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Abstract
Prostate cancer is the most commonly diagnosed cancer and second most common cause of cancer death in American men. Although high-risk disease accounts for less than 15% of diagnoses, high-risk prostate cancer patients have a cancer-specific mortality rate of 15% at 10 years. There is currently no consensus on the optimal management of high-risk disease because (1) there are different primary modalities available (ie, surgery, radiation), for which there are no randomized trials comparing efficacy; and (2) unstandardized timing of different therapies (ie, neoadjuvant v concurrent v adjuvant), which makes comparisons of efficacy problematic. Increased understanding into the mechanisms leading to the formation of advanced metastatic disease has spurred the development of agents to target these pathways. However, new questions regarding optimal management of disease arise with regard to the role of these therapies in combination with "conventional" primary modalities for earlier stage, high-risk prostate cancer patients. In this article, we review the transforming world of multimodality therapy in high-risk prostate cancer.

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