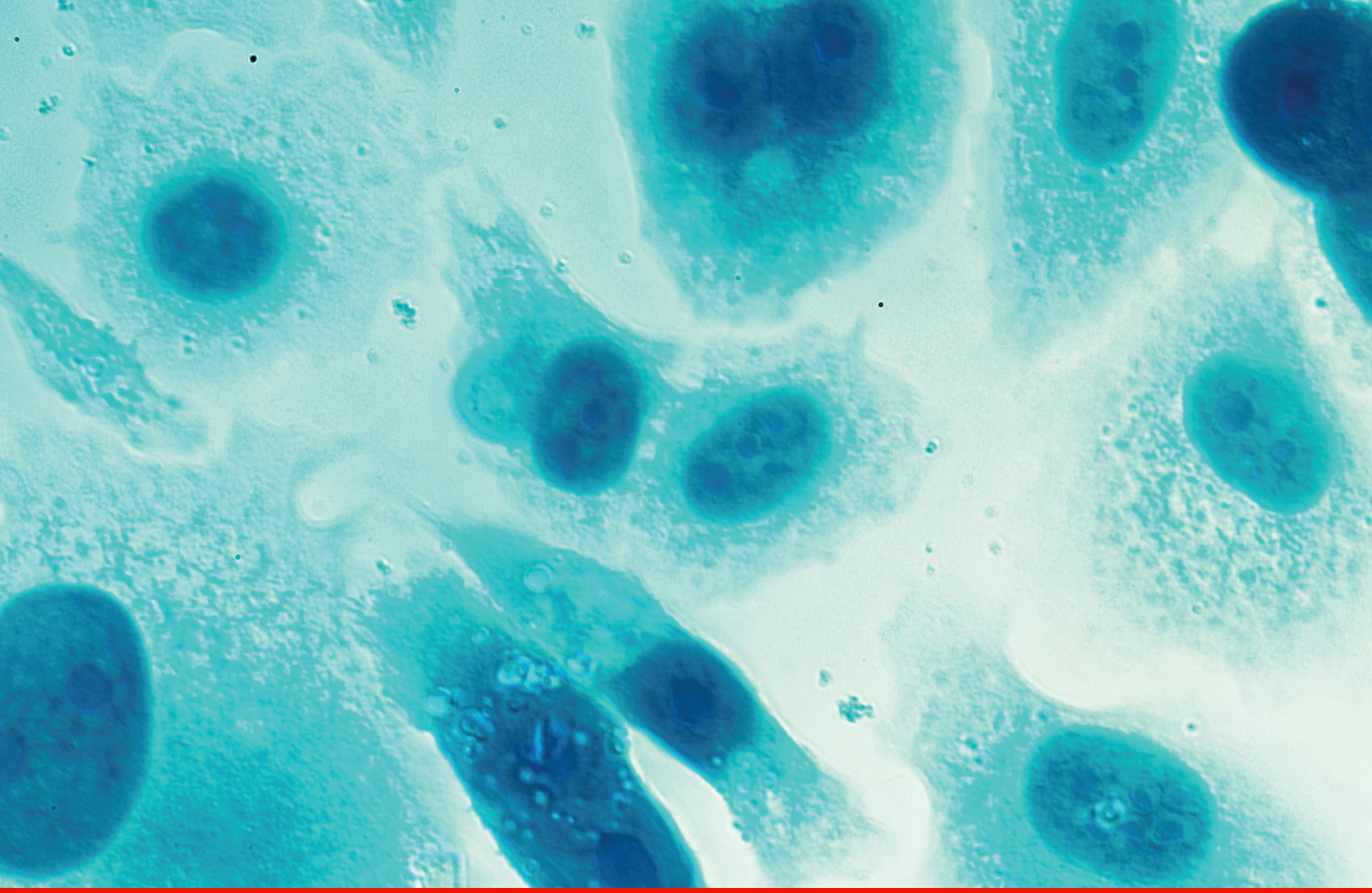


Genitourinary Cancer Overview

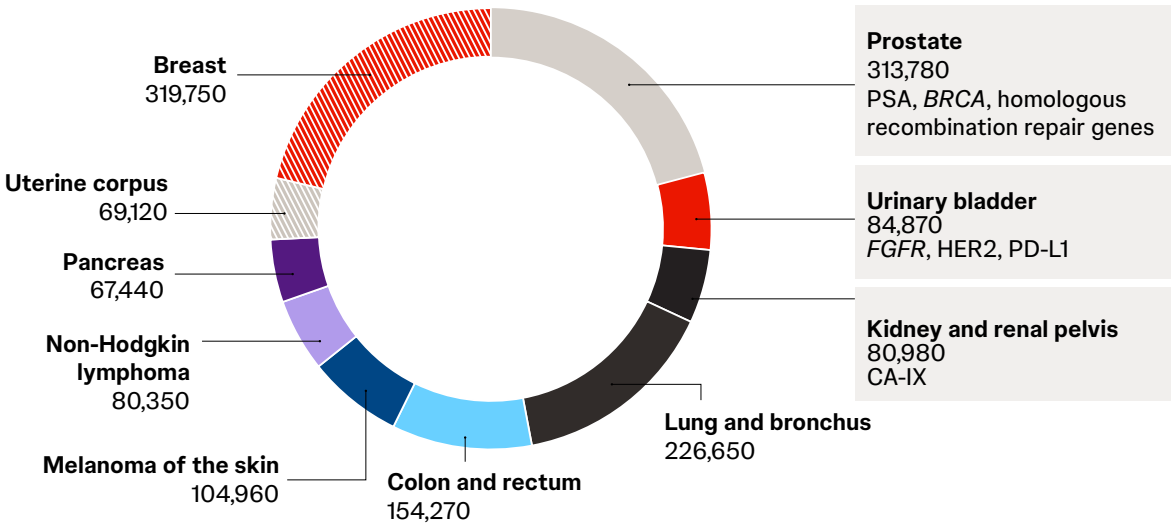
Biomarkers in Prostate Cancer and Bladder Cancer Precision Medicine

J&J
Precision Medicine

Genitourinary cancers are among the most common cancers in the United States[1]

Prostate cancer and bladder cancer have the highest incidence and mortality of all genitourinary cancers[2–5]

Top 10 cancers in the United States
Cancer site, estimated new cases,[1] example biomarkers[6–11]



Molecular alterations serve as biomarkers for prostate and bladder cancers[12,13]

Biomarkers are measurable indicators of clinical or biological characteristics and may be diagnostic, prognostic, or predictive of therapeutic response[6,13]

	Actionable biomarkers in genitourinary cancers may be detected by different assays with unique capabilities[9,14–22]			
	Single-biomarker test			Broad-based panel
Test type	**Immunohistochemistry (IHC)[14,23]**	**Fluorescence in situ hybridization (FISH)[24]**	**Polymerase chain reaction (PCR)[25]**	**Next generation sequencing (NGS)[26]**
Target	Protein	Chromosome	DNA, RNA	DNA, RNA

Opportunity to optimize

Understand molecular biomarkers of prostate cancer and bladder cancer to help inform precision medicine approaches that tailor treatment to the patient.[27,28]

