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Editorial Comment

As a greater proportion of men are diagnosed with high-risk prostate cancer, there is increasing need to elucidate the optimal management strategy for these patients. In metastatic hormone-sensitive disease, intensification of treatment using docetaxel and/or androgen receptor signaling inhibitors has been shown to improve survival. It stands to reason that in men with localized disease at high risk for treatment failure, many of whom may harbor micrometastatic disease, intensifying therapy may similarly provide oncologic benefit. This has been shown to be true for addition of abiraterone to radiation and androgen deprivation therapy (ADT).[1] Prior studies using neoadjuvant ADT have shown improvement in surgical margins but not oncologic outcomes.[2] CALGB 90203 investigated neoadjuvant chemohormonal therapy and showed improvement in biochemical progression-free survival (bPFS), metastasis-free survival, and overall survival, though not in the primary end point of 3-year bPFS.[3] The primary barrier to acceptance was likely the significant toxicity (26% grade 3 and 19% grade 4). There are now several phase 3 trials in process, including PROTEUS, investigating neoadjuvant androgen receptor signaling inhibitors in high-risk disease.

The authors should be commended on a well-designed prospective randomized trial investigating neoadjuvant docetaxel and ADT vs neoadjuvant ADT alone for high-risk prostate cancer.[4] They found a significant improvement in 3-year bPFS (29% vs 9.5%, $P = .002$) in a population notably at very high risk, with over 50% having clinically node-positive disease. Optimism about these results should be tempered by the lack of more meaningful end points such as overall survival and metastasis-free survival, in addition to the still significant grade 3 to 4 toxicity.

We are on the cusp of integration of systemic treatment for high-risk localized disease. Randomized trials such as this one are paving the way toward a future of improved survival. Once efficacy is proven, tailoring agents to minimize toxicity and maximize benefit will be the next frontier.

Benjamin V. Stone[1] **and Adam S. Kibel**[1]
[1]*Department of Urology, Brigham and Women's Hospital Boston, Massachusetts*

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