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Re: Activity of Cabazitaxel in Castration-resistant Prostate Cancer Progressing After Docetaxel and Next-generation Endocrine Agents

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Experts' summary

The authors addressed sequencing treatments for castration-resistant prostate cancer (CaP) in the postdocetaxel setting. Antitumor activity of cabazitaxel in 59 patients treated between January 2008 and August 2013 was analyzed retrospectively. Forty-one patients had previously received abiraterone (n = 32), sequential abiraterone and enzalutamide (n = 5), or enzalutamide (n = 4). Antitumor activity was reported before and after novel endocrine drugs, and it appeared less in abiraterone- and enzalutamide-naive patients (decreased median overall survival by 6.2 mo and decreased median progression-free survival by 1.1 mo).

Experts' comments

The authors validated cabazitaxel as a treatment option in this setting and emphasized the need for predictive biomarkers to optimize treatment decision making. However, treatment decision making and biomarker development will be more difficult if the terminology used to describe CaP does not evolve as fast as the treatment options. Current nomenclature does not characterize precisely CaPs that recur during androgen deprivation therapy (ADT). The available descriptors (androgen independent, castration resistant, hormone resistant, androgen depletion independent, hormone relapsed) do not acknowledge the sustained role for androgens for CaP cell growth, do not distinguish between CaP responsiveness to androgens versus other steroids, and do not appreciate a cancer's sensitivity to further therapeutic manipulation of its intracrine androgenic milieu [1,2]. *Castration-recurrent CaP* is a more accurate designation than *castration-resistant*, which seems to have become the preferred term [3], since it characterizes best the continuum of advanced CaP treated by ADT: regression on initiating ADT followed by growth despite castrate levels of circulating androgens to produce clinical recurrence. However, this term also seems to lump too many

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advanced CaPs together. Castration-recurrent prostate cancer does not [1] discriminate between CaP that fails first-, second-, or third-line ADT; [2] distinguish surgical from medical castration; [3] indicate whether “complete” androgen blockade was administered; or [4] specify whether ADT was administered continuously or intermittently. These nuances are relevant because the method of ADT may differentially affect CaP progression and response to newer agents. Repositioning, sequencing, and/or combination of traditional or novel ADTs [4], alone or in combination with radiation, chemotherapy, or immunotherapy, further complicate the accurate description of an individual patient’s CaP.

We introduce a nomenclature method that summarizes the timing, sequence, and combination of treatments and specifies the drugs that have been administered. This nomenclature allows for an initial assessment of the treatment course, facilitates recognition of side effects from the various interventions, and enables consideration of further therapeutic interventions, their implications for future disease management, disease monitoring, patient stratification, and biomarker development. The advantages are obvious when comparing *castration-resistant* with radical prostatectomy-recurrent, luteinizing hormone-releasing hormone agonist-recurrent, bicalutamide-recurrent, sipuleucel-T–recurrent, docetaxel-recurrent, abiraterone-recurrent, or enzalutamide-recurrent CaP.

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