Overview of Prostate Cancer

Prostate cancer is the second most prevalent cancer in the United States[2]

Prevalence: 3,399,229 men in 2021[2]*
~12.8% of men diagnosed with prostate cancer during their lifetime

Incidence: 313,780 cases in 2025[29]*
15.4% of all new cancer cases
- Second only to breast cancer

Deaths: 35,770 deaths in 2025[29]*
5.8% of all cancer deaths

5-Year relative survival rates (2014–2020)[2]
Overall: 97.5%
- Localized (stage I): 100%
- **Metastatic** (stage IV): **36.6%**

Risk factors[30–32†]

- Older age
- Family history
- Race
- Diet
- Alcohol‡
- Certain mutations

*Estimated. †NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. ‡Data across studies are inconsistent on whether alcohol consumption increases overall or aggressive prostate cancer risk.[31,32]

The high prevalence of prostate cancer has drawn attention to the disease, with a long history of scientific, clinical, and biomarker research[2,33–35]

PSA screening improved prostate cancer survival due to earlier diagnosis[7,36,37]

Five-year prostate cancer survival[2,36]

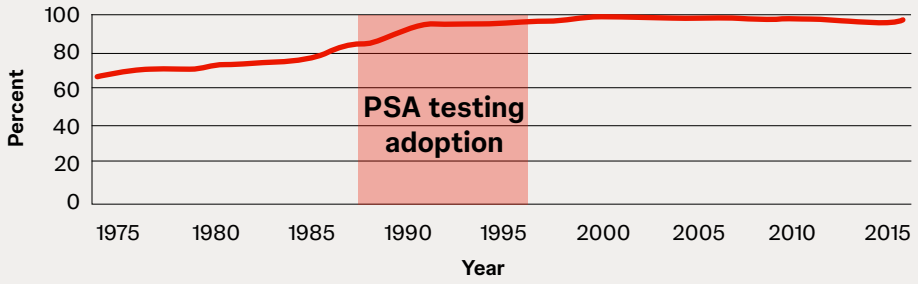


Image adapted from the National Cancer Institute

Introduction of PSA screening led to a **reduction in prostate cancer mortality by 46.0%–63.7%**[36]

