



Precision Medicine in *Prostate Cancer*
Informing Treatment Through Genomic Testing

Approximately **1 in 4** men with advanced prostate cancer has an HRR mutation¹⁻³

Have you tested your patients for **HRR mutations**?

Mutations in HRR genes, such as *BRCA1/2*, *ATM*, and *CDK12*, may help predict prognosis in prostate cancer

Prostate cancer is the 2nd leading cause of cancer death among men in the US⁴

Men with metastatic prostate cancer face a reduced **5-year relative survival rate**⁵

from **100%**
in local/regional
disease

to **30%**
in metastatic
disease

Up to **40%** of men
with prostate cancer will develop
metastatic disease despite treatment,
with most progressing to CRPC⁶

Certain HRR gene mutations have been associated with progression of prostate cancer

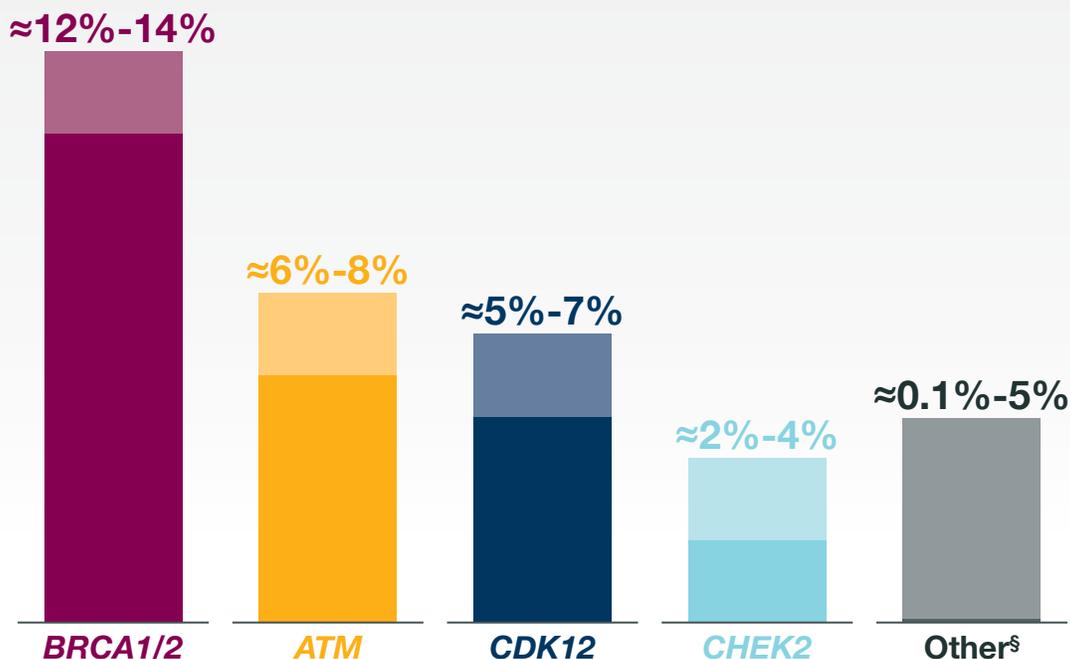
In different retrospective analyses,

- **5-year metastasis-free survival was significantly lower for carriers of *BRCA1/2* mutations (77%) compared with noncarriers (93%)^{7,*}**
- **Median overall survival after diagnosis was 5 years for men with *BRCA1/2* or *ATM* mutations compared with 16 years in noncarriers^{3,†}**

*Demonstrated in a retrospective analysis of outcomes for germline *BRCA1/2* mutation carriers and noncarriers (N=2019).

†Demonstrated in a retrospective case study analysis of patients with lethal prostate cancer and patients with low-risk localized disease (N=799).

FREQUENCY OF CERTAIN HRR MUTATIONS IN ADVANCED PROSTATE CANCER^{1,6,8-10,‡}



[§]Other HRR gene mutations may include: *RAD51B*, *RAD51C*, *RAD51D*, *PALB2*, *FANCA*, *BRIP1*, *GEN1*, *MRE11A*, and *NBN*.^{1,8,10}

[‡]Data are derived from multiple sources, and there are differences in factors such as study populations and demographics.

