Urine Test May Detect Aggressive Prostate Ca

BY ELIZABETH MECHCATIE

A molecular urine test that detects the fusion of two genes associated with more aggressive prostate cancers was highly specific for prostate cancer in a study in men undergoing prostate biopsies, investigators report based on an interim review.

The test, which is not available commercially, detects fusions between TMPRSS2 (T2), an androgen-responsive gene, and the oncogenic transcription factor ERG. This fusion is found in about half of all prostate tumors, and has been associated with adverse clinical outcomes.

Initially reported at the end of 2005, this fusion was the first specific chromosomal rearrangement identified in prostate tumors, and appears to be "an ideal target for a diagnostic test because of the high specificity for prostate cancer," according to Jack Groskopf, Ph.D., director of research and development in the cancer diagnostics division of Gen-Probe Inc., the San Diego-based company developing the test.

The test, known as the T2:ERG test, may eventually be useful in determining prognosis and selecting treatment in men diagnosed with prostate cancer, Dr. Groskopf said at a press briefing in advance of the study's presentation at a symposium on genitourinary cancers. He cited the need for a test that can help determine which prostate cancers require aggressive treatment and which could be managed conservatively.

To date, the test has been used on urine specimens collected in 556 men at three medical centers following a digital rectal exam and before prostate biopsy. The test predicted the presence of prostate cancer on biopsy with a specificity of 84%, compared with a specificity of 27% for serum prostate-specific antigen (PSA), with similar results at all three sites, he said.

The gene fusion has been present in about 42% of all positive biopsies to date, an indication that the test is "doing pretty well" in terms of sensitivity, as this correlates to the prevalence of the gene fusion in about half of all prostate cancers, he noted.

The test predicted the presence of prostate cancer on biopsy with a specificity of 84%, compared with a specificity of 27% for serum prostate-specific antigen.

In addition, there have been significant correlations between a positive test and indicators of cancer aggressiveness, Gleason score, percent of prostate cancer involvement, and percent positive core, providing preliminary evidence indicating that T2:ERG status correlates with the criteria for aggressive cancers, he said.

The next step is to follow up and confirm these findings, and "perhaps more importantly," to start studying the correlation between the urine test and pathologic features in prostatectomy tissue, such as tumor volume, stage, and grade, Dr. Groskopf said.

Describing this work as an "important first step," Dr. Howard Sandler, moderator of the briefing, remarked that it represents "an amazingly short interval between the basic fundamental discovery and potential clinical utility of a diagnostic test."

If it turns out that gene fusion is related to progression of prostate cancer in half of all men who develop prostate cancer, the molecular change will have major implications for diagnosis and possibly treatment as well, because it may also be a therapeutic target, said Dr. Sandler, chairman of radiation oncology at the Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles. "There is interest in targeting our diagnostic strategies towards patients who will have cancers that really need to be treated, not those that are overdiagnosed and are never destined to cause clinical harm," he added.

The annual Genitourinary Cancers Symposium is sponsored by the American Society of Clinical Oncology, American Society for Therapeutic Radiology and Oncology, and Society of Urologic Oncology. ■