UROAMP

Urinary Comprehensive Genomic Profiling Test for Urothelial Cancer

Patient ID:

Surveillance Monitoring Report

PATIENT

Name: Sample Patient
DOB: 1943-05-01
Age & Gender: 79, Male
MRN: GW0117
Collection Date: 2022-07-03
Received Date: 2022-07-05
Report Date: 2022-07-18

PHYSICIAN

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Account: Sample Clinic
Practice Name: Sample Clinic
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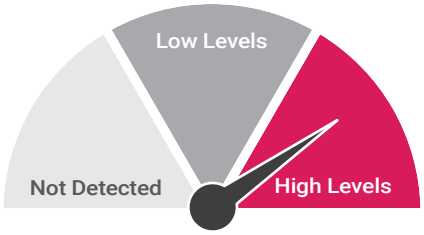
High-Grade Features

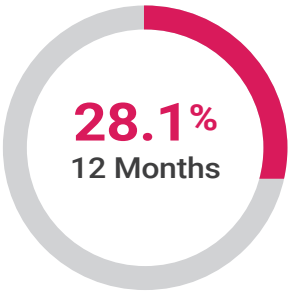


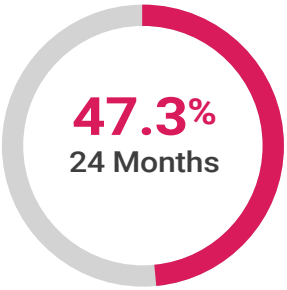
Detected

High-grade features detected at high levels.

Recurrence Risk

HIGH



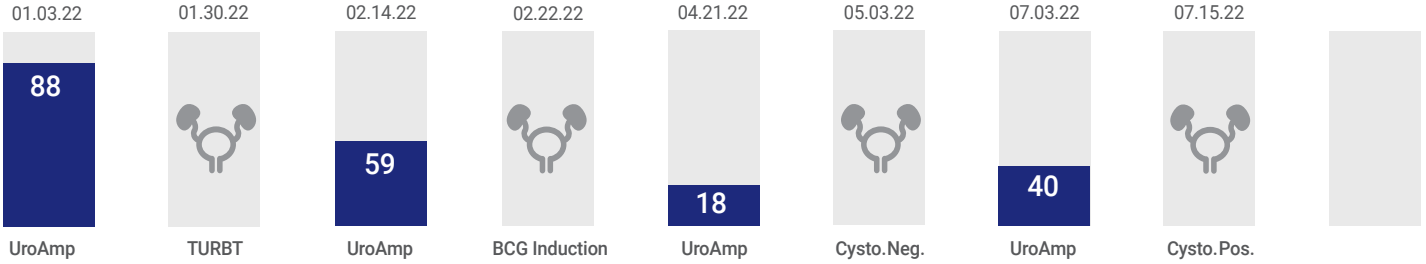


UroAmp Risk Categories Reference

Recurrence Risk	12-Month Rate	24-Month Rate
High	**28.1%**	**47.3%**
Intermediate	2.5%	23.7%
Low	0%	4.2%

Genomic Disease Burden

Monitor disease progression and therapeutic response over time



Patient is in the **40th percentile** for disease burden, meaning that 39% of bladder cancer patients tested with UroAmp had less disease burden, and 60% had more disease burden.

UroAmp Prognostic Insights

- UroAmp test results are consistent with the presence of high-grade urothelial carcinoma.
- Longitudinal monitoring is consistent with persistent disease, an increase in genomic disease burden shortly after BCG induction increases the risk for refractory disease.
- Favorably, a mutation risk factor for CIS was cleared in response to BCG (ERBB2 event no longer detected).
- Results should be correlated with cystoscopy, other standard of care testing, and consideration for biopsy and re-induction therapy.

