

# Metastatic Castrate-Resistant Prostate Cancer Practical Review



Abby Moeller, PA-C\*, Michael Cookson, MD, MMHC,  
Sanjay G. Patel, MD

## KEYWORDS

- Castrate-resistant prostate cancer • CRPC • Androgen deprivation therapy • ADT
- LHRH • Immune therapy • Skeletal-related event (SRE)

## KEY POINTS

- Androgen deprivation therapy, with goals of creating a castrate-level testosterone, is the primary baseline treatment of metastatic prostate cancer and should be continued indefinitely.
- There are many different therapies now available for men with metastatic castrate-resistant prostate cancer (CRPC). Optimal selection of each therapy depends on the patient's clinical assessment and performance status.
- In addition to treatment of metastatic disease, attention should also be directed toward therapies that optimize the patient's bone health and quality of life.

## DEFINITIONS

Castrate: serum total testosterone level of less than 50 ng/dL.<sup>1</sup>

Castrate-resistant prostate cancer (CRPC): patient with prostate cancer that has an increasing PSA level or worsening radiographic changes in the face of a total testosterone level of less than 50 ng/dL.<sup>2</sup>

Hormone-sensitive prostate cancer: patient with prostate cancer and a detectable PSA level that is stable or decreasing despite androgen deprivation therapy (ADT).

Metastasis: visible signs of cancer on imaging, beyond the primary cancer.

Prostate-specific antigen (PSA): enzyme secreted from prostate epithelial cells.<sup>3</sup>

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Department of Urology, Stephenson Cancer Center, The University of Oklahoma Health Sciences Center, 800 North East 10th Street, Suite 4300, Oklahoma City, OK 73104, USA

\* Corresponding author.

E-mail address: [Abby-Moeller@ouhsc.edu](mailto:Abby-Moeller@ouhsc.edu)

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## INTRODUCTION

Prostate cancer remains the most commonly diagnosed malignancy in men and is diagnosed and monitored using serum PSA.<sup>4</sup> Patients with prostate cancer are broadly categorized as having localized or metastatic disease. Patients diagnosed with localized prostate cancer typically undergo primary treatment with cryotherapy, radiation therapy, or surgery and should have a persistently undetectable or stable low PSA, which indicates treatment success. It is recommended to follow the PSA for at least 20 years after primary therapy because increases in PSA indicate primary treatment failure and may necessitate further adjuvant therapies.<sup>5</sup> A small subset of patients who undergo primary treatment undergo disease progression and develop metastatic disease. Patients initially diagnosed with metastatic disease or who progress to metastatic disease after primary treatment have increasing and often markedly elevated levels of PSA.<sup>6</sup>

The mainstay treatment of patients with metastatic prostate cancer is lifelong ADT. ADT aims to lower the total testosterone (T) level to castrate levels, defined as less than 50 ng/dL. ADT can be accomplished through surgical castration (bilateral orchiectomy) or medically through manipulation of the hypothalamic-pituitary axis (luteinizing hormone-releasing hormone [LHRH] agonist/antagonist).<sup>7</sup>

While a patient is responding to ADT, PSA levels decline and stabilize and metastatic disease burden on imaging decreases in size. Patients in this disease state are considered to have hormone-sensitive prostate cancer. Unfortunately, the patient may experience an increasing PSA level and worsening of disease burden on imaging. Patients in this disease state are considered to have CRPC. CRPC is defined as having a total testosterone level of less than 50 ng/dL, with 2 consecutive rises in PSA with a PSA level of 2 ng/mL or more.<sup>8</sup> Generally, the average time it takes a patient with hormone-sensitive prostate cancer to develop CRPC is on average 2 years and thus these patients require close monitoring with physical examination, laboratory tests, and imaging.<sup>1</sup>

Over the last decade, advances in metastatic CRPC research have led to the development of several therapies designed to slow the progression of disease and improve the overall bone health of patients with CRPC. This article discusses relevant patient and treatment considerations in men with metastatic CRPC.

## EVALUATION OF PATIENTS WITH METASTATIC CASTRATE-RESISTANT PROSTATE CANCER

### *General Considerations*

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#### *History*

The history in a patient with CRPC should include a discussion of urinary symptoms including, but not limited to, force of urine stream, urinary incontinence, hematuria, ability to empty, urinary frequency, and dysuria. Also, assess for weight loss, constipation, or bone pain. It is also important to evaluate neurologic symptoms such as fecal incontinence, saddle anesthesia, or numbness or tingling, because these can indicate signs of spinal cord compression, which requires urgent evaluation and management. Assessment of treatment-related specific side effects should be performed and are discussed later.

#### *Physical examination*

In addition to a standard physical examination, palpation of bony areas such as spinal column and hips may indicate bone metastases, which may require further evaluation and treatment.

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