



Decipher Bladder

Genomic Classifier



What is Decipher Bladder?

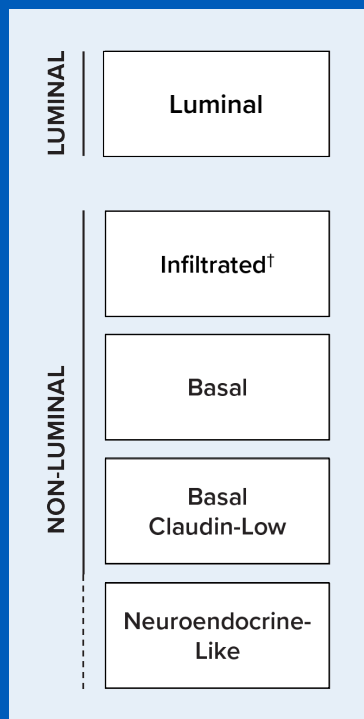
Decipher Bladder is:

- A transcriptomic subtyping tool that provides a deep biological characterization of your patients' bladder cancer
- Intended for men and women diagnosed with:
 - high-grade T1 non-muscle invasive bladder cancer through T4a muscle invasive bladder cancer
 - and who are candidates for definitive local therapy
- Derived from 219 genes
- Performed on tumor tissue collected during a trans urethral resection of a bladder tumor (TURBT)



Decipher Bladder provides the tumor molecular subtype of your patient's bladder cancer, which:

- May help determine a **patient's risk of upstaging** at time of radical cystectomy¹
- May help identify patients **who might benefit most from cisplatin-based neoadjuvant chemotherapy (NAC)** prior to radical cystectomy²
- Identifies patients with **neuroendocrine-like tumors**, which are associated with a poor prognosis and may benefit from rapid referral to medical oncology³
- May be useful in identifying optimal **candidates for immune checkpoint inhibitor therapy**⁴





1

Molecular Subtype

- The molecular subtype in which the patient tumor has the highest probability of belonging
- Luminal tumors tend to be associated with less aggressive disease while non-luminal tend to be associated with more aggressive disease

2

Interpretation

- Summary based on the patient's tumor molecular subtype and relevant clinical findings
- Includes the risk of upstaging the patient may have at RC and benefit from NAC prior to RC

The Decipher Bladder Report

PAGE 2

Decipher
BLADDER GENOMIC CLASSIFIER

Name: **Sample Patient**
Date of Birth: **--/--/----**
Accession ID: **MC-123456**

PATIENT REPORT
REPORT STATUS: FINAL
PAGE: 2 OF 2

1

SUBTYPE PROBABILITIES

Subtype	Probability
Luminal	87%
Infiltrated ¹	5%
Basal	3%
Basal Claudin-Low	5%
Neuroendocrine-Like	0%

Luminal. These tumors more frequently have a papillary morphology^{2,4,6} with urothelial differentiation and express markers associated with luminal cells (e.g., *FGFR3*, *GATA3*, *KRT20*). Luminal tumors may have higher *FGFR3* activity and/or *NECTIN4* gene expression.^{4,11}

Infiltrated¹. These tumors tend to show higher levels of stromal and / or immune cell infiltration.²

Basal. These tumors are generally poorly differentiated, with higher expression of basal cell markers (e.g., *KRT5/6*, *KRT14*).^{2,4,6}

Basal Claudin-Low. These tumors are an aggressive variant of the basal subtype that shows lower expression of claudin genes.^{2,9} These tumors are enriched with immune cells, but their anti-tumor function is actively suppressed. In a retrospective analysis of a Phase 2 clinical trial (NCT02736266), basal claudin-low tumors were found to derive greater benefit from neoadjuvant pembrolizumab as compared to other subtypes.²⁰

Neuroendocrine-Like. These tumors have a histological appearance consistent with conventional urothelial carcinoma, but have similar gene expression profiles as small cell / neuroendocrine carcinoma (e.g., high *SYP*, *ENO2*).^{4,6,12}

¹ Luminal Infiltrated

2

FINDINGS FROM CLINICAL STUDIES RELEVANT TO THIS PATIENT

In a clinical study of 206 patients with node-negative, non-metastatic cT1 and cT2 bladder cancer who received radical cystectomy alone, pathological upstaging occurred in 23% of cT1 and 57% of cT2 patients.¹

- Patients with luminal subtype tumors had lower rates of upstaging to non-organ confined disease (node-positive or pT3 or greater) than those with non-luminal subtype disease.
 - 34% of patients with luminal subtype disease were upstaged at radical cystectomy.
 - 51% of patients with non-luminal subtype disease were upstaged at radical cystectomy.

