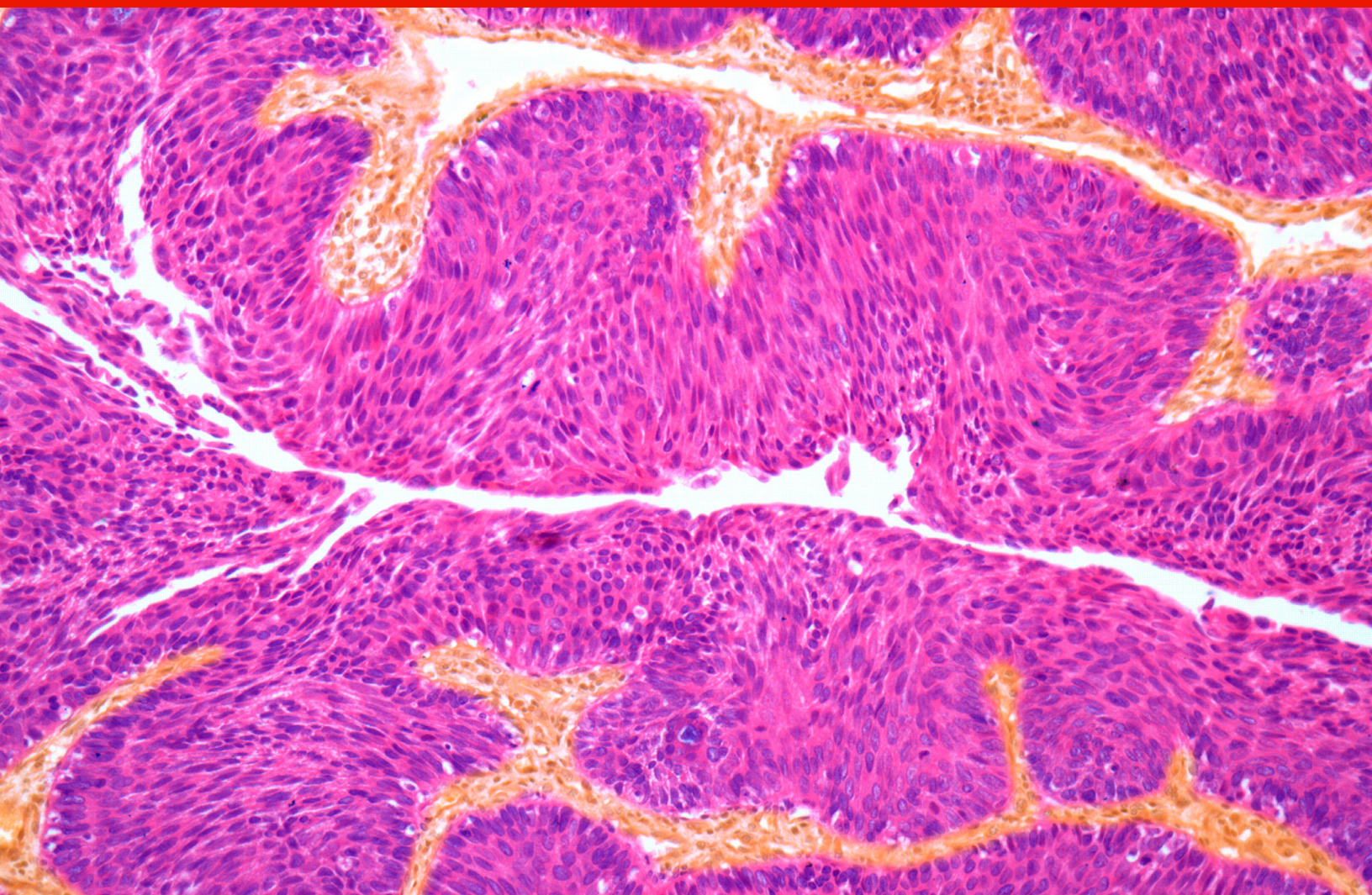
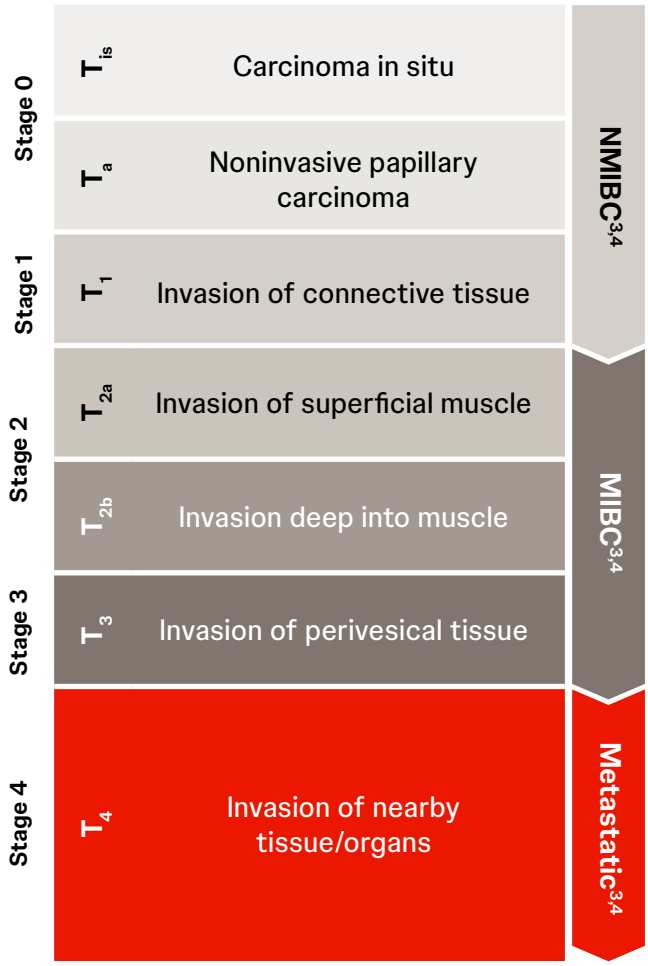
Bladder Cancer Biomarkers and Guideline Recommendations

