GENOMICA
Next Generation Genetics

An advanced non-invasive genetic test for the detection of tumor DNA mutations in urine related with bladder cancer

UROADVANCE

www.uroadvance.it

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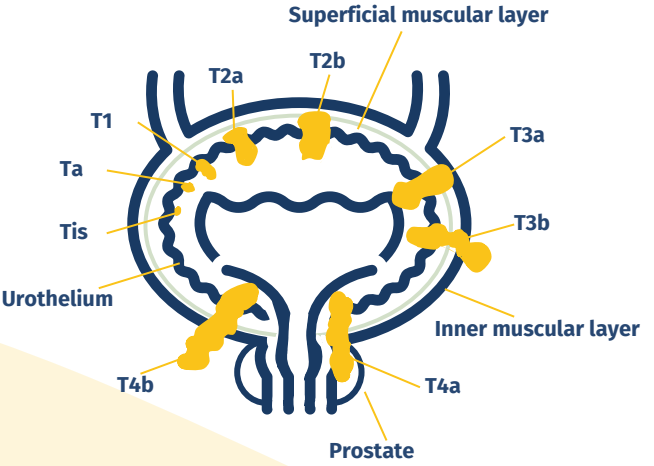
BLADDER CANCER

Bladder cancer consists of the neoplastic transformation of the cells lining the internal surface of the bladder. The most common form of bladder cancer, named **urothelial**, is a tumor that begins in the urothelial cells, which line the urethra, bladder, ureters, renal pelvis, and some other organs. The majority (**>90%**[1]) of bladder cancers are **urothelial carcinomas**.

Bladder tumors are distinguished according to the depth they reach and whether they are limited to the internal surface of the bladder (**superficial** or **non-invasive tumors** - **NMIBC**, diagnosed in approximately **85%** of cases), or whether they have invaded the muscular wall of the bladder (**muscle invasive tumors** - **MIBC**, which represent approximately **15%** of cases).



TNM STAGES OF BLADDER CANCER

1. AIOM-AIRTUM-SIAPEC-IAP. I numeri del cancro in Italia, Ottobre 2020

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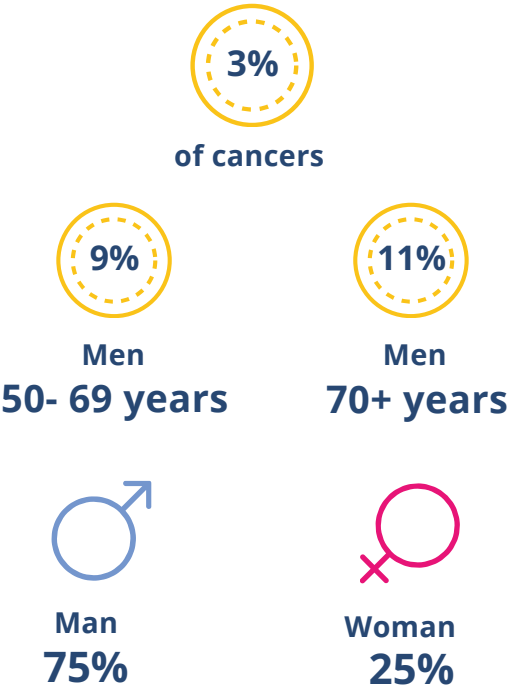
EPIDEMIOLOGY OF BLADDER CANCER

Bladder cancer represents approximately **3%** of all cancers, affecting over **313,500** individuals. An incidence of around **30,000** cases/year is estimated, with onset prevalent in old age, between 60 and 70 years old.

In men, bladder cancer is **3 times more frequent** than in women and represents the **fourth most common neoplasm** in terms of incidence and alone accounts for **9%** of tumors affecting men aged between 50 and 69, a percentage which rises to **11%** of tumors in the age group aged over 70 years.

The probability of **recurrence**, i.e. the reappearance of the tumor after some time, is very frequent and has been estimated between **50%** and **80%**[1].



1.AIOM-AIRTUM-SIAPEC-IAP. I numeri del cancro in Italia, Ottobre 2020

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THE IMPORTANCE OF EARLY DIAGNOSIS

An early and accurate diagnosis of bladder cancer is **essential** for the effectiveness of treatment, because it can broaden the spectrum of therapeutic options available and therefore increase the chances of recovery.

When an **early diagnosis** is achieved, especially in the early stages of tumor development, before it has invaded the muscular wall of the bladder, the long-term **survival rate is very high**.

