Decipher® BLADDER

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# Decipher Bladder Report

## Patient Details:

Patient Name:
MRN/Patient ID #:
Date of Birth:
Gender:

Pathology Laboratory:
Pathologist:
Address:

## TURBT Specimen Order Information:

Order Date:
Specimen Received Date:
GenomeDx Accession ID:
Specimen ID:
Ordering Physician:
Clinic/Hospital Name:
Clinic/Hospital Address:
Additional Physician:

## Clinical Details

**Date of TURBT:**
12 / 01 / 2016

Tumor Type: Muscle Invasive Carcinoma with Carcinoma In-Situ
Tumor Grade: High Grade
Histology Type: Urothelial / Transitional Cell Carcinoma
Lymph-Vascular Invasion: Not Identified



Bladder

## Your Decipher Result – Luminal Subtype

| Subtype | Subtype Probability | Interpretation |
|---|---|---|
| Luminal | 93% | **Patients may be considered for immediate radical cystectomy**<br>• **Favorable prognosis** following surgery and may have limited benefit from cisplatin-based neoadjuvant chemotherapy[1,2]<br>• 3-year overall survival for these patients with cisplatin-based neoadjuvant chemotherapy was similar to those with surgery alone[2] |
| Luminal Infiltrated | 2% | **Patients may be considered for immediate radical cystectomy and enrollment into immunotherapy clinical trials**<br>• **Unfavorable prognosis** and may have limited benefit from cisplatin-based neoadjuvant chemotherapy[2,3]<br>• 3-year overall survival for these patients with cisplatin-based neoadjuvant chemotherapy was similar to those with surgery alone[2]<br>• Patients with this subtype have been shown to most likely benefit from anti-PD-L1 immunotherapy in the locally advanced and metastatic setting[4] |
| Basal | 1% | **Patients may be prioritized to cisplatin-based neoadjuvant chemotherapy**<br>• **Unfavorable prognosis** but may receive substantial benefit from cisplatin-based neoadjuvant chemotherapy[1,2]<br>• 3-year overall survival for these patients with cisplatin-based neoadjuvant chemotherapy was substantially higher than those with surgery alone[2] |
| Basal Claudin-Low | 4% | **Patients may be considered for cisplatin-based neoadjuvant chemotherapy and enrollment into clinical trials of novel agents**<br>• **Unfavorable prognosis** and may benefit from cisplatin-based neoadjuvant chemotherapy[2,5]<br>• 3-year overall survival for these patients with cisplatin-based neoadjuvant chemotherapy was moderately higher than those with surgery alone[2] |

References on reverse

Assay Description. Decipher Genomic Subtyping Classifier (GSC), a microarray gene expression assay is used to classify formalin-fixed paraffin-embedded (FFPE) bladder tumor samples into one of four molecular subtypes (Luminal, Luminal Infiltrated, Basal, Basal Claudin-Low) based on functional molecular pathways. The GSC has been developed and validated in 305 neoadjuvant chemotherapy and 476 radical cystectomy alone patients from 10 leading cancer centers in North America and Europe. GSC measures RNA expression levels of 149 genes used to calculate multinomial probabilities of the tumor sample belonging to each of the four molecular subtypes. The higher the score, the more certain the sample w ill belong to assigned subtype. The patient tumor samples are classified as belonging to the subtype with the highest probability. The Decipher GSC molecular subtypes are based on a consensus classification derived from The Cancer Genome Atlas project and other previously published schema.[1,6-8] The GSC has AUCs ranging from 0.85 to 0.97 for classifying a tumor sample into one of the four molecular subtypes in two independent validation cohorts (n=558).[2]

**GenomeDx Medical Director (Signature)**
Medical Directors: Timothy J. Triche, MD, PhD | Doug Dolginow, MD

**Date**

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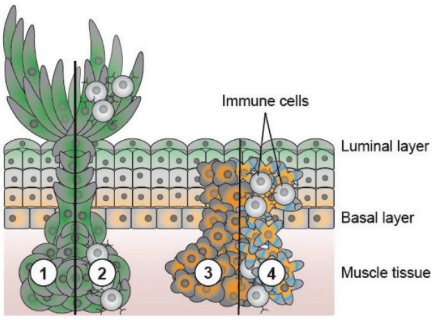
## Subtype Description

Decipher Bladder uses oligonucleotide microarrays to measure 149 RNA expression biomarkers, extracted from formalin-fixed paraffin-embedded (FFPE) bladder tumor specimens, to derive probability of a patient tumor sample belonging to each of the four molecular subtypes:

1. **Luminal**
   Luminal tumors originate from the inner surface of the bladder. These tumors are often papillary, growing outwards from the bladder wall into the lumen.
2. **Luminal Infiltrated**
   Similar to Luminal tumors, Luminal Infiltrated tumors originate from the inner surface of the bladder. However, unlike Luminal tumors, these tend to be enriched with immune cells.
3. **Basal**
   Basal tumors originate from cells lining the bladder wall (basal layer) above the smooth muscle surrounding the bladder.
4. **Basal Claudin-Low**
   An aggressive variant of the basal subtype which shows lower expression of claudin genes and increased invasive potential. These tumors are enriched for immune cells, but their anti-tumor function is actively suppressed.




Note: Mixed subtype test results are reported when the difference between the two highest predicted subtype probabilities is within 15%. Indeterminate results are reported when the difference between more than two predicted subtype probabilities is within 15%. This threshold is used to ensure the most accurate subtype classification. In the GSC validation study, mixed subtype test results between any luminal and any basal subtype were observed in 3% of cases (5/145), while indeterminate results were observed in <1% of the cases.[2]

## 3-Year Overall Survival Probabilities Post Radical Cystectomy

Estimates of 3-year overall survival post radical cystectomy were obtained using the Kaplan-Meier method. The overall survival estimates associated with patients treated with radical cystectomy alone are based on a cohort of 476 patients pooled from 3 cancer centers. Overall survival estimates for patients treated with cisplatin-based neoadjuvant chemotherapy are based on a cohort of 269 patients pooled from 7 leading cancer centers.[2] Note, overall survival estimates reported here reflect a high-risk cohort with >50% clinical stage T3/4 and 30% clinical lymph node stage N1-3.

Estimates of hazard ratios post radical cystectomy were obtained using Cox proportional hazards regression adjusting for clinical risk factors including patient age and gender. Among patients who received radical cystectomy alone, Luminal Infiltrated, Basal and Basal Claudin-Low patients had two- to three-fold increased risk of death compared to Luminal subtype patients. Among those who received cisplatin-based neoadjuvant chemotherapy, patients with a Basal subtype had as favorable an outcome as Luminal subtype patients.

**3-Year Overall Survival**

| Subtype | Radical Cystectomy (n=476)* | Cisplatin-based Neoadjuvant Chemotherapy + Radical Cystectomy (n=269)** |
|---|---|---|
| Luminal | 76.6% | 74.7% |
| Luminal Infiltrated | 59.4% | 50.6% |
| Basal | 49.2% | 77.8% |
| Basal Claudin-Low | 43.1% | 57.9% |

*p < 0.0001, **p = 0.0002

## References

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## Disclaimer

The Decipher test was developed and its performance characteristics were determined by GenomeDx Biosciences Laboratory. The GenomeDx Biosciences Laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88) to perform high complexity testing. This test has not been cleared or approved by the U.S. Food and Drug Administration.

Summary of TURBT or surgical pathology report provided for convenience of Ordering Physician. Please refer to Referring Pathologist's original pathology report to guide treatment decisions.

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