State-of-the-Art Management for the Patient with Castration-Resistant Prostate Cancer in 2012.

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Abstract

Much progress has been made in metastatic castration-resistant prostate cancer (CRPC), and multiple new U.S. Food and Drug Administration (FDA)-approved survival-prolonging drugs are now available. In 2004, docetaxel/prednisone was the first therapy shown to prolong survival. In 2010 and 2011, sipuleucel-T, cabazitaxel/prednisone, and abiraterone/prednisone were FDA approved. Two new agents, radium-223 and MDV-3100, have recently reported large phase III trials prolonging overall survival and will be submitted for regulatory approval in 2012. One can now begin to ask, is there an optimal sequence for therapies in metastatic CRPC? Despite the recent progress, there is much we do not know and virtually no information on this important question. We know that abiraterone/prednisone and cabazitaxel/prednisone are appropriate choices for a patient after receiving docetaxel, but we do not know what, if anything, represents the optimal sequence for abiraterone and cabazitaxel. In fact we do not understand how one therapy may affect the response to a subsequent therapy. We are also aware that the pre- and postdocetaxel spaces represent regulatory rather than biologic divisions. In addition, despite the proven role of docetaxel/prednisone, many patients with CRPC are not considered to be suitable for chemotherapy, and worldwide many never receive any form of chemotherapy. What is the optimal management for these patients? Taken together it is reasonable to assess patient preferences, prior therapies and response/tolerance to prior therapies, burden of disease, comorbidities, current symptoms, drug toxicities, out-of-pocket costs, etc., in clinical decision making. Given the many factors we do not know, it is hard to be dogmatic in approaching the therapeutic options for the patient with CRPC. We will likely soon move beyond the current sequencing paradigm and begin to assess new combinations in a systematic and rational fashion. Perhaps one day, in the not too distant future, we will develop molecular "stratification systems" to better guide therapeutic choices in CRPC.