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Report Status: **FINAL**
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Mutated Genes Identified

Gene	Description	Mutation Fraction	References
TERT	TERT mutations are commonly seen in early bladder cancer development and in some cases are associated with increased tumor recurrence (hazard ratio=5). TERT mutations are associated with future recurrence in patients with negative cystoscopy (P=0.034).	1.8%	3
FOXA1	FOXA1 loss of function is associated with squamous differentiation, increased risk for HG cancers, and a higher proliferative cell rate.	2.1%	4
KMT2C	Mutations in this gene affect the expression of DNA repair genes, leading to increased risk of chromosomal instability and elevated DNA damage. Cancer cells with this gene mutated have been shown more susceptible to PARP inhibitors in cell line studies.	1.7%	5

Test Validation and Studies

Next-generation DNA sequencing analysis was performed using the UroAmp assay to assess over 250,000 locations in the genome, across 60 recurrent urologic cancer genes. The UroAmp disease classifier was developed and validated in a multi-institutional study consisting of 593 subjects. UroAmp demonstrated a sensitivity for initial diagnosis of bladder cancer of 95.5%, and a specificity of 89.6% in urology patients without cancer. Molecular grading was developed and validated in a multi-institutional academic study of 197 subjects with bladder cancer. UroAmp high-grade prediction had a positive predictive value of 93.3% (93.3% of UroAmp urinary HG predictions were confirmed by pathology tissue grading) and a specificity of 95.2% (95.2% of pathologically low-grade cancers were not classified as molecularly HG by UroAmp's urinary risk assessment) [1, 2].

UroAmp recurrence risk categories were validated across multiple multi-institutional studies of 111 patients with a history of bladder cancer and urine collected at time of negative cystoscopy. Long-term surveillance outcomes were available for all patients (average follow-up 16 months, range 3 months to 164 months). Study demographics included patients across AUA clinical risk categories and also included patients undergoing BCG treatment.

UroAmp predicted high risk in 24% of patients, intermediate risk in 52%, and low risk in 24%. The description of outcomes in each risk group are summarized in the UroAmp Risk Categories table provided on the back of all UroAmp Bladder Cancer Surveillance test reports.

Genomic Disease Burden: this score compares this patient's urine mutational intensity to all previous UroAmp studies of patients with a history of bladder cancer. It has been shown to decrease in response to intravesical therapy and surgical interventions as well as increase over time in subjects with expanding residual disease. This score provides a single value which can be tracked longitudinally in subjects and correlated to standard of care intervention.

For additional validation and studies scan or visit convergentgenomics.com/validation

References

1 Salari K. et al., Comprehensive genomic profiling of urine DNA for urothelial carcinoma detection and risk prediction. J Clin Oncol 40, 2022 (suppl 6; abstr 450).

2 Bicocca, V. et al., Urinary comprehensive genomic profiling correlates urothelial carcinoma mutations with clinical risk and efficacy of intervention. J. Clin. Med. 2022, 11(19), 5827.

3 Hayashi, Y. et al., Clinical significance of hotspot mutation analysis of urinary cell-free DNA in urothelial bladder cancer. Front. Oncol., 19 May 2020.; Descotes, F., Non-invasive prediction of recurrence in bladder cancer by detecting somatic TERT promoter mutations in urine. Br J Cancer 117, 583-587 (2017).

4 DeGraff, DJ et al., Loss of the urothelial differentiation marker FOXA 1 is associated with high grade, late stage bladder cancer and increased tumor proliferation. PLoS ONE 7(5): e36669.

5 Rampias, T. et al., The lysine-specific methyltransferase KMT2C/MLL3 regulates DNA repair components in cancer, EMBO Reports (2019)20:e46821.

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This test was developed and its performance characteristics were determined by Convergent Genomics. The Lab is regulated under CLIA88 as qualified to perform high-complexity clinical testing. This test has not been cleared nor approved by the FDA; FDA clearance or approval is not required. This test is used for clinical purposes and clinical correlation of its results are recommended. a copy of this form shall be as valid as the original.

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