Genetic biomarker test predicts recurrence and survival outcomes for men with high-risk prostate cancer

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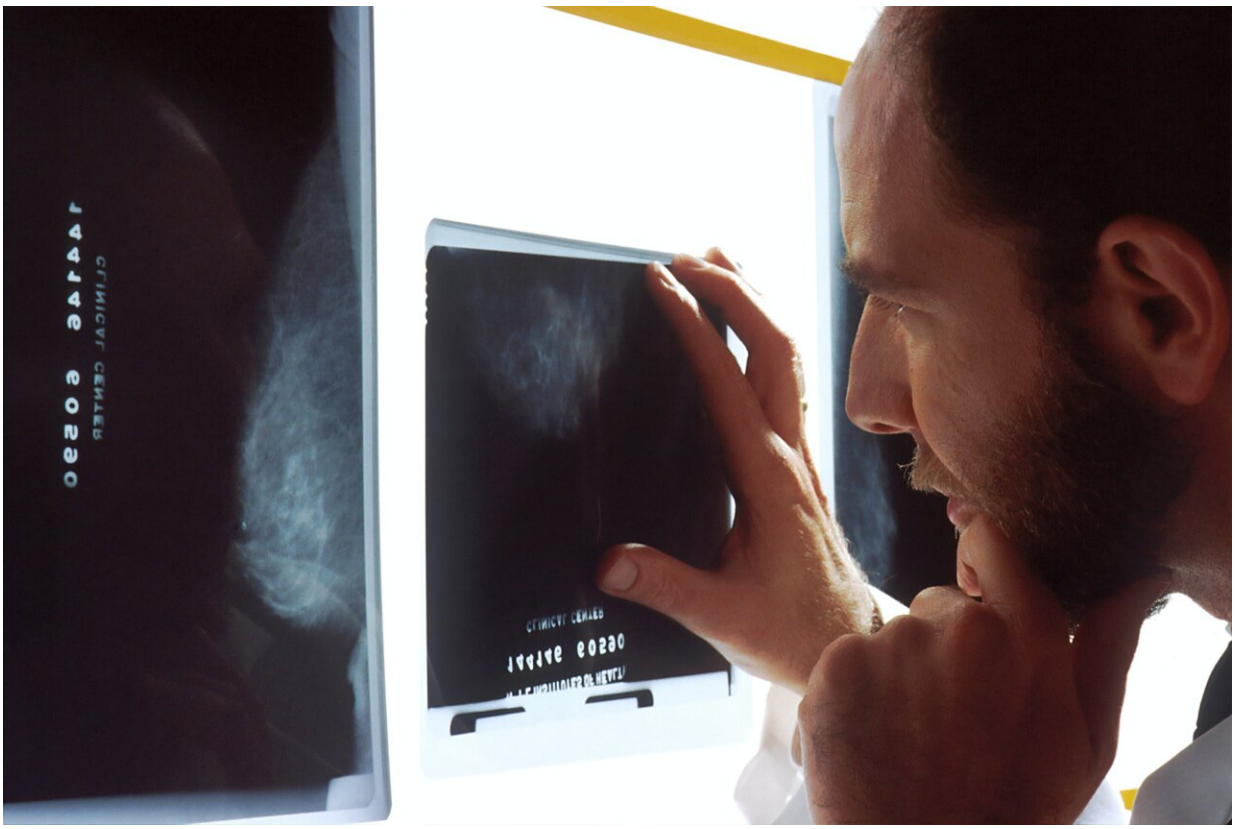

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A new meta-analysis finds that a genetic biomarker test accurately predicts how men with high-risk prostate cancer will respond to

treatment with radiation and hormone therapy. The study, which examined biopsy samples collected from three large, randomized clinical trials, indicates that physicians potentially can use genetic test scores to personalize treatment for men with the most aggressive form of prostate cancer. Findings will be presented today at the American Society for Radiation Oncology (ASTRO) Annual Meeting.

Two-thirds of prostate cancer deaths occur in patients with high-risk prostate cancer, for whom standard treatment involves radiation therapy and two years of hormone therapy. Balancing survival risk with quality of life is an important consideration for many men with this disease. Hormone therapy can cause difficult side effects, including hot flashes, loss of libido and possible cardiovascular and cognitive changes. Researchers believe that biomarkers could potentially be used to develop more precise treatment guidelines and designate who might benefit from less therapy or who might benefit from additional treatment with newer hormonal agents.

"When a man is diagnosed with high-risk prostate cancer, we don't have a widely accepted way to sub-classify their cancer and truly personalize their therapy, but we think we will in the near future," said lead author Paul L. Nguyen, MD, a professor at Harvard Medical School and vice chair for clinical research in the department of radiation oncology at Brigham and Women's Hospital/Dana-Farber Cancer Institute in Boston.

Dr. Nguyen and his team utilized the Decipher biopsy test, which analyzes the activity of 22 genes in prostate tumors to produce a score reflecting how aggressive a patient's cancer is. "We are optimistic that this score can tell us which men should have their treatment de-intensified, meaning they will get less hormone therapy, and which men should have their therapy intensified, meaning they will get an additional, second-generation hormone therapy," said Dr. Nguyen. "With this genetic marker, we hope to personalize therapy for men with high-

risk prostate cancer rather than having a one-size-fits-all approach."

Researchers calculated Decipher scores using RNA extracted from archival biopsy samples collected in three major prostate cancer trials (RTOG-9202, n=90; RTOG-9413, n=172; RTOG-9902, n=123). Then, they examined how closely these Decipher scores were associated with long-term outcomes.

The genetic signature predicted which patients were more likely to develop distant metastases (HR 1.24, 95% CI 1.11-1.39), which were more likely to die of their prostate cancer (HR 1.27, 95% CI 1.13-1.43) and which were more likely to die from any cause (HR 1.12, 95% CI 1.05-1.20). For example, the rate of distant cancer metastasis at 10 years was 29% for patients whose scores indicated they had more aggressive cancer, compared to 13% for those whose scores signaled lower risk.

While the Decipher test was previously validated using tissue samples taken after radical prostatectomy, the current meta-analysis examined tissue taken before treatment, at the time of initial diagnosis. "This study is the first to validate a genetic biomarker for high-risk prostate cancer using pre-treatment archival tissue from large prospective randomized trials," said Dr. Nguyen. "Using archival tissue samples from a wide range of centers and patients—hundreds of cancer centers across the country—shows that this test can be helpful for many men with high-risk disease."

The age of the samples also meant that researchers could examine very long-term outcomes on the patients with high-risk prostate tumors. "A strength of using this tissue is that we have the complete follow-up for 20 to 30 years on these patients," said Dr. Nguyen.

Dr. Nguyen emphasized that the test needs further validation before it can become widely adopted. To that end, the NRG-GU009/PREDICT-

RT trial led by Dr. Nguyen and Dr. Oliver Sartor is currently enrolling patients with high-risk prostate cancer to test Decipher's predictive validity in a prospective randomized trial.

"For a man with high-risk prostate cancer, this genetic score can be a very powerful prognostic tool that can tell us whether he is likely to be cured from treatment or is likely to see his cancer return again," said Dr. Nguyen. "I see this as a great opportunity to change the standard of care for patients in the future by using genomics to personalize therapy."

More information: Conference: www.astro.org/Meetings-and-Edu …/2021/Annual-Meeting

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