In a clinical study of 601 patients with muscle-invasive bladder cancer, 247 were treated with NAC and radical cystectomy and 354 underwent radical cystectomy without NAC.³

- With NAC, the overall net benefit to overall survival (OS) and cancer-specific survival (CSS) at three years was 7% and 5%, respectively.
- After controlling for clinicopathologic variables, non-luminal subtype tumors had greatest benefit from NAC with 10% greater OS at 3 years (71% vs 61%) and 11% greater CSS at 3 years (77% vs 66%), whereas luminal subtype tumors did not have a statistically significant benefit.

3

TEST DESCRIPTION

Hematoxylin and Eosin (H&E) slides are microscopically reviewed by a pathologist to identify the optimal area of tumor that satisfies specimen requirements. The selected region of the tumor is microdissected from surrounding non-neoplastic tissue and submitted for testing. Decipher Bladder Genomic Subtyping Classifier (GSC) uses an oligonucleotide microarray to measure 219 genes to determine the probability of a patient tumor sample belonging to each of five molecular subtypes (Luminal, Luminal Infiltrated, Basal, Basal Claudin-Low, and Neuroendocrine-Like) based on functional molecular pathways. The tumor samples are classified as belonging to the subtype with the highest calculated probability.^{1,12}

4

INTENDED USE

Decipher Bladder GSC is intended for use in patients with American Joint Committee on Cancer (AJCC) Stage I to IIIA bladder cancer who are candidates for definitive local therapy such as chemoradiation, radical cystectomy, or chemoradiation, and have not yet received pelvic radiation or chemotherapy for treatment of bladder cancer. Results are intended for use as an adjunct to conventional clinical variables and nomograms currently used in determining treatment for these patients.

5

REFERENCES

1. Lotan Y, et al. Eur Urol 76(2):200-206, (2019).
2. Seiler R, et al. Eur Urol 72(4):544-554, (2017).
3. Lotan Y, et al. J Urol, (2021).
4. Kamoun A, et al. Eur Urol 77(4):420-433, (2020).
5. Sjödaahl G, et al. J Pathol 242(1):113-125, (2017).
6. Robertson AG, et al. Cell 174(4):1033, (2018).
7. Chiu CE, et al. Clin Cancer Res 20(21), (2021).
8. de Jong JJ, et al. Genome Med, 11(1):60, (2019).
9. Kiaros J, et al. JCI Insight 13(8):e85902, (2016).
10. Necchi A, et al. Eur Urol 77(6):701-710, (2020).
11. Bandini M, et al. Ann Oncol 31(12):1755-1763, (2020).
12. Batista da Costa J, et al. Clin Cancer Res 25(13):3908-3920, (2019).

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Lab Director: [Lab Director Name, MD]

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1

Subtype Probabilities

The probabilities of the patient tumor belonging to each of the 5 molecular subtypes

2

Clinical Findings

Clinical study results relevant to this patient

3

Test Description

An overview of how the test is performed

4

Intended Use

Decipher Bladder is intended for use in patients with AJCC Stage I to IIIA bladder cancer who are candidates for definitive therapy

5

References

References for each of the clinical studies cited in the report.