Ongoing biomarker research has led to continuing advancement in prostate cancer biomarker technology since the initial breakthrough with PSA screening in the 1990s[38–40]

Molecular testing for key biomarkers informs multiple aspects of prostate cancer management[21,30,41]*

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer recommend molecular testing to:

- Understand genetic disposition[21,30,41]*
- Identify and manage high-risk individuals[21,30,41]*
- Predict treatment response[21,30,41]*

NCCN Guidelines® for Prostate Cancer molecular testing overview[30,41]*

Who to test

Germline testing

- Relevant personal and/or family history
- High-risk tumor/mutation characteristics

Metastatic prostate cancer

Somatic testing

Consider for regional (N1) prostate cancer

What to test for

Germline testing†

TP53 *HOXB13*

BRCA1 *CHEK2*
BRCA2 *ATM*

Somatic testing

RAD51D *CDK12* TMB‡
FANCA *PALB2* MSI-H
dMMR/MMR genes§

Opportunity to optimize

Consider somatic and germline testing in appropriate patients to help inform a personalized prostate cancer treatment plan[21,30,41]*

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Genes in the HRR pathway are valuable prostate cancer biomarkers[41,42*]

23% **of men with mCRPC** have somatic mutations in the **HRR pathway**, with most being found in *BRCA2* and *ATM*[41*]

- **7%–26%** of males with germline ***BRCA1*** alterations and **19%–61%** of males with germline ***BRCA2*** alterations **will develop prostate cancer**[30,43*]
- In one large, retrospective study, 12-year **survival rate in patients with a *BRCA2* alteration was >30% lower** compared with those without a *BRCA* alteration[44]
- In a separate study, ***BRCA1/2* alterations were associated with significantly lower progression free survival and overall survival** compared with patients without *BRCA* alterations[45]
- *BRCA* alterations may predict **response to PARPis**[41*]

Prostate cancer biomarkers may guide decision-making throughout the course of disease[41*]

Biomarkers	CSPC (hormone-sensitive prostate cancer, HSPC)	CRPC	mCRPC or mCSPC	
Pre-cancerous	**Early localized proliferation**[46]	**Acquired or de novo ADT resistance**[47,48]	**Metastases to nearby tissue**[49]	**Metastases to bone and viscera**[49]
Informing therapeutic selection[41*]	Somatic testing may be considered for[41*]: • **Alterations in HRR genes** ◦ *BRCA1/2, PALB2, ATM, FANCA, RAD51D, CHEK2, CDK12* • **MSI-H or dMMR** in regional CSPC		Somatic testing is recommended for[41*]: • **Alterations in HRR genes** ◦ *BRCA1/2, PALB2, ATM, FANCA, RAD51D, CHEK2, CDK12* • **MSI-H or dMMR** in mCRPC • **TMB** in mCRPC Somatic testing may be considered for[41*]: • **MSI-H or dMMR** in mCSPC Somatic testing for **HER2** following progression after prior treatment[50,51]	
Staging	**PSMA-PET** is a sensitive and specific targeted imaging modality for both initial staging and biochemical recurrence[27]			

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Biomarker testing may improve risk stratification[7,27]

PSMA-PET[7,27]

Targeted imaging **provides more accurate staging than** conventional imaging

Gene expression tools[7,27]

22-gene genomic classifier

31-gene cell cycle progression assay

17-gene genomic assay

Aid in treatment decisions of active surveillance vs radical therapy, radiotherapy, and ADT

For unfavorable intermediate through very high-risk groups

Germline and somatic testing[41,52–54]*

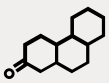
- Provide additional prognostic information
- **Predict therapeutic response** to PARPis, chemotherapy, and immune checkpoint inhibitors (ICI)

Opportunity to optimize

Use biomarker testing in combination with clinical and pathological features when appropriate to improve risk stratification[41]*

Summary of prostate cancer

Prostate cancer is a complex disease and is the most commonly diagnosed cancer in men in the United States[27,41]*



During the course of prostate cancer, the molecular profile may change[41]*

Molecular biomarker testing is recommended for use in clinical decision-making for prostate cancer[27,41]*

