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REVIEW ARTICLE

Castration-resistant prostate cancer: Where are we going?☆

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Abstract

Context: Hormonal therapy allows effective control of cancer-related symptoms in advanced stages. However, the disease will progress in almost all these metastatic prostate cancer patient until becoming resistant to androgen suppression. The emergence of new drugs will most probably have open up new expectations regarding the treatment of this cancer.

Objective: The aim of the present review has been to provide an overview of the current status of castration-resistant prostate cancer and to share the high expectations created with the new treatments.

Evidence acquisition: Evidence was obtained from multidisciplinary meetings with the participation of urologists and oncologists, where they pooled the analysis of original articles in the literature and defined the content of the article.

Evidence synthesis: Chemotherapy with docetaxel was a turning point in castration-resistant prostate cancer after the failure of hormonal therapy failure. For the first time, it achieved increased survival time in comparison with mitoxantrone and prednisone. Combination therapy with docetaxel and prednisone is the first-line choice treatment. Once the cancer has progressed, there is no clear alternative, although some novel agents have created expectations for the treatment of this type of cancer.

Conclusions: The range of therapeutic options for castration-resistant prostate cancer has increased dramatically with the arrival of new drugs. At present, cabazitaxel, and in the near future, abiraterone, have been found to be effective drugs in second-line treatment after progression to docetaxel, increasing survival by 2–4 months and reducing risk of death by 30–35%.

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Cáncer de próstata resistente a castración: ¿hacia dónde vamos?

Resumen
Contexto: El tratamiento hormonal permite un control eficaz de los síntomas relacionados con el cáncer de próstata metastásico; sin embargo, la práctica totalidad de estos pacientes sufrirán progresión de su enfermedad cuando esta se hace resistente a la supresión androgénica. La aparición de nuevos fármacos permite abrir nuevas expectativas en el tratamiento de esta enfermedad.
Objetivo: Elaborar un documento de revisión sobre la situación actual del cáncer de próstata resistente a castración y compartir las grandes expectativas que se muestran con los nuevos tratamientos.
Adquisición de la evidencia: Reuniones multidisciplinares con la participación de urólogos y oncólogos, donde se pusieron en común el análisis bibliográfico de artículos originales y se definió el contenido del artículo.
Síntesis de la evidencia: Tras el fracaso de la hormonoterapia, la quimioterapia con docetaxel supuso un punto de inflexión en el cáncer de próstata resistente a castración, consiguiendo por primera vez beneficio en la supervivencia sobre mitoxantrone y prednisona. La combinación de docetaxel y prednisona es el tratamiento de elección en primera línea. Cuando progresa no hay alternativa clara, aunque nuevos agentes están generando expectativas en el tratamiento de esta enfermedad.
Conclusiones: El horizonte terapéutico del cáncer de próstata resistente a la castración se abre de forma espectacular con la llegada de nuevos fármacos. Por el momento, cabazitaxel y en el futuro próximo abiraterona se han mostrado como fármacos eficaces en el tratamiento de segunda línea tras la progresión a docetaxel, añadiendo más de 2-4 meses de supervivencia y reduciendo un 30-35% el riesgo de muerte.

Introduction

Prostate cancer (PCa) is the most common tumor among the western male population if we exclude skin cancer. Its incidence has been increasing, reaching a peak in 1992, decreasing until 1995, and then increasing by 1% annually.[1] Although the considerable increase in the use of the determination of the prostate specific antigen (PSA) may be one of the reasons for this growth, there may also be genetic and environmental factors involved.[2]

The incorporation of the PSA determination as an early diagnostic method makes it possible to detect many cases of PCa in localized stages, where surgery or radiotherapy are potentially curative. However, between 20 and 40% of the patients undergoing local treatment will have a biochemical relapse (PSA > 0.2 ng/ml after surgery), and of those, between 30 and 70% will develop metastases 10 years after local treatment.[3] When the PCa progresses after local treatment or is diagnosed in advanced stages, the possibility of healing becomes more complicated. In fact, PCa is the second leading cause of cancer death in the male population in North America and the western world, and the third in developing countries.[1]

Hormone treatment allows for lasting and effective control of disease-related symptoms in its advanced stage. However, virtually all the patients with metastatic PCa will suffer from progression of their disease when it becomes resistant to androgen suppression.[4] This situation is called castration resistance. The term hormone refractory is often used interchangeably, but they represent different disease situations.

Traditionally, chemotherapy showed modest efficacy in castration-resistant PCa (CPRC), with response rates of 10–20%, with no impact in increased survival, which was estimated around the year.[5] The arrival of docetaxel was a turning point in the treatment of this disease. Docetaxel achieved a higher response rate and improved biochemical control by reducing PSA levels, and, above all, a benefit in metastatic PCa survival on mitoxantrone and prednisone.[6–8] Therefore, the combination of docetaxel and prednisone is the treatment of choice in first line in CRPC. However, there is no clear alternative when progression to docetaxel occurs. Recently, new agents such as cabazitaxel, abiraterone, and sipuleucel have proved able to improve the survival of our patients, both before and after docetaxel, which opens new prospects in the treatment of this disease.

This review updates the treatment of metastatic PCa in progression with castration levels of testosterone, how this clinical situation is defined, its prognosis and first-line treatment, and new options of second-line treatment.

Definition of the terms castration-resistant prostate cancer/hormone-refractory prostate cancer

Classically, the term hormone-refractory PCa (HRPC) was used to define the PCa that experiences a progression in a patient undergoing gonadal androgen deprivation. However, within this concept of HRPC, there is great heterogeneity with different types of patients according to their clinical situation, the PSA elevation, the possibility or not of new hormone treatments, and the presence or absence of metastases. The estimated mean survival ranges from 4 years for a patient with only PSA recurrence to 9–16 months for a