1*, *RAD51C*, *RAD51D*, *CDK12*, and *TP53*.[5]

[e] Tissue-based testing is HRR genes: *BRCA1*, *BRCA2*, *ATM*, *PALB2*, *CHEK2*, *BRIP1*, *RAD51C*, *RAD51D*, *RAD21*, *RAD51B*, *RAD54L*, *HDAC2*, and *TP53*.[5]

Test the Tumor at Metastatic Diagnosis for HRRm – Including *BRCA1/2*[6]

These biomarkers are actionable in metastatic castration-resistant prostate cancer[6].

What to test?	Where to test?	How to test?[7,8]	What to test?
Somatic mutations in HRR genes: *BRCA1*, *BRCA2*, *ATM*, *PALB2*, *CHEK2*, *RAD51C*, *CDK12*, and *TP53*[5]	• All patients with metastatic castration-resistant prostate cancer[5] • Consider considering in patients with regional disease	FDA-approved CGP[9]: • FoundationOne®CDx • FoundationOne®Liquid CDx • Guardant Info 500 NGS CG and RT-PCR	Recommended in patients with metastatic prostate cancer and consider considering patients with regional prostate cancer
Germline mutations in HRR genes, such as *BRCA1/2*	• All patients with metastatic castration-resistant prostate cancer[5] • Consider considering in patients with regional disease • Consider considering in metastatic cancer and a positive family history, or hereditary, breast cancer, or a personal history of breast cancer[5]	FDA-approved CGP[9]: • Foundation Medicine® Tumor Genetics Comprehensive, Test	Criteria for germline testing should be considered in patients with regional and metastatic and if relevant or recurrence
MSI and *dMMR* genes: *BRCA1*, *BRCA2*, *ERRB*, and *PMS2*	• Patients with metastatic castration-resistant prostate cancer • Can be considered in patients with regional or castration-resistant metastatic prostate cancer	FDA-approved CGP[9]: • Foundation Medicine FoundationOne MSI Suite, Panel • MSK PyroSequence®CDx	

ATM, ataxia telangiectasia mutated; *BRCA1/2*, *BRCA1* DNA repair associated gene; CT, CGH-U, array-dependent known CG; CGH-U, array-dependent known CG; *CHEK2*, checkpoint kinase 2; *dMMR*, deficient mismatch repair; FISH-U, fluorescence-mediated in situ; FISH, fluorescence in situ hybridization; HPR, homologous recombination repair; HRRm, homologous recombination repair mutation; *MSI*, microsatellite instability; NGS, next-generation sequencing; PCR, polymerase chain reaction; PMS2, postmeiotic segregation increased 2; RAD51C, RAD51 paralog C; TMB, tumor mutational burden.

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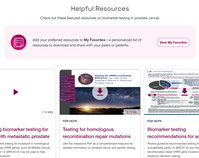
ATM, ataxia telangiectasia mutated; *BRCA1/2*, *BRCA1* DNA repair associated gene; CT, CGH-U, array-dependent known CG; CGH, comparative genomic hybridization; CGH-U, array-dependent known CG; *CHEK2*, checkpoint kinase 2; *dMMR*, deficient mismatch repair; FISH-U, fluorescence-mediated in situ; FISH, fluorescence in situ hybridization; HPR, homologous recombination repair; HRRm, homologous recombination repair mutation; *MSI*, microsatellite instability; NGS, next-generation sequencing; PCR, polymerase chain reaction; PMS2, postmeiotic segregation increased 2; RAD51C, RAD51 paralog C; TMB, tumor mutational burden.

Nearly a Third of Patients With Primary or Metastatic Prostate Cancer Have an HRR Mutation[10]

***BRCA1/2* mutations are seen in ~10% of patients with advanced disease[10]**



*BRCA1 and BRCA2 (prevalence in 13% and 12.2%, respectively).[11]

BRCA1/2, Breast Cancer susceptibility gene 1/2; DDR, DNA damage response; HRR, homologous recombination repair; *MMR*, mismatch repair.

Testing for HRR Mutations Provides Predictive, Prognostic, and Familial Insights

Mutations in the *BRCA1/2* genes of the HRR pathway can indicate eligibility for targeted treatment in certain patients with prostate cancer.[12]

Why test for *BRCA1/2*?

BRCA1/2, Breast Cancer susceptibility gene 1/2; DDR,DNA damage response; HRR, homologous recombination repair.

Considerations for Your Practice

As recommended by NCCN Guidelines®:

- Include somatic multigene tumor testing to detect alterations in HRR genes in metastatic prostate cancer. It can also be considered in regional disease.
- Review criteria for germline multigene testing at initial diagnosis and, if relevant, at recurrence
- Arrange for prompt genetic counseling if a pathogenic variant is identified, or if there is positive family history

Review protocols for identifying patients eligible for biomarker testing, such as *BRCA1/2* mutations. Involve the HRT team to enable optimal workflow for specimen collection and preservation at time of diagnosis and ensure suitability for testing at the critical point of clinical decision-making.[13]

BRCA1/2, Breast Cancer susceptibility gene 1/2; HRT, Homologous repair; NCCN, National Comprehensive Cancer Network® NCCN®.

Helpful Resources

Check out these featured resources on biomarker testing in prostate cancer.

Add your preferred resources to **My Favorites** – a personalized list of resources to download and share with your peers or patients.

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FOR HCPS

Optimizing biomarker testing for patients with metastatic prostate

Learn how biomarker testing for homologous recombination repair (HRR) gene mutations in metastatic castration-resistant prostate cancer (mCRPC) patients may be used to help guide treatment decisions.

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FOR HCPS

Testing for homologous recombination repair mutations

Use this interactive PDF as a comprehensive resource for detailed information on prostate cancer and genetic testing.

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FOR HCPS

Biomarker testing recommendations for advanced

Review prostate cancer biomarker testing in Where Clinical Evidence Meets Practice Guidelines. Learn how to use the NCCN Guidelines® to identify patients with metastatic castration-resistant prostate (mCRPC) gene mutations to help inform treatment decision-making.

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7. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreas V.1.2024. 2024©. National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed November 27, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org.
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