J&J
Precision Medicine



Bladder cancer is a prevalent, commonly recurring disease[1,2]

Bladder cancer is the sixth most prevalent cancer in the United States[1]



Condition at diagnosis

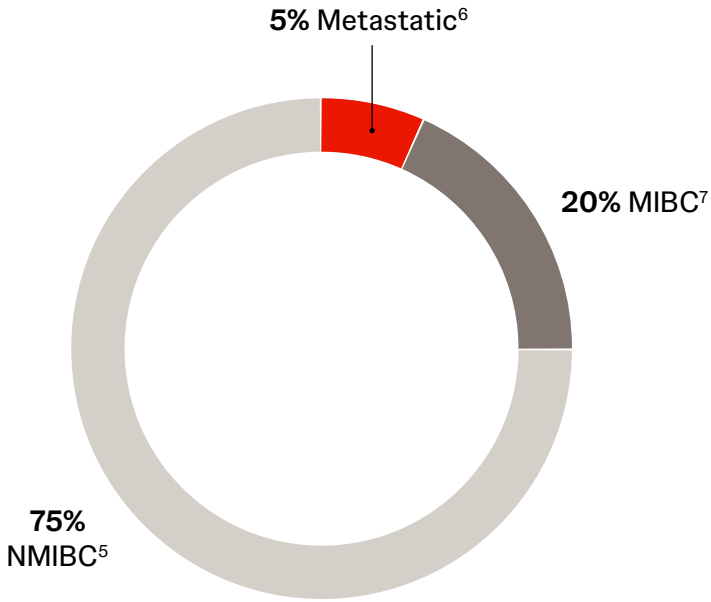


Image adapted from: Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. *CA Cancer J Clin*. 2024;74(1):12–49.

90% of bladder cancer cases are categorized as urothelial carcinoma[8]

Although bladder cancer is often caught in early stages, **recurrence rates are high and survival rates in metastatic disease are low[1,2,5]**

Recurrence rates

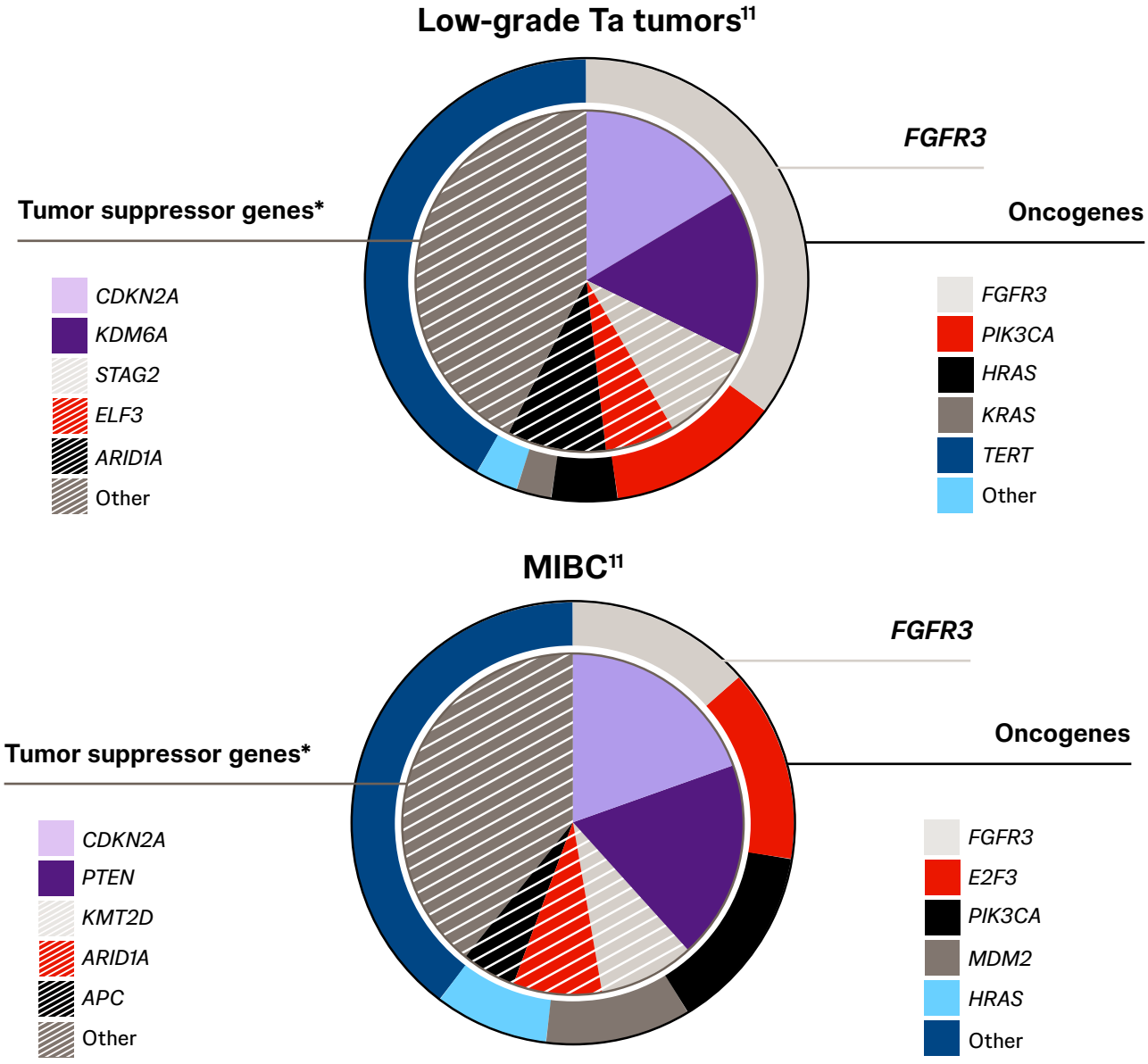
NMIBC following TURBT[9]