Testing for HRR mutations in advanced prostate cancer can guide the development of a treatment plan

HRR mutation testing can inform^{1,3,10-12}:



Prognosis



Treatment decisions



Hereditary risk



Eligibility for clinical trials

Recommendations for HRR mutation testing in prostate cancer

According to NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)¹¹

- **Tumor testing is recommended for men with metastatic disease**
 - Testing should include *BRCA1*, *BRCA2*, *ATM*, *PALB2*, *FANCA*, *RAD51D*, *CDK12*, and *CHEK2*
- **Germline testing is recommended for all men with strong family history or intraductal/criform histology and men with high-/very high-risk local disease, regional disease, or metastatic disease**
 - Testing should include *BRCA1*, *BRCA2*, *ATM*, *PALB2*, and *CHEK2*

Expert consensus from the inaugural Philadelphia Prostate Cancer Consensus Conference¹³

- **Germline testing for *BRCA1*, *BRCA2*, and *ATM* is recommended for all men with mCRPC or a family history**

Men with prostate cancer and their families may be at risk for other certain cancers.¹⁰ All patients confirmed to have germline HRR mutations should receive genetic counseling; pre-test genetic counseling is preferred.^{11,13}

Did you know?

HRR proteins play an essential role in DNA damage repair mechanisms.^{14,15} Mutations in HRR genes can increase a tumor's reliance on PARP-mediated DNA repair pathways for survival.^{14,15}

ATM, ataxia-telangiectasia mutated; *BRCA*, breast cancer susceptibility gene; *BRIP1*, *BRCA1* interacting protein c-terminal helicase 1; *CDK12*, cyclin-dependent kinase 12; *CHEK2*, checkpoint kinase 2; CRPC, castration-resistant prostate cancer; *FANCA*, Fanconi anemia complementation group A; *GEN1*, Gen endonuclease homolog 1; mCRPC, metastatic castration-resistant prostate cancer; *MRE11A*, *MRE11A* homolog, double strand break repair nuclease; *NBN*, nibrin; NCCN, National Comprehensive Cancer Network; *PALB2*, partner and localizer of *BRCA2*; PARP, poly (ADP-ribose) polymerase; *RAD51*, *RAD51* recombinase.

How to test for HRR mutations in advanced prostate cancer

Remember: Tumor testing can identify both germline and somatic HRR mutations but does not distinguish between them.¹⁶ Only germline testing can assess hereditary risk.^{16,17}

HRR MUTATION TESTING IN 3 STEPS

1. CHOOSE a sample type

Tumor tissue, plasma, whole blood, or saliva can be used to detect HRR mutations.^{12,18-20} Select the required sample type for the test you plan to use.

2. COLLECT the sample

For germline testing



Whole blood, saliva, or buccal samples can be used¹⁸



Prepare samples according to test instructions as soon as possible to prevent degradation¹⁹

For tumor testing



A freshly extracted piece of the tumor or archival tissue can be used in genomic testing^{12,19,20}



The tumor specimen is prepared to be evaluated for somatic and germline mutations¹²

For plasma testing



Obtain a blood sample and separate plasma from blood for ctDNA analysis¹⁹



Refer to test instructions for any sample preparation before evaluating it for somatic and germline mutations

How to test for HRR mutations in advanced prostate cancer

3. CHOOSE a test

Several assays are available for somatic or germline HRR mutation detection by germline, tissue, or ctDNA analysis.

Refer to each manufacturer's test specifications for guidance on the required sample.

Laboratory*	Contact Information Direct any questions regarding these tests to customer service at:
Ambry²¹	(949) 900-5500
Caris²²	(866) 771-8946
Foundation Medicine²³	(888) 988-3639
GenPath/GeneDx²⁴	(888) 729-1206
Guardant Health²⁵	(855) 698-8887
Invitae²⁶	(800) 436-3037
Myriad²⁷	(800) 469-7423
NeoGenomics^{®28}	(866) 776-5907
Tempus²⁹	(800) 739-4137

Test your patients with advanced prostate cancer for HRR mutations!

*These laboratories and their tests are not affiliated with AstraZeneca.

Knowing your patient's HRR gene mutation status, including *BRCA1/2*, *ATM*, and *CDK12*, is critical

HRR mutation status can provide:



Predictive Insights

HRR mutation status may aid development of a comprehensive treatment plan¹⁰⁻¹²



Predispositional Insights

HRR mutation status can guide assessment of familial risk for certain cancers^{10,11}



Prognostic Insights

Mutations to certain HRR genes may be associated with the development and progression of prostate cancer^{1,3}

Does your institution have a process in place for HRRm testing in patients with advanced prostate cancer?

Optimal management requires multidisciplinary team collaboration²⁰



Timely team collaboration is critical throughout the patient journey

HRRm, homologous recombination repair mutation.

Learn more at [HRRinPrCa.com](https://www.hrrinprca.com)

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