# Time to biochemical failure could be used as surrogate endpoint in treatment: LA prostate cancer

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An analysis of the NRG Oncology clinical trial NRG-RTOG 9202 showed that the interval of time to biochemical failure (IBF), or the time it takes for previously treated cancer to return as indicated by prostate specific antigen (PSA) rise, could be used as a surrogate endpoint for locally advanced prostate cancer. Previously, surrogate endpoints based on PSA, which are alternate endpoints that could determine the effectiveness of a treatment earlier than traditional clinical endpoints, have been tested and evaluated with radiotherapy and short-term androgen deprivation. However, surrogate endpoints for long-term androgen deprivation, a proven therapy in high-risk, localized cancers, have not been investigated. The results of this analysis are published in the *Journal of Clinical Oncology*.

"The main goal of this trial study was to determine if time interval free of biochemical failure could stand as a surrogate endpoint for the effect of long-term androgen deprivation on two clinical endpoints: prostate cancer-specific survival and overall survival," stated James Dignam, Ph.D., of the Department of Public Health Sciences at University of Chicago and the NRG Oncology Statistics and Data Management Center, a member of the Cancer Prevention and Control research program at the University of Chicago Medicine Comprehensive Cancer Center, and the lead author of the NRG-RTOG 9202 analysis.

NRG-RTOG 9202 randomly assigned 1,520 men to one of two

treatment arms. Treatment Arm 1 received short-term androgen deprivation (AD) therapy for four months; whereas Treatment Arm 2 received long-term AD for approximately 28 months. Survival modeling and landmark analysis methods were applied to evaluate the associations between long-term AD, IBF, prostate-specific survival, and overall survival.

"Men who remained free of biochemical failure for three years had significantly more favorable overall survival and prostate cancer-specific survival," added Dr. Dignam. "Additionally, data showed that 50% of the men who experienced biochemical failure by three years died of prostate cancer as of 15 years, as opposed to 19% among the men who were still free of biochemical failure at three years."

Accounting for three-year IBF status reduced the long-term AD overall survival benefit from 12% (hazard ratio (HR, 0.88; 95% CI, 0.79 to 0.98) to 6% (HR, 0.94; 95% CI, 0.83 to 1.07). For prostate cancer-specific survival, long-term AD benefit was reduced from 30% (HR, 0.70; 95% CI, 0.52 to 0.82) to 6% (HR, 0.94; 95% CI, 0.72 to 1.22). These findings satisfied the surrogacy criteria, as IBF identified the benefit for long-term AD on disease-specific and overall survival, suggesting that IBF has the potential to serve as a valid primary endpoint if validated in a proper meta-analysis. Even if not used as a primary endpoint, IBF is an informative intermediate endpoint in Phase II/III clinical trials, and may aid in patient risk monitoring after initial treatment.

**More information:** James J. Dignam et al. Time Interval to Biochemical Failure as a Surrogate End Point in Locally Advanced Prostate Cancer: Analysis of Randomized Trial NRG/RTOG 9202, *Journal of Clinical Oncology* (2018). DOI: 10.1200/JCO.18.00154

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