MIBC following RC[2]

8.8% 5-year survival rate in metastatic disease[1]

The understanding and approach to bladder cancer is evolving with precision medicine[10]

Urothelial carcinoma is driven by a variety of stage-dependent biomarkers[11]



Images adapted from: Sanli O, Dobruch J, Knowles MA, et al. Bladder cancer. *Nat Rev Dis Primers*. 2017;3:17022. doi:10.1038/nrdp.2017.22

Opportunity to optimize

Biomarker testing may identify patients at risk of recurrence or progression and help guide treatment decisions[10]

*Summed percentages exceed 100% since patients can express more than 1 mutation.

Biomarkers are emerging as useful diagnostic, prognostic, and predictive tools in the management of bladder cancer[12–14]*

Biomarker testing at different stages of disease can inform the management of bladder cancer[12,13]*

Diagnosis
(eg, NMP22)[14]

Understanding genetic disposition[12,15]*
(eg, MSH2)[15,16]*

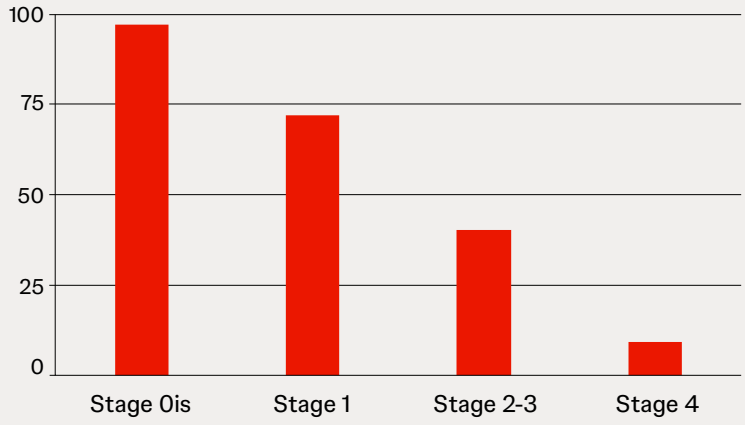
Risk stratification and prognosis
(eg, CDKN2A)[17]

Predict likelihood of treatment response
(eg, FGFR3)[12]*

Screen for clinical trials[12]*
(eg, ARID1A)[18]

Early diagnosis is associated with better clinical outcomes[1]

Five-year relative survival rates[1,19]



Survival rates are correlated with cancer stage at detection[1]

Biomarker analysis from liquid biopsies are emerging as potential noninvasive diagnostic tools[20]

*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.

Biomarker testing can significantly improve accuracy and overcome current limitations in bladder cancer evaluation[20–22]

- Testing may aid in interpreting equivocal results from cytology[13]
- Repeat testing may help monitor patients' response to therapy[13,22,23]
- Matching patients with bladder cancer to biomarker-informed treatments can lead to clinical benefits[24–27]

Clinical guidelines for bladder cancer recommend biomarker testing at diagnosis and when monitoring treatment response[12,13,28]*

When to order testing:	Following diagnosis	When monitoring treatment response
National Comprehensive Cancer Network® (NCCN®)[12]*	At time of diagnosis of advanced disease • Facilitate treatment selection • Prevent delays in: - Later lines of therapy - Entry into clinical trials	
American Urological Association (AUA)/ Society of Urologic Oncology (SUO)[13]	Following initial diagnosis • Resolve equivocal cytology (UroVysion® FISH and ImmunoCyt)	• Assess treatment response to intravesical BCG in NMIBC
Emerging evidence: **NCCN[12]***		• Can be considered for the surveillance of high-risk NMIBC patients
AUA/American Society of Clinical Oncology (ASCO)/SUO[13,28,29]		• To identify early recurrences post surgery using ctDNA - Determine patients that are likely (or not likely) to benefit from adjuvant treatment

*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.

Noninvasive biomarkers for bladder cancer detection are continuing to emerge[14,28]

As of 2024, there are currently **6 FDA-approved tests for bladder cancer diagnosis and monitoring based on urinary biomarkers,** including:

UroVysion®, ImmunoCyt®, BTA Stat, BTA TRAK, NMP22® BladderChek®, and NMP22® Bladder Cancer Test[14,30]

Recommended by AUA/SUO NMIBC guideline[13]

UroVysion®

Chromosomal alterations[14]

Chromosome 3, 7, or 17 aneuploidy and loss of the 9p21 locus[14]

Used to assess response to intravesical BCG and resolve equivocal cytology[13]

ImmunoCyt®

Bladder cancer cell antigens[14]

Detection of cells positive for **carcinoembryonic antigens and sulfated mucin glycoproteins** may aid in bladder cancer management[14]

Used to resolve equivocal cytology[13]

Did you know?