Understanding the molecular profile of prostate cancer will help inform precision medicine approaches that are tailored to the patient[27,41]*

Overview of Bladder Cancer

Bladder cancer is the sixth most prevalent cancer in the United States[3]

Incidence: 84,870 cases in 2025[29]*
4.2% of all new cancer cases

Prevalence: 730,044 people in 2021[3]*
~2.2% of people will be diagnosed with bladder cancer at some point during their lifetime

Deaths: 17,420 deaths in 2025[29]*
2.8% of all cancer deaths

5-Year relative survival rates (2014–2020)[2]
Overall: 78.4%
- Localized (stage I): 71.7%
- **Metastatic** (stage IV): **8.8%**

Risk factors[55,56]

- Smoking
- Older age
- Family history
- Certain mutations
- Prior radiation or certain anticancer drugs
- Race
- Chronic urinary tract infections
- Environmental factors, including common workplace exposures

Advancements in precision medicine have the potential to impact clinical understanding and treatment of bladder cancer[57]

Bladder cancer biomarkers can indicate targeted therapy approaches for advanced disease[58†]

Localized						Metastatic	
NMIBC			MIBC			mMIBC	
Stage 0is‡	Stage 0a	Stage I	Stage II	Stage IIIa	Stage IIIb	Stage IVa	Stage IVb
Biomarkers informing therapeutic selection[58†]:			Somatic testing may be considered for[58†]: • ***FGFR3* genetic alterations**§ in stage IIIb • **HER2 overexpression** in stage IIIb • **MSI-H or MMR status** in stage IIIb			Somatic testing is recommended for[58†]: • ***FGFR3* genetic alterations**§ • **HER2 overexpression** • **MSI-H or MMR status**	

*Estimated. †NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. ‡Carcinoma in situ (CIS). §A larger panel may be preferred to identify rare mutations that may have approved therapies or allow for clinical trial eligibility.[58]

Molecular testing for key biomarkers informs multiple aspects of bladder cancer management[58]*

NCCN Guidelines for Bladder Cancer recommend molecular testing to:

- Understand genetic disposition[58,59]*
- Predict likelihood of treatment response[58]*
- Screen for clinical trials[58]*

NCCN Guidelines for Bladder Cancer molecular testing overview[58,59]*

Who to test

Germline testing

Relevant personal and/or family history of Lynch syndrome

Patients presenting at a young age

Somatic testing

mMIBC

Consider for advanced nonmetastatic MIBC

What to test for

Germline testing

Multigene sequencing for:

MLH1 *MSH6* *EPCAM*
MSH2 *PMS2*

MMR gene deletions/ rearrangements

Somatic testing

FGFR3 genetic alterations§

HER2 overexpression

MSI-H status

Opportunity to optimize

Consider somatic and germline testing in appropriate patients to help inform a personalized bladder cancer treatment plan[58,59]*

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§A larger panel may be preferred to identify rare mutations that may have approved therapies or allow for clinical trial eligibility.[58]

Emerging biomarkers may improve risk stratification

Did you know?

NMIBC has a ~45%–50% recurrence rate, with high-grade lesions more likely to progress, and MIBC has up to a 54% local recurrence rate following RC[60–62]

Risk stratification can help identify which patients with bladder cancer to treat and monitor[28,63]

Current roles for urinary biomarkers in NMIBC are limited, but future directions are promising[60]:

- Advances in sensitivity for **detection of high-grade disease** in a surveillance population using genomic testing
- Potential applications of urinary cell-free DNA in both **detection and molecular risk stratification**

Several studies have identified a wide range of **emerging biomarkers with potential prognostic value**, such as[63–66]:

- Neutrophil-to-lymphocyte ratio
- Certain genes
- Protein markers

Summary of bladder cancer

Bladder cancer is the sixth most prevalent cancer in the United States[3]

Actionable mutations continue to be identified, and some have therapeutic value in bladder cancer[28,67]

Risk stratification along with biomarkers may help clinicians optimally treat their patients[28]

Understanding the molecular profile of bladder cancer has the potential to inform precision medicine approaches that are tailored to the patient[28,67]

Precision medicine tailors treatments to your patients

Biomarker-informed decision-making for genitourinary cancers can aid in **treatment selection**, understanding **prognosis**, determining **clinical trial eligibility**, and **identifying cancer susceptibility** in patients and their families[41,58]*