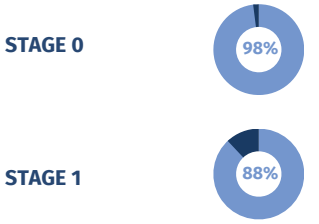
In general, **5-year survival** is approximately **80%** for both men and women, which must be interpreted in light of the large prevalence of superficial forms (with better prognosis) compared to those infiltrating the muscle wall, for which the survival rate is drastically reduced.

There is also a strong gradient by age: **96%** in **<45 years** which reduces to **66%** in **75+ years**[2].

NON MUSCLE-INVASIVE

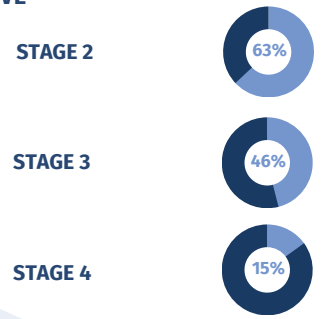
5 YEARS SURVIVAL RATES

if cought early, long-term survival is good



MUSCLE-INVASIVE

5 YEARS SURVIVAL RATES



2.AIRTUM Working Group (2017). La sopravvivenza dei pazienti oncologici in Italia.

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DIAGNOSIS OF BLADDER CANCER

1

Urinary Cytology[3]

- Diagnosis of urothelial carcinomas
- Follow-up of high-grade bladder
- tumors Low cost
- Non-invasive

SENSITIVITY: ~50-60% **HG cancers** | 16% **LG cancers**

2

Urinary cystoscopy[4]
with cytological examination

- Expensive
- Invasive
- Does not detect all lesions[3]
- Operator dependent
- Low patient compliance

SENSITIVITY: ~87-100% **All cancers**

The scientific community showed the need for a **non-invasive** and **highly accurate** test to improve the management of patients with bladder cancer by **reducing the number of cystoscopies** required for triage of patients with hematuria and for **monitoring** patients with bladder cancer.

3.Yafi et al. 2015. UrolOncol 2015;33, 66 e25-31.
4. W. Devlies, J.J. de Jong, F. Hofmann et al., (....) A Systematic Review from the European Association of Urology Guidelines Office, Eur Urol Focus (2023)

UROADVANCE

AN ADVANCED GENETIC TEST FOR EARLY DIAGNOSIS OF BLADDER CANCER

UROADVANCE is an advanced genetic test that allows the **non-invasive** identification of somatic mutations of **urinary tumor DNA (utDNA)** deriving from urothelial cells, associated with bladder cancer, through the analysis of a simple **urine sample**.

The **UROADVANCE** test allows for **early identification of bladder cancer**, significantly increasing the chances of therapeutic success.

The test uses the **latest technological innovations** developed for liquid biopsy. Thanks to **Next Generation Sequencing (NGS)** sequencing technology, it is now possible to effectively identify somatic mutations even in the presence of **small quantities of tumor cells**.

UROADVANCE is able to detect somatic mutations present in minimal percentages (up to **0.5% of Mutant Allele Frequency - MAF**).

Providing **sensitivity >90%**[4-6], the **UROADVANCE** test allows urologists to make an informed and confident decision to determine which patients may need further investigation and which may not.

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AIMS OF THE TEST

Used throughout the entire bladder cancer treatment pathway, including patient monitoring, surveillance for recurrence and minimal residual disease (MRD), as well as haematuria triage [4-6]

Identification of patients positive for bladder cancer-related mutations[4-6]

Identification of patients positive for mutations related to the presence of residual disease after radical cystectomy[6]

Identification of patients who are candidates for treatments with new generation drugs[6]

4.Ward DG, et al. (BJUI, 2019)
5.Ward DG, et al. (EurUrolOncol. 2023)
6.Chauhan PS, et al. (PLoS Med. 2021)

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INDICATIONS FOR TESTING

Patients with urinary symptoms and clinical picture suspicious for bladder cancer

Patients undergoing radical cystectomy who require monitoring for residual disease and recurrence

Patients who need to identify eligibility for targeted therapies and new generation anticancer drugs

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GENES AND MUTATIONS SCREENED

Genes screened:
promoterTERT, FGFR3, PIK3CA, TP53, ERCC2, RHOB, ERBB2, HRAS, RXRA, ELF3, CDKN1A, KRAS, KDM6A, AKT1, FBXW7, ERBB3, SF3B1, CTNNB1, BRAF, C3orf70, CREBBP, and NRAS.

