

UroVysion™ FISH

FOR DIAGNOSIS AND MONITORING OF UROTHELIAL CARCINOMA

Test Highlights

- Detects amplifications of chromosomes 3, 7, and 17, as well as deletions of the 9p21 locus.
- Can aid in the initial diagnosis of urothelial carcinoma or in the monitoring of tumor recurrence in patients previously diagnosed with urothelial carcinoma.

Clinical Background

- Patients complaining of mild hematuria have traditionally been tested by cytology and/or cystoscopy for the presence of neoplastic lesions. Cystoscopy can detect low-grade papillary tumors, but may miss high-grade carcinoma in situ, whereas cytology is more sensitive to high-grade lesions, but may miss low-grade papillary tumors. Urothelial carcinoma shows a high recurrence rate, with approximately 70 percent of cases showing recurring lesions after initial treatments. Molecular methodologies can serve as adjunctive or primary tests to diagnose transitional cell carcinoma (TCC) or monitor recurrence.
- The Vysis UroVysion™ FISH assay, which uses multitarget, multicolored FISH for the detection of numerical chromosomal abnormalities common to bladder cancer, has demonstrated high sensitivity (68-81 percent) and specificity (79-96 percent) for the detection of urothelial cell carcinoma in voided urine samples (Alvarez and Lokeshwar, 2007).

Disease Overview

- Urinary neoplasms are associated with a variety of chromosomal aberrations, the most common of which are amplifications of chromosomes, 3, 7, and 17, as well as the deletion of 9p21, the locus of the tumor suppressor gene, P16^{INK4a} (Sokolova, et al., 2000). The UroVysion™ Bladder Cancer Kit by Vysis has been designed to detect these aberrations by fluorescence in situ hybridization (FISH), and has been FDA approved based on the ability of the test to detect polysomy for chromosomes 3, 7, and 17, or the homozygous deletion of 9p21.
- In a recent study, approximately 27 percent of patients undergoing bladder carcinoma surveillance without immediate evidence of tumor recurrence showed a positive FISH result, defined as “anticipatory positive” patients. In about 65 percent of this anticipatory positive group, recurrent bladder urothelial carcinoma developed within 29 months (Yoder, et al., 2007). The UroVysion™ FISH assay provides high sensitivity and specificity to detect urothelial carcinoma in cytologically equivocal (e.g., “atypical”) and negative urine samples.

Epidemiology

- Bladder cancer, also called urothelial carcinoma (UC) or transitional cell carcinoma (TCC), is the fifth most common cancer in the United States, with approximately 50,000 new cases and 12,000 deaths each year (Ries, et al., 2006).
- Caucasians are affected twice as frequently as African-Americans.

- Age: 65 years and older.
- Gender: the ratio of affected males to affected females is 4:1.

Pathophysiology

Like many cancers, the progression of urothelial carcinoma is believed to occur through the accumulation of mutations over time that impact the regulation of cell proliferation and cell death. The suite of genetic defects detected by UroVysion™ FISH may occur in approximately 84 percent of patients with urothelial carcinoma.

Indications for Ordering

The UroVysion™ FISH test is intended for use as an aid for initial diagnosis of urothelial carcinoma in patients with hematuria and to monitor for tumor recurrence in patients previously diagnosed with urothelial carcinoma. Results from the UroVysion™ FISH test are intended to be used in conjunction with current standard diagnostic procedures.

Additional Ordering Notes

- UroVysion™ FISH is FDA approved for use on voided urine samples.
- Specimens should be fixed in Saccomanno or PreservCyt® and refrigerated.
- For specific collection, transport, and testing information, refer to the ARUP Web site at www.aruplab.com.

Interpretation

- The UroVysion™ FISH test detects chromosomal abnormalities associated with urothelial cell carcinoma from voided urine samples. Through enumeration of morphologically abnormal cells for aneuploidy of chromosomes 3, 7, and 17 or the loss of both chromosomal 9p21 segments, bladder cancer can be detected. Specimens from patients with bladder cancer show ≥ 4 cells with multiple chromosomal gains or ≥ 12 cells with the loss of both copies of 9p21.
- Negative: No evidence of numeric chromosomal aberrations associated with urothelial carcinoma identified. Negative results indicate a lack of evidence for the presence of numeric chromosomal abnormalities commonly associated with urothelial carcinoma within the cells collected in this specimen. Although the Vysis UroVysion™ kit was designed to detect genetic abnormality associated with most urothelial cancers, there will be some urothelial cancers for which genetic changes cannot be detected by the UroVysion™ test.

- Positive: Numeric chromosomal aberrations associated with urothelial carcinoma identified. Positive results indicate the presence of one or more numeric chromosomal abnormalities commonly associated with urothelial carcinoma within the cells collected in this specimen. Positive results in the absence of clinical documentation of urothelial carcinoma within the bladder suggest the possibility of urothelial carcinoma or other urologic malignancy from another site (including ureter, kidney, urethra, and prostate). In this circumstance, further clinical evaluation to exclude these as a source of the abnormal cells is justified.

Limitations

- Negative results in the presence of other symptoms/signs of urothelial carcinoma may suggest the possibility of a false-negative test. In this circumstance, additional clinical studies to exclude urothelial carcinoma should be pursued, as clinically indicated.
- Mutations or genetic defects other than amplification of chromosomes 3, 7, or 17 or deletions of 9p21, will not be detected by UroVysion™ FISH.

Methodology

- Microscope slides are prepared from urinary samples, followed by fluorescence in situ hybridization (FISH) using the UroVysion™ Bladder Cancer kit from Vysis®.
- Slides are subsequently evaluated by a pathologist with the aid of the BioView Duet™ instrument, an automated scanning fluorescence microscope and image analysis system.

Related Tests

- Cytology, Urologic (8209704)
- NMP22® (0080281)
- Bladder Tumor Associated Antigen (8100500)

References

1. Alvarez A, Lokeshwar VB. Bladder cancer biomarkers: current developments and future implementation. *Curr Opin Urol* 2007;17(5):341-6.
2. Ries LAG, Harkins D, Krapcho M, et al (eds). SEER Cancer Statistics Review, 1975-2003, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2003/, based on November 2005 SEER data submission, posted to the SEER web site, 2006.
3. Sokolova IA, Halling KC, Jenkins RB, et al. The development of a multitarget, multicolored fluorescence in situ hybridization assay for the detection of urothelial carcinoma in urine. *J Mol Diag* 2000;2:116-123.
4. Yoder BJ, Skacel M, Hedgepeth R. Reflex UroVysion™ testing of bladder cancer surveillance patients with equivocal or negative urine cytology: a prospective study with focus on the natural history of anticipatory positive findings. *Am J Clin Pathol* 2007;127(2):295-301.
5. Vysis®, Inc. UroVysion™ Bladder Cancer Kit Package Insert.

Test Information

8100600

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For specific collection, transport, and testing information, refer to the ARUP Web site at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.