According to NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), urinary biomarkers may be considered in the first 2 years of surveillance for high-risk NMIBC[12]*

Biomarker testing may inform the likelihood of treatment response in advanced disease[12]*

Biomarker	Prevalence in locally advanced or metastatic disease	Testing methods†	Predict response to
FGFR3 alteration‡	15%[31]	RT-PCR, NGS, FISH[32–34]	FGFR inhibitors[12,24]*
HER2 overexpression	13%[35]	IHC, FISH[35]	HER2-targeted therapy[12,35]*
MSI-H	<1%[27]	NGS, RT-PCR[27]	Immune checkpoint inhibitors[12,27,36]*
High TMB	30%[36]	NGS[37]	
PD-L1 overexpression	35%[38]	IHC[38]	

*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.
†ctDNA is not currently utilized in clinical care to inform treatment decisions.[33,39]
‡A larger panel may be preferred to identify rare mutations that may have approved therapies or allow for clinical trial eligibility.[12]*

FGFR3 alterations are predictive biomarkers in bladder cancer[12]*

Oncogenic *FGFR* alterations, including point mutations and fusions, may cause constitutive signaling[32,40]

- Promotes tumorigenesis by increasing survival, migration, proliferation, angiogenesis, and invasion

FGFR physiology[40,41]

Activation of FGFR3

↓

Intracellular signaling

↓

Cell growth, proliferation, and angiogenesis

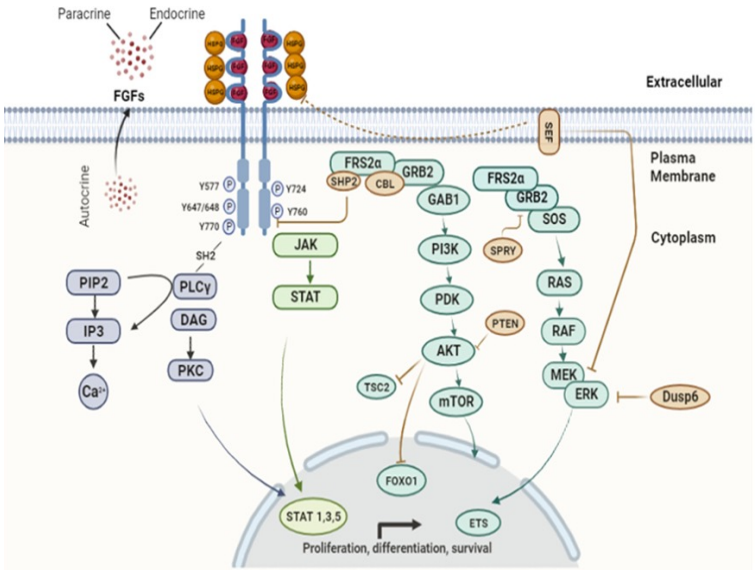


Image adapted from: Ascione CM, Napolitano F, Esposito D, et al. Role of *FGFR3* in bladder cancer: treatment landscape and future challenges. *Cancer Treat Rev*. 2023;115:102530. doi:10.1016/j.ctrv.2023.102530

Clinically relevant *FGFR3* alterations

***FGFR3* mutations:**
p.R248C, p.S249C, p.G370C, and p.Y373C[42]
- Frequency is stage-dependent
  - ~75% in NMIBC; ~20% in MIBC; ~9% in mMIBC[43,44]

***FGFR3* fusions:**
FGFR3-TACC3v1 and FGFR3-TACC3v3[33,43]
- 2–6% in patients with MIBC or mMIBC[42,43]

Did you know?

FGFR3 alterations, including clinically relevant point mutations and fusions, can be detected with PCR, NGS, and FISH[32–34]

Some urothelial tumors express predictive biomarkers for treatments with pan tumor indications[12,16,45,46]*

Predictive biomarkers (pan tumor)

	HER2[12]*	TMB[47]	MSI and dMMR[45]
Method	**IHC** – overexpression[48] **FISH** – amplification[48] **NGS** – overexpression and amplification[49,50]	**NGS** – whole-genome sequencing (WGS)[51]	**PCR** – microsatellite markers[16,45] **IHC** – expression of MMR proteins[16,45] **NGS** – targeted gene panels[16,45]
Clinical considerations	• IHC 2+ scores are equivocal[48] - follow up with FISH[48]	• High TMB >10 mutations/MB[36]	• Loss of ≥1 MMR protein defines dMMR[45] - MLH1, PMS2, MSH2 and MSH6[16] • MSI-H: instability at >30% of loci[52]

Did you know?

Although less common in bladder cancer, treatments are available for solid tumors that have metastasized and express specific alterations in *NTRK1/2/3*, *RET*, or *BRAF*[53–55]

Testing for biomarkers including *FGFR3*, *HER2*, MSI, dMMR, and TMB can identify patients who are eligible for biomarker-informed therapies[12,45,47]*

Emerging Biomarkers and Future Directions

New biomarkers are being identified that can potentially improve multiple domains of bladder cancer management[18,56–70]

Extracellular vesicles are emerging as useful sources of biomarkers[56,57]

	DNA[18,58–60] Mutations, fusions, methylation	**RNA**[61–63] mRNA, miRNA, ncRNA, lncRNA	**Protein**[57,64–70] Overexpression
Diagnosis*	*FGFR3, PIK3CA, KRAS, TERT, TP53*	MALAT, PCAT-1, SPRY4-IT1	alpha-1-anti-trypsin, BLCA-1/4, H2B1K
Prognosis*	*CDKN2A, CTSV, FOXM1*	H19, PCAT-1, UBC1	EphA2, ERCC1/2, Rab1a
Prediction of treatment response*	*ARID1A, KDM6A, KMT2D*		EphA2, HER2, HER3

Opportunity to optimize

An MDT approach can help ensure that patients' biomarker profiles are continuously updated based on current approvals[71]

*This is not an exhaustive list of emerging biomarkers for bladder cancer.