How to Order Decipher Bladder

Email

orders@decipherbio.com

Fax

1.858.766.6575

Contact Customer Support

Phone: 1.888.792.1601

Email: cs@decipherbio.com

What to Include

- Requisition form
- Pathology report
- Demographic information
- Office notes

Sample Types Accepted

- TURBT and
- Patient has not received local therapy

What to Expect from the Testing Process



Physician orders
Decipher



Decipher handles tissue
collection, processing,
and analysis as well as
billing to insurance



Decipher Bladder
report generated
and sent to
ordering physician

Decipher Testing Insurance Coverage

Medicare covers Decipher Bladder for men and women with AJCC Stage I to IIIA bladder cancer

Financial assistance is available via the **Decipher Assist Program***

**see page 11*

AJCC Stage	Stage Grouping	Medicare Coverage
Oa	Ta, N0, M0	
Ois	Tis (CIS), N0, M0	
I	T1, N0, M0	✓
II	T2a/T2b, N0, M0	✓
IIIA	T3a/T3b/T4a, N0, M0 OR T1-4a, N1, M0	✓
IIIB	T1-T4a, N2/N3, M0	
IVA	T4b, Any N, M0	
IVB	Any T, Any N, M1b	



How Veracyte Handles the Insurance Process

STEP 1

A claim is submitted to your patient's insurer

STEP 2

The patient will receive an Explanation of Benefits (EOB) from insurer*

****This is not a bill***

STEP 3

In many cases, insurance pays for the complete cost of the test

STEP 4

In the event the patient's insurance company does not pay for the complete cost of the test, Decipher will appeal it on their behalf

STEP 5

After the appeal, if the patient's balance exceeds \$395, a Decipher Representative will guide them through their options

Veracyte’s Decipher Assist

We are committed to ensuring access for all eligible patients

We offer two programs to ensure testing is affordable for patients:

- 1. **Financial assistance** for patients with demonstrated financial need
- 2. **Tailored payment plans** to accommodate certain financial circumstances

Financial Assistance

Designed for qualified patients with commercial insurance

- Patients may be eligible for a reduction to non-covered costs
- Eligibility requirements include:
 - Determination of medical necessity for Decipher testing by a physician
 - Completed Decipher Assist application
 - Financial qualification

Payment Plans

Customized for patients at specific income levels

Household Size	COST TO PATIENT		
	\$0	\$100	\$295
1	\$40,770	\$54,360	\$67,950
2	\$54,930	\$73,240	\$91,550
3	\$69,090	\$92,120	\$115,150
4	\$83,250	\$111,000	\$138,750
5	\$97,410	\$129,880	\$162,350
maximum household income*			

*Decipher Assist eligibility is based on total annual household income, insurance status, and household size. Some eligibility restrictions apply.

Decipher Assist offers certain Decipher tests at a reduced cost to eligible applicants except where otherwise restricted. Residents of the United States, District of Columbia and Puerto Rico are eligible to apply. Decipher Assist does not constitute health insurance. You must meet certain income requirements set forth above. We may request documentation to verify your income, including recently filed tax returns and other supporting documentation. By requesting assistance, you certify, to the best of your knowledge, that you are eligible for assistance and that you have insufficient financial resources to pay for the ordered test. We may discontinue or change this program at any time for any reason without notice.



To learn more about Decipher Bladder contact us today
at **1.888.792.1601** or **cs@decipherbio.com**

REFERENCES:

1. Lotan Y et al., Molecular Subtyping of Clinically Localized Urothelial Carcinoma Reveals Lower Rates of Pathological Upstaging at Radical Cystectomy Among Luminal Tumors. European Association of Urology, Vol. 76, Issue 2, 2019, Pages 200-206. <https://doi.org/10.1016/j.eururo.2019.04.036>
2. Lotan Y et al., Patients with Muscle-Invasive Bladder Cancer with Nonluminal Subtype Derive Greatest Benefit from Platinum Based Neoadjuvant Chemotherapy. The Journal of Urology, Vol. 207, 2021, Pages 541-550. www.auajournals.org/doi/10.1097/JU.0000000000002261
3. Grivas P et al., Validation of a neuroendocrine-like classifier confirms poor outcomes in patients with bladder cancer treated with cisplatin-based neoadjuvant chemotherapy. Urologic Oncology: Seminars and Original Investigations, Vol. 38, Issue 4, 2020, Pages 262-268. <https://doi.org/10.1016/j.urolonc.2019.11.004>
4. Necchi A et al., Molecular Subtyping and immune-gene signatures identify a subset of early bladder tumors as candidates for single-agent immune-checkpoint inhibition. Urologic Oncology: Seminars and Original Investigations, Vol. 39, Issue 10, 2021, Pages 734.e11-735.e17. <https://doi.org/10.1016/j.urolonc.2021.06.011>