



## EDITORIAL COMMENT

Monitoring prostate-specific antigen (PSA) is the mainstay of evaluating definitive therapy in that a rising PSA is predictive of developing distant metastases and prostate cancer-specific mortality (PCSM). Recent studies have identified post treatment PSA based surrogates for PCSM which is important given that it takes 10-20 years to die after unsuccessful definitive therapy.<sup>1,2</sup> In this article, investigators describe an analysis of 204 men with unfavorable prostate cancer enrolled in a randomized clinical trial comparing 70.2 Gy external beam radiotherapy with or without 6 months of androgen deprivation (ADT). With a median follow-up more than 18 years, men with a PSA nadir >0.2 ng/mL and a time to nadir (TTN) <12 months had a statistically significant increased PCSM rate. The authors conclude that these observations infer a high likelihood of castrate resistant prostate cancer (CRPC) and propose that men with a measurable PSA nadir and a short TTN be considered for randomized trials evaluating the impact on survival of salvage ADT with or without novel agents shown to prolonged survival in men with CRPC.

The authors are to be congratulated on a well-written thought-provoking article that adds to the literature on PSA based surrogates for PCSM. Strengths of this study include its prospective design, long median follow-up, and consistency in the designation of PCSM. The authors address some of the study limitations. Additionally, given the inclusion of men that would now be considered intermediate risk, small number of men receiving external beam radiotherapy/ADT who had a PSA nadir >0.2, and more importantly-the limited duration of ADT and the low dose of radiotherapy, alternate conclusions could be reached. It is therefore problematic to extrapolate results from patients who did not receive the current recommendations of ADT and were treated with suboptimal radiation dose to an era of modern therapy.

Nevertheless, this long-term study significantly adds to the growing data regarding PCSM surrogates. These indicate that post treatment PSA kinetics including TTN, PSA nadir >0.5, PSA doubling time, PSA bounce, and a shorter interval to PSA failure can predict the risk of CRPC. If these predictors continue to be confirmed on external validation, it will change how we identify those men in need for prostate cancer trials.

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## References

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<https://doi.org/10.1016/j.urology.2018.11.057>  
UROLOGY 126: 151, 2019. © 2019 Elsevier Inc.



## AUTHOR REPLY

We thank Dr. Gejerman for recognizing the importance of this work. Indeed, we agree that the results of the present study are hypothesis generating. Thus, we enthusiastically await the long-term results of RTOG0815 which, with a planned enrollment of 1520 men with intermediate-risk prostate cancer, randomized men to either dose-escalated RT alone vs dose-escalated RT combined with 6 months of androgen deprivation, stratified by the number of risk factors, ACE-27, Adult Comorbidity Evaluation 27 comorbidity status, and RT modality. These data will validate or refute the hypothesis-generating finding in the present study, which suggests that a higher prostate-specific antigen nadir and shorter time to prostate-specific antigen nadir are prognostic factors and potential surrogates for prostate cancer-specific mortality, in a population treated with dose-escalated RT.

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<https://doi.org/10.1016/j.urology.2018.11.058>  
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