Summary

Bladder cancer is a molecularly heterogeneous disease; different tumor subtypes and stages express unique molecular signatures[11]

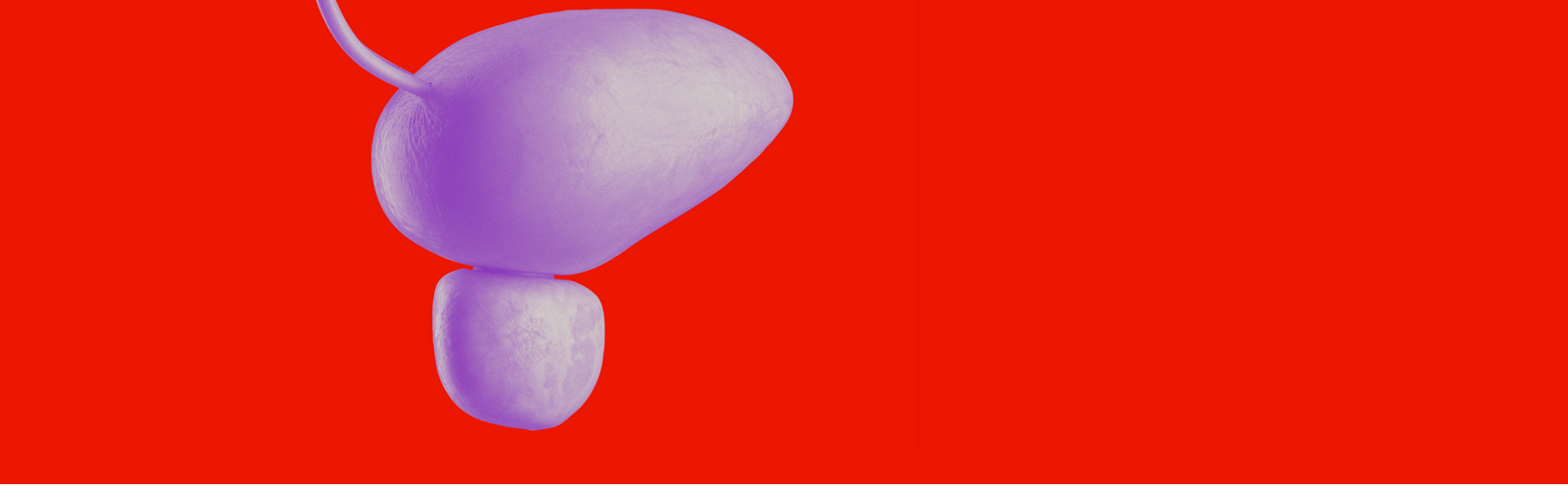
Multiple guidelines recommend that biomarker testing may be utilized to aid in diagnosis and prognosis or to inform treatment decisions in select bladder cancer patients[12,13]*

Biomarkers may play an instrumental role in diagnosis, risk stratification, surveillance, and identifying treatment options[12,13,28]*

*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.

APC, adenomatous polyposis coli; ARID1A, AT-rich interactive domain-containing protein 1A; AUA, American Urological Association; BCG, Bacillus Calmette-Guérin; BLCA, bladder cancer; BRAF, B-Raf proto-oncogene; CDKN2A, cyclin-dependent kinase inhibitor 2A; ctDNA, circulating tumor deoxyribonucleic acid; CTSV, cathepsin V; dMMR, deficient DNA mismatch repair; DNA, deoxyribonucleic acid; E2F3, E2F transcription factor 3; ELF3, E74-like factor 3; EphA2, ephrin type-A receptor 2; ERCC, excision repair 1, endonuclease non-catalytic subunit; FDA, Food and Drug Administration; FGFR, fibroblast growth factor receptor; FISH, fluorescence in situ hybridization; FOXM1, forkhead box M1; H2B1K, histone H2B type 1-K; HER2, human epidermal growth factor receptor 2; HER3, human epidermal growth factor receptor 3; HRAS, Harvey rat sarcoma viral oncogene homologue; IHC, immunohistochemistry; KDM6A, lysine-specific demethylase 6A; KMT2D, Histone-lysine N-methyltransferase 2D; KRAS, Kirsten rat sarcoma viral oncogene homologue; lncRNA, long non-coding ribonucleic acid; MALAT, metastasis associated lung adenocarcinoma transcript; MB, megabase; MDM2, murine double minute 2; MDT, multidisciplinary team; MIBC, muscle-invasive bladder cancer; miRNA, micro ribonucleic acid; mMIBC, metastatic muscle-invasive bladder cancer; MLH1, MutL homologue 1; MMR, mismatch repair; mRNA, messenger ribonucleic acid; MSH, MutS homologue; MSI, microsatellite instability; MSI-H, microsatellite instability–high; NCCN, National Comprehensive Cancer Network; ncRNA, non-coding ribonucleic acid; NGS, next-generation sequencing; NMIBC, non–muscle-invasive bladder cancer; NMP22, nuclear matrix protein 22; NTRK, neurotrophic tyrosine receptor kinase; PCAT-1, prostate cancer associated transcript 1; PCR, polymerase chain reaction; PD-L1, programmed cell death ligand 1; PIK3CA, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; PMS2, postmeiotic segregation increased 2; Rab1a, Ras-related protein Rab-1A; RC, radical cystectomy; RET, rearranged during transfection; RNA, ribonucleic acid; RT-PCR, reverse transcription polymerase chain reaction; SPRY4-T1, sprouty receptor tyrosine kinase signaling antagonist 4 transcript 1; STAG2, stromal antigen 2; SUO, Society of Urologic Oncology; TACC3, transforming acidic coiled-coil-containing protein 3; TERT, telomerase reverse transcriptase; TMB, tumor mutational burden; TP53, tumor protein p53; TURBT, transurethral resection of bladder tumor; UBC1, Ubiquitin-conjugating enzyme E2 1.