Urinary Tumor DNA (**utDNA**) extracted from urine sample pellets

22

22 genes related to bladder cancer

450+

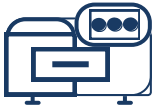
450+ hotspot mutations related to bladder cancer

THE TESTING PROCESS

1

utDNA extraction

2



Next Generation Sequencing

3

Data interpretation and Reporting

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TEST RESULTS

POSITIVE

This test result indicates that one or more **pathogenic mutations have been detected** in the targeted genes screened.

NEGATIVE

This test result indicates that **no pathogenic mutations have been detected** in the targeted genes screened.

The identification of a somatic mutation can have different implications, depending on the variant detected. Our geneticist, during genetic counseling, will explain in detail the meaning of the test result.

UROADVANCE

CLINICAL VALIDITY DEMONSTRATED BY SCIENTIFIC STUDIES ON LARGE COHORTS OF PATIENTS

A recent study[5] has demonstrated the sensitivity of sequencing techniques for the identification of somatic mutations of urinary tumor DNA (**utDNA**), useful for detecting the presence of tumors in the bladder.

The test was validated on a sample of almost **1000 patients**, enrolled in 10 highly specialized centers, simultaneously identified by a new cystoscopic diagnosis of urothelial carcinoma.

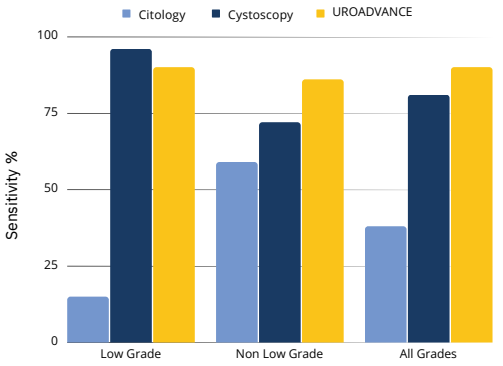
Among the hotspot mutations under study, investigated with the **UROADVANCE** test, **96%** of enrolled patients presented on average **2.5 somatic mutations** related to urothelial carcinoma regardless of grade and stage.

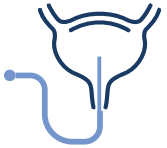
Healthy patients do not have utDNA in their urine[7]

UROADVANCE test is effective in the non-invasive detection of bladder cancer in the context of haematuria investigations and non-muscle invasive bladder cancer (NMIBC) surveillance[6]

5.Ward DG, et al. (BJUI, 2019)
6.Ward DG, et al. (EurUrolOncol. 2023)
7.Chauhan PS, et al. (PLoS Med. 2021)

HIGH SENSITIVITY AND SPECIFICITY IN ALL STAGES OF BLADDER CANCER





CYSTOSCOPY[3]

Sensitivity **84%**
Specificity 86%
NPV 96%

UROADVANCE (MIBC)[4-5]

Sensitivity **86%**
Specificity 85%
NPV 96%

UROADVANCE (NMIBC)[4-5]

Sensitivity **90%**
Specificity 85%
NPV 94%

	SENSITIVITY	SPECIFICITY
pTa	87%	85%
T1	95%	85%
T2+	86%	85%
G1	78%	85%
G2	91%	85%
G3	91%	85%
NMIBC	90%	85%
MIBC	86%	85%

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5 EASY STEPS TO GET TESTED

1. Order a test kit
2. Complete the test requisition form
3. Collect the samples (urine)
4. Ship the samples to Genomica Lab
5. Sample's processing and reporting of test results

Turnaround time **15 working days**

GENOMICA
Next Generation Genetics

Advanced molecular diagnostics solutions using state-of-the art technologies

GENOMICA is recognized as one of the most advanced molecular diagnostics laboratory in Europe, both for the state-of-the- art instruments and technologies, as well as for its high quality standards. With a comprehensive portfolio of over 10.000 genetic tests, GENOMICA is able to satisfy increasingly specialised requests in the field of molecular genetics, providing physicians and their patients with innovative and highly specialised diagnostic solutions for any clinical need.

Worldwide genetic testing provider

Laboratories with **groundbreaking technologies** and high quality standards

Dedicated R&D team

Professionals with 20+ years experience in the field of genetics and molecular diagnostics

Personalized genetic counseling with genetic counselors experts in discussing genetic test results and familial risks

Fast TAT **15 days**

UroAdvance M ENG rev.00

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