Decipher
BLADDER GENOMIC CLASSIFIER

Sample Report:
NOT A REAL PATIENT

PATIENT REPORT

PATIENT

Name: **Sample Patient**
Date of Birth: **--/--/----**
Medical Record **#:** **----------**
Sex**: _**

SPECIMEN INFORMATION

Order Date: **--/--/----**
Specimen ID: **----------**
Specimen Received Date: **--/--/----**
Accession ID: **MC-123456**

ORDERING PHYSICIAN

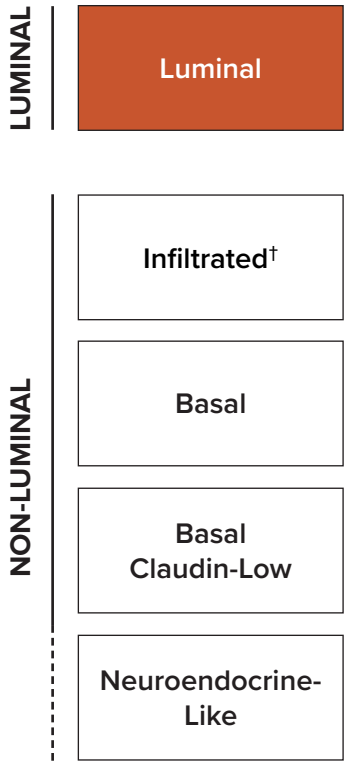
Name: **Sample Physician, MD**
Clinic: **Sample Clinic**
Address: **123 Birch Avenue, Suite A, Anytown, CA 54321**

CLINICAL AND PATHOLOGY DETAILS

For reference only, not used in calculation of genomic subtype

Date of Procedure: **01/02/2021**
Specimen Type: **TURBT**
Tumor Type: **Muscle Invasive Bladder Carcinoma**
Tumor Stage: **cT2**

DECIPHER GENOMIC RESULTS



BLADDER CANCER SUBTYPE: LUMINAL

INTERPRETATION

Luminal subtype bladder cancer is associated with a more favorable prognosis.[1,2] In comparison with non-luminal subtype disease:

Risk of Upstaging	Luminal subtype bladder cancer is more likely to be organ-confined (node-negative and pT2 or less) at radical cystectomy.[1]
Benefit from NAC‡	Patients with luminal subtype muscle-invasive bladder cancer may receive less benefit from cisplatin-based neoadjuvant chemotherapy (NAC).[3]

Approved By:
SIGNED BY NAME, CREDENTIAL ON DATE AT TIME

CLIA ID# 05D2055897
CAP # 8859006
Lab Director: [Lab Director Name, MD]

† Luminal Infiltrated ‡ Neoadjuvant chemotherapy

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veracyte

Veracyte Labs SD
6925 Lusk Boulevard, Suite 200
San Diego, CA 92121
T 1.888.792.1601
F 1.858.766.6575
E cs@decipherbio.com
W www.decipherbio.com

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SUBTYPE PROBABILITIES

Subtype	Probability
Luminal	87%
Infiltrated†	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.[4,7,8]

Infiltrated†. 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 (i.e., *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.[10,11]

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]

† Luminal Infiltrated

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.

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.[1-3,12]

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 chemotherapy, 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.

REFERENCES

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3. Lotan Y, et al. J Urol, (2021).
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Lab Director: [Lab Director Name, MD]