References: 1. National Cancer Institute. Accessed March 14, 2025. https://seer.cancer.gov/statfacts/html/urinb.html **2.** Mari A, Campi R, Tellini R, et al. Patterns and predictors of recurrence after open radical cystectomy for bladder cancer: a comprehensive review of the literature. *World J Urol*. 2018;36(2):157–170. **3.** Kanmalar M, Abdul Sani SF, Kamri NINB, et al. Raman spectroscopy biochemical characterisation of bladder cancer cisplatin resistance regulated by FDFT1: a review. *Cell Mol Biol Lett*. 2022;27(1):9. doi:10.1186/s11658-022-00307-x **4.** American Cancer Society. Accessed March 14, 2025. https://www.cancer.org/cancer/types/bladder-cancer/detection-diagnosis-staging/staging.html **5.** Grabe-Heyne K, Henne C, Mariappan P, et al. Intermediate and high-risk non-muscle-invasive bladder cancer: an overview of epidemiology, burden, and unmet needs. *Front Oncol*. 2023;13:1170124. doi:10.3389/fonc.2023.1170124 **6.** Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. *CA Cancer J Clin*. 2024;74(1):12–49. **7.** Patel VG, Oh WK, Galsky MD. Treatment of muscle-invasive and advanced bladder cancer in 2020. *CA Cancer J Clin*. 2020;70(5):404–423. **8.** Scholtes MP, de Jong FC, Zuiverloon TCM, et al. Role of bladder cancer metabolic reprogramming in the effectiveness of immunotherapy. *Cancers (Basel)*. 2021;13(2):288. doi:10.3390/cancers13020288 **9.** Cao M, Yang G, Pan J, et al. Repeated transurethral resection for non-muscle invasive bladder cancer. *Int J Clin Exp Med*. 2015;8(1):1416–1419. **10.** Minoli M, Kiener M, Thalmann GN, et al. Evolution of urothelial bladder cancer in the context of molecular classifications. *Int J Mol Sci*. 2020;21:5670. doi:10.3390/ijms21165670 **11.** Sanli O, Dobruch J, Knowles MA, et al. Bladder cancer. *Nat Rev Dis Primers*. 2017;3:17022. doi:10.1038/nrdp.2017.22 **12.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer V.1.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed March 26, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. **13.** Holzbeierlein J, Bixler BR, Buckley DI, et al. Diagnosis and treatment of non-muscle invasive bladder cancer: AUA/SUO guideline: 2024 amendment. *J Urol*. 2024;211(4):533–538. **14.** Flores Monar GV, Reynolds T, Gordon M, et al. Molecular markers for bladder cancer screening: an insight into bladder cancer and FDA-approved biomarkers. *Int J Mol Sci*. 2023;24(18):14374. doi:10.3390/ijms241814374 **15.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric Cancer V.4.2024. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed April 7, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org **16.** Li K, Luo H, Huang L, et al. Microsatellite instability: a review of what the oncologist should know. *Cancer Cell Int*. 2020;20:16. doi:10.1186/s12935-019-1091-8 **17.** Verma S, Shankar E, Lin S, et al. Identification of key genes associated with progression and prognosis of bladder cancer through integrated bioinformatics analysis. *Cancers (Basel)*. 2021;13(23):5931. doi:10.3390/cancers13235931 **18.** National Cancer Institute. Accessed March 14, 2025. https://www.cancer.gov/research/participate/clinical-trials-search/v?id=NCI-2021-05785&r=1 **19.** National Cancer Institute. Accessed March 14, 2025. https://www.cancer.gov/about-cancer/diagnosis-staging/staging **20.** Lodewijk I, Dueñas M, Rubio C, et al. Liquid biopsy biomarkers in bladder cancer: a current need for patient diagnosis and monitoring. Int J Mol Sci. 2018;19(9):2514. doi:10.3390/ijms19092514 **21.** Zhu CZ, Ting HN, Ng KH, et al. A review on the accuracy of bladder cancer detection methods. *J Cancer*. 2019;10(17):4038–4044. **22.** Meeks JJ, Al-Ahmadie H, Faltas BM, et al. Genomic heterogeneity in bladder cancer: challenges and possible solutions to improve outcomes. *Nat Rev Urol*. 2020;17(5):259–270. **23.** Lee D, Lee W, Kim HP, et al. Accurate detection of urothelial bladder cancer using targeted deep sequencing of urine DNA. *Cancers (Basel)*. 2023;15(10):2868. doi:10.3390/cancers15102868 **24.** Loriot Y, Matsubara N, Park SH, et al. Erdafitinib or chemotherapy in advanced or metastatic urothelial carcinoma. *N Engl J Med*. 2023;389(21):1961–1971. **25.** Meric-Bernstam F, Makker V, Oaknin A, et al. Efficacy and safety of trastuzumab deruxtecan in patients with HER2-expressing solid tumors: primary results from the destiny-pantumor02 phase II trial. *J Clin Oncol*. 2024;42(1):47–58. **26.** McGrail DJ, Pilié PG, Rashid NU, et al. High tumor mutation burden fails to predict immune checkpoint blockade response across all cancer types. *Ann Oncol*. 