Urothelial Carcinoma by UroVysion FISH

Indications for Ordering

- May aid in diagnosis of urothelial carcinoma in individuals with hematuria
- Monitor for tumor recurrence in patients previously diagnosed with urothelial carcinoma

Test Description

Fluorescence in situ hybridization/computer-assisted analysis/microscopy

Tests to Consider

Primary test

UroVysion FISH 2001181
- Detects
  - Amplifications of chromosomes 3, 7, 17
  - Deletions of the 9p21 locus

Related tests

Bladder Tumor Associated Antigen 2000183
- Aid in management of bladder cancer patients in conjunction with cystoscopy
- Qualitative assay detects bladder tumor-associated antigen in urine of patients diagnosed with bladder cancer

Cytology, Non-Gynecologic 2000623

NMP22, Urine 0080281
- Aid in diagnosis of urothelial carcinoma in conjunction with standard diagnostic procedures and monitoring for tumor recurrence

Disease Overview

Incidence

- ~143,000 new cases of cancer in urinary system/year in U.S. (American Cancer Society, 2016)
  - Bladder cancer – ~77,000
  - Kidney and renal pelvis – ~63,000
  - Ureter and other urinary organs – ~3,500
- Caucasians:African Americans = 2:1
- Males:females = 4:1

Age of onset – ≥65 years

Symptoms

- Hematuria
- Irritative voiding

Screening/diagnosis issues

- Individuals complaining of mild hematuria traditionally tested for the presence of neoplastic lesions by
  - Cytology
    - More sensitive to high-grade lesions
    - May miss low-grade papillary tumors
  - Cystoscopy
    - Can detect low-grade papillary tumors
    - May miss high-grade carcinoma in situ
- Urothelial carcinoma shows high recurrence rate
  - ~70% of cases show recurring lesions after initial treatments
  - Necessitates ongoing, lifelong surveillance
- Bladder cancer can be detected by
  - Enumeration of morphologically abnormal cells for aneuploidy of chromosomes 3, 7, 17
  - Loss of both chromosomal 9p21 segments
- Molecular testing can serve as primary or adjuvant tests
  - Noninvasive when compared to cystoscopy
  - May be used to diagnose urothelial carcinoma
  - May be used to monitor recurrence of urothelial carcinoma
- UroVysion detects chromosomal abnormalities associated with urothelial cell carcinoma from voided urine specimens

Genetics

Variants

- Amplifications of chromosomes 3, 7, 17
- Deletions of the 9p21 locus

Test Interpretation

Sensitivity/specificity

- Clinical sensitivity – 68-81%
- Clinical specificity – 79-96%
Results
• Positive
  o One or more numeric chromosomal abnormalities commonly associated with urothelial carcinoma detected
    ▪ ≥4 cells show gains for 2 or more chromosomes (3, 7, or 17) in the same cell, or
    ▪ ≥12 cells have zero 9p21 signals
  o In the absence of clinical documentation of urothelial carcinoma within the bladder, positive result suggests
    ▪ Possibility of urothelial carcinoma or other urological malignancy
      • Ureter
      • Urethra
      • Kidney
      • Prostate
    ▪ Further clinical evaluation to exclude these tissues as a source of abnormal cells is recommended
• Negative
  o Lack of evidence for presence of numeric chromosomal abnormalities commonly associated with urothelial carcinoma within cells collected in specimen

Limitations
• Some urothelial cancers will not be detected
• Negative results in the presence of other symptoms/signs of urothelial carcinoma may suggest possibility of false-negative test result
• Not detected
  o Gene variants or defects other than
    ▪ Amplification of chromosomes 3, 7, or 17
    ▪ Deletion (loss) of 9p21 locus