Understanding the molecular profile of complex diseases like prostate cancer and bladder cancer can **inform precision medicine approaches** that are tailored to the patient[27,28,41,58,67]*

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ADT, androgen deprivation therapy; ATM, ataxia telangiectasia mutated; BRCA, breast cancer gene; CA, carbonic anhydrase; CDK, cyclin-dependent kinase; CHEK2, checkpoint kinase 2; CIS, carcinoma in situ; CRPC, castration-resistant prostate cancer; CSPC, castration-sensitive prostate cancer; dMMR, deficient DNA mismatch repair; DNA, deoxyribonucleic acid; EPCAM, epithelial cellular adhesion molecule; FANCA, Fanconi anemia; FISH, fluorescence in situ hybridization; FGFR, fibroblast growth factor receptor; HER2, human epidermal growth factor receptor 2; HOXB, homebox B; HRR, homologous recombination repair; HSPC, hormone sensitive prostate cancer; ICI, immune checkpoint inhibitor; IHC, immunohistochemistry; mCRPC, metastatic castration-resistant prostate cancer; mCSPC, metastatic castration-sensitive prostate cancer; MIBC, muscle-invasive bladder cancer; MLH, MutL homologue; mMIBC, metastatic muscle-invasive bladder cancer; MMR, mismatch repair; MSH, MutS homologue; MSI-H, microsatellite instability–high; NCCN, National Comprehensive Cancer Network; NGS, next-generation sequencing; NMIBC, non–muscle-invasive bladder cancer; PALB2, partner and localizer of BRCA2; PARPi, poly (ADP-ribose) polymerase inhibitor; PCR, polymerase chain reaction; PD-L1, programmed cell death ligand 1; PET, positron emission tomography; PMS2, postmeiotic segregation increased 2; PSA, prostate-specific antigen; PSMA, prostate-specific membrane antigen; RAD, restriction-site associated DNA; RC, radical cystectomy; RNA, ribonucleic acid; TMB, tumor mutational burden; TP53, tumor protein p53.

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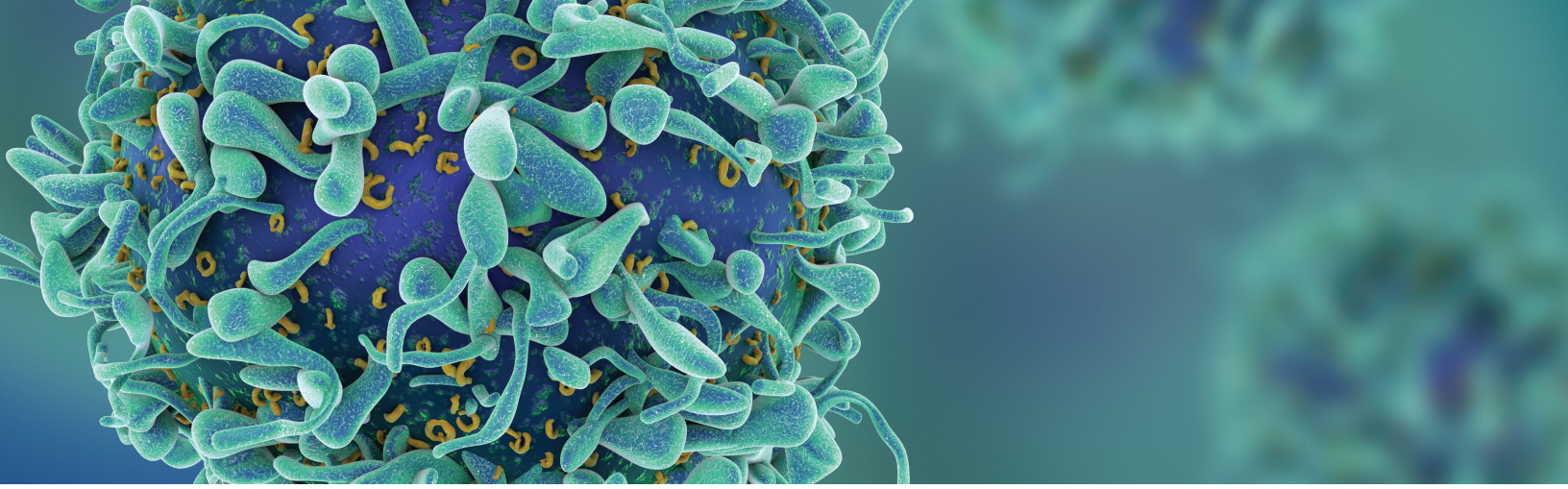

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