2021;32(5):661–672. **27.** Chandran EBA, Iannantuono GM, Atiq SO, et al. Mismatch repair deficiency and microsatellite instability in urothelial carcinoma: a systematic review and meta-analysis. *BMJ Oncol*. 2024;3(1):e000335. doi:10.1136/bmjonc-2024-000335 **28.** Hemenway G, Anker JF, Riviere P, et al. Advancements in urothelial cancer care: optimizing treatment for your patient. *Am Soc Clin Oncol Educ Book*. 2024;44(3):e432054. doi:10.1200/EDBK_432054 **29.** Holzbeierlein J, Bixler BR, Buckley DI, et al. Treatment of non-metastatic muscle-invasive bladder cancer: AUA/ASCO/SUO guideline (2017; amended 2020, 2024). *J Urol*. 2024;212(1):3–10. **30.** Tomiyama E, Fujita K, Hashimoto M, Uemura H, Nonomura N. Urinary markers for bladder cancer diagnosis: A review of current status and future challenges. *Int J Urol*. 2024;31(3):208–219 **31.** Teo MY, Mota JM, Whiting KA, et al. Fibroblast growth factor receptor 3 alteration status is associated with differential sensitivity to platinum-based chemotherapy in locally advanced and metastatic urothelial carcinoma. *Eur Urol*. 2020;78(6):907–915. **32.** Karkera JD, Cardona GM, Bell K, et al. Oncogenic characterization and pharmacologic sensitivity of activating fibroblast growth factor receptor (FGFR) genetic alterations to the selective FGFR inhibitor erdafitinib. *Mol Cancer Ther*. 2017;16(8):1717–1726. **33.** Therascreen® FGFR RGQ RT-PCR Kit, Instructions for use (Handbook). Version 2, October 2021. Germantown, MD: QIAGEN N.V. **34.** Yu SH, Kim SS, Kim S, et al. FGFR3 mutations in urothelial carcinoma: a single-center study using next-generation sequencing. *J Clin Med*. 2024;13(5):1305. doi:10.3390/jcm13051305 **35.** Scherrer E, Kang A, Bloudek LM, et al. HER2 expression in urothelial carcinoma, a systematic literature review. *Front Oncol*. 2022;12:1011885. doi:10.3389/fonc.2022.1011885 **36.** Voutsadakis IA. Urothelial bladder carcinomas with high tumor mutation burden have a better prognosis and targetable molecular defects beyond immunotherapies. *Curr Oncol*. 2022;29(3):1390–1407. **37.** Aggarwal C, Ben-Shachar R, Gao Y, et al. Assessment of tumor mutational burden and outcomes in patients with diverse advanced cancers treated with immunotherapy. *JAMA Netw Open*. 2023;6(5):e2311181. doi:10.1001/jamanetworkopen.2023.11181 **38.** Nakanishi J, Wada Y, Matsumoto K, et al. Overexpression of B7-H1 (PD-L1) significantly associates with tumor grade and postoperative prognosis in human urothelial cancers. *Cancer Immunol Immunother*. 2007;56(8):1173–1182. **39.** U.S. Food and Drug Administration. Accessed March 14, 2025. https://www.fda.gov/medical-devices/in-vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-in-vitro-and-imaging-tools **40.** Perera TPS, Jovcheva E, Mevellec L, et al. Discovery and pharmacological characterization of JNJ-42756493 (erdafitinib), a functionally selective small-molecule FGFR family inhibitor. *Mol Cancer Ther*. 2017;16(6):1010–1020. **41.** Ascione CM, Napolitano F, Esposito D, et al. Role of FGFR3 in bladder cancer: treatment landscape and future challenges. *Cancer Treat Rev*. 2023;115:102530. doi:10.1016/j.ctrv.2023.102530 **42.** Knowles MA. FGFR3 – a central player in bladder cancer pathogenesis? *Bladder Cancer*. 2020;6(4):403–423. **43.** Guancial EA, Werner L, Bellmunt J, et al. FGFR3 expression in primary and metastatic urothelial carcinoma of the bladder. *Cancer Med*. 2014;3(4):835–844. **44.** Gust KM, McConkey DJ, Awrey S, et al. Fibroblast growth factor receptor 3 is a rational therapeutic target in bladder cancer. *Mol Cancer Ther*. 2013;12(7):1245–1254. **45.** Gilson P, Merlin JL, Harlé A. Detection of microsatellite instability: state of the art and future applications in circulating tumour DNA (ctDNA). *Cancers (Basel)*. 2021;13(7):1491. doi:10.3390/cancers13071491 **46.** Boll LM, Perera-Bel J, Rodriguez-Vida A, et al. The impact of mutational clonality in predicting the response to immune checkpoint inhibitors in advanced urothelial cancer. *Sci Rep*. 2023;13(1):15287. doi:10.1038/s41598-023-42495-2 **47.** Peng M, Chu X, Peng Y, et al. Targeted therapies in bladder cancer: signaling pathways, applications, and challenges. *MedComm* (2020). 2023;4(6):e455. doi:10.1002/mco2.455 **48.** Laé M, Couturier J, Oudard S, et al. Assessing HER2 gene amplification as a potential target for therapy in invasive urothelial bladder cancer with a standardized methodology: results in 1005 patients. *Ann Oncol*. 2010;21(4):815–819. **49.