

Table 1. Recommendations from international guidelines for genetic testing in patients with castration-resistant prostate cancer (mCRPC).

Guidelines	Germline testing	Tumour testing
NCCN (v1.2023) ²⁵	In patients with metastatic, regional (node-positive), very high- or high-risk localised prostate cancer. Any patient with prostate cancer who has Ashkenazi Jewish ancestry, strong family history of cancer ^a or breast cancer. Intraductal/ciribriform histology.	In patients with metastatic prostate cancer for HRR mutations such as <i>BRCA1</i> , <i>BRC2</i> , <i>ATM</i> , <i>PALB2</i> , <i>FANCA</i> , <i>RAD51D</i> , <i>CHEK2</i> , <i>CDK12</i> . In patients with mCRPC that is MSI-H or dMMR.
ESMO (2020) ²⁶	Testing for <i>BRCA2</i> and other DDR genes associated with cancer predisposition syndromes is recommended in patients with a family history of cancer and should be considered in all patients with metastatic prostate cancer.	Testing for homologous recombination genes and dMMR (or MSI) in patients with mCRPC.
AUA/ ASTRO/ SUO (2020) ²⁸	In patients with mHSPC, regardless of age and family history, clinicians should offer genetic counselling and germline testing. In patients with mCRPC, clinicians should offer germline genetic testing to identify DNA repair deficiency mutations and MSI status that may inform prognosis and counselling regarding family risk as well as potential targeted therapies.	In patients with mCRPC, clinicians should offer somatic tumour genetic testing to identify DNA repair deficiency mutations and MSI status that may inform prognosis and counselling regarding family risk as well as potential targeted therapies.
Philadelphia Prostate Cancer Consensus Conference (2019) ²⁷	In patients with metastatic prostate cancer (either castration-resistant or castration-sensitive). Men with 1 brother or father or 2 or more male relatives diagnosed with prostate cancer at age <60 years, died of prostate cancer or had metastatic prostate cancer. Patients should undergo genetic testing for the following genes: <ul style="list-style-type: none"> • Comprehensive (large) panel testing for therapy/clinical trial eligibility • Priority germline testing (metastatic prostate cancer): <ul style="list-style-type: none"> ◦ <i>BRCA2/BRCA1</i> ◦ DNA MMR genes ◦ Test additional genes on the basis of personal or family history 	Next-generation sequencing for all men with metastatic prostate cancer, followed by confirmatory germline testing.

ASTRO: American Society for Radiation Oncology; AUA: American Urological Association; DDR: DNA damage response and repair; dMMR: deficient mismatch repair; DNA: deoxyribonucleic acid; ESMO: European Society for Medical Oncology; HRR: homologous recombination repair; mCRPC: metastatic castration-resistant prostate cancer; mHSPC: metastatic hormone-sensitive prostate cancer; MMR: mismatch repair; MSI: microsatellite instability; MSI-H: microsatellite instability - high; NCCN: National Comprehensive Cancer Network; SUO: Society of Urologic Oncology

^a Family history and/or ancestry with ≥1 first-, second- or third-degree relative with breast, colorectal or endometrial cancer at age ≤50 years, male breast cancer or ovarian cancer or exocrine pancreatic cancer or metastatic, regional, very high-risk or high-risk prostate cancer at any age; ≥1 first-degree relative with prostate cancer at age ≤60 years; ≥2 first-, second- or third-degree relatives with breast cancer or prostate cancer at any age; ≥3 first- or second-degree relatives with Lynch syndrome-related cancers, especially if diagnosed at age <50 years; a known family history of familial cancer risk mutations, especially in *BRCA1*, *BRCA2*, *ATM*, *PALB2*, *CHEK2*, *MLH1*, *MSH2*, *MSH6*, *PMS2*, *EPCAM*.