** Jung J, Kim ST, Ko J, et al. Clinical implication of HER2 aberration in patients with metastatic cancer using next-generation sequencing: a pan-tumor analysis. *JCO Precis Oncol*. 2023;7:e2200537. doi:10.1200/PO.22.00537 **50.** Kim ST, Banks KC, Lee SH, et al. Prospective feasibility study for using cell-free circulating tumor DNA-guided therapy in refractory metastatic solid cancers: an interim analysis. *JCO Precis Oncol*. 2017;1:PO.16.00059. doi:10.1200/PO.16.00059 **51.** Thermo Fisher. Accessed March 14, 2025. https://www.thermofisher.com/us/en/home/life-science/sequencing/sequencing-learning-center/next-generation-sequencing-information/cancer-research/basics **52.** Vaish M, Mandhani A, Mittal RD, et al. Microsatellite instability as prognostic marker in bladder tumors: a clinical significance. *BMC Urol*. 2005;5:2. doi:10.1186/1471-2490-5-2 **53.** U.S. Food and Drug Administration. Accessed March 14, 2025. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-repotrectinib-adult-and-pediatric-patients-ntrk-gene-fusion-positive **54.** Duke ES, Bradford D, Marcovitz M, et al. FDA approval summary: selpercatinib for the treatment of advanced RET fusion-positive solid tumors. *Clin Cancer Res*. 2023;29(18):3573–3578. **55.** U.S. Food and Drug Administration. Accessed March 14, 2025. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-dabrafenib-combination-trametinib-unresectable-or-metastatic-solid **56.** Teixeira Marques A, Lourenço C, Oliveira MC, et al. Extracellular vesicles as potential bladder cancer biomarkers: take it or leave it? *Int J Mol Sci*. 2023;24(7):6757. doi:10.3390/ijms24076757 **57.** Leiblich A. Recent developments in the search for urinary biomarkers in bladder cancer. *Curr Urol Rep*. 2017;18(12):100. doi:10.1007/s11934-017-0748-x **58.** Ou Z, Li K, Yang T, et al. Detection of bladder cancer using urinary cell-free DNA and cellular DNA. *Clin Transl Med*. 2020;9(1):4. doi:10.1186/s40169-020-0257-2 **59.** Verma S, Shankar E, Lin S, et al. Identification of key genes associated with progression and prognosis of bladder cancer through integrated bioinformatics analysis. *Cancers (Basel)*. 2021;13(23):5931. doi:10.3390/cancers13235931 **60.** National Cancer Institute. Accessed March 14, 2025. https://www.cancer.gov/research/participate/clinical-trials-search/v?id=NCI-2024-07862&r=1 **61.** Zhan Y, Du L, Wang L, et al. Expression signatures of exosomal long non-coding RNAs in urine serve as novel non-invasive biomarkers for diagnosis and recurrence prediction of bladder cancer. *Mol Cancer*. 2018;17(1):142. doi:10.1186/s12943-018-0893-y **62.** Zhang S, Du L, Wang L, et al. Evaluation of serum exosomal LncRNA-based biomarker panel for diagnosis and recurrence prediction of bladder cancer. *J Cell Mol Med*. 2019;23(2):1396–1405. **63.** Wang J, Yang K, Yuan W, et al. Determination of serum exosomal H19 as a noninvasive biomarker for bladder cancer diagnosis and prognosis. *Med Sci Monit*. 2018;24:9307–9316. **64.** Koizumi M, Sato S, Yoshihara M, et al. Chronological change in EPHA2 protein expression is associated with recurrence of bladder cancer. *Anticancer Res*. 2022;42(12):5783–5794. **65.** Lin SY, Chang CH, Wu HC, et al. Proteome profiling of urinary exosomes identifies alpha 1-antitrypsin and H2B1K as diagnostic and prognostic biomarkers for urothelial carcinoma. *Sci Rep*. 2016;6:34446. doi:10.1038/srep34446 **66.** Su H, Li T, Li C, et al. Expression of Rab1A in bladder cancer and its clinical implications. *Exp Ther Med*. 2020;20(5):44. doi:10.3892/etm.2020.9174 **67.** Castaneda PR, Theodorescu D, Rosser CJ, et al. Identifying novel biomarkers associated with bladder cancer treatment outcomes. *Front Oncol*. 2023;13:1114203. doi:10.3389/fonc.2023.1114203 **68.** National Cancer Institute. Accessed March 14, 2025. https://www.cancer.gov/research/participate/clinical-trials-search/v?id=NCI-2022-03375&r=1 **69.** National Cancer Institute. Accessed March 14, 2025. https://www.cancer.gov/research/participate/clinical-trials-search/v?id=NCI-2020-02918&r=1 **70.** National Cancer Institute. Accessed March 14, 2025 https://www.cancer.gov/research/participate/clinical-trials-search/v?id=NCI-2022-04337&r=1 **71.** Mark JR, Gomella LG, Lallas CD, et al. Enhancing bladder cancer care through the multidisciplinary clinic approach. *Can J Urol*. 2023;30(3):11526–11531.



Visit our website!

For additional resources on **Precision Medicine,** visit jnjprecisionmedicine.com

Data rates may apply

Solutions start with a conversation

Data rates may apply

Take action and speak to **J&J Precision Medicine** jnjprecisionmedicine.com/contact

Johnson&Johnson