Prostate Int 5 (2017) 1–7

Contents lists available at ScienceDirect

Prostate International

journal homepage: https://www.journals.elsevier.com/prostate-international

Review Article

Management of metastatic castration-resistant prostate cancer: Insights from urology experts in Thailand

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ARTICLE INFO

Article history:
Received 20 December 2016
Accepted 2 January 2017
Available online 11 January 2017

Keywords:
Abiraterone acetate
Androgen receptor
Metastatic castration-resistant prostate cancer
Prostate-specific antigen
Urology expert

ABSTRACT

Treatment options for castration-resistant prostate cancer (CRPC) are available, but clear instructions for the selection of appropriate treatment are lacking. A meeting of urology experts based in Thailand was convened with the following objectives: (1) to reach a consensus and share real-life experiences about how to identify CRPC; (2) to choose the appropriate treatment for CRPC patients; (3) to evaluate disease progression using novel inhibitors of the androgen receptor pathway; (4) to identify the frequency of monitoring disease; and (5) to promote rational use of corticosteroids in CRPC patients. This consensus document can provide guidance to other urologists in Thailand to provide appropriate treatment to metastatic CRPC patients in a timely manner.

1. Introduction

Twelve urology experts from Thailand met to share their experiences of the management of castration-resistant prostate cancer (CRPC). These urologists work in medical schools and large public hospitals in Bangkok, Chiang Mai, and Khon Kaen, and have considerable experience in the management of prostate cancer (PC) and other genitourinary diseases.

A voting system was used during the whole meeting. Voting was based on scientific evidence and not on financial/patient factors related to treatment prescription.

Standard treatment for biochemical-recurrent PC and advanced-stage PC is androgen-deprivation therapy (ADT). Once disease status shifts from hormone-sensitive prostate cancer (HSPC) to CRPC, new treatment should be offered to the patient. Various treatments for metastatic castration-resistant prostate cancer (mCRPC) are available in Thailand, including hormonal therapy and chemotherapy. In some hospitals in Thailand, the first-line treatment is secondary hormonal therapy using ketoconazole, corticosteroids, or cyproterone acetate owing to the affordability of these agents to patients. Such treatments provide only short-term decline in prostate-specific antigen (PSA) levels but no increase in overall survival (OS).

Pivotal studies of current treatments have shown an OS benefit in mCRPC patients. Also, novel inhibitors of the androgen receptor pathway (IARP), such as abiraterone acetate and enzalutamide, have shown an OS benefit and an improvement of other parameters, especially quality of life (QoL); hence, the role of IARP is

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http://dx.doi.org/10.1016/j.prnil.2017.01.002

attracting increasing interest in Thailand, and such agents are being selected more widely for mCRPC patients. Currently, the IARP approved by the Food and Drug Administration of Thailand are abiraterone acetate and enzalutamide.

2. Key topics of the urology experts' meeting

Six issues were discussed in this meeting of urology experts, as described in the following sections.

2.1. Upfront chemohormonal therapy for high-tumor volume metastatic HSPC in Thailand is promising

The urology experts agreed that chemohormonal therapy should be selected on a case-by-case basis. Only 60% of urology experts considered chemohormonal therapy in high-tumor volume metastatic HSPC because they were concerned about the side effects of chemotherapy. Patients who are fit and young, and have a survival time of >15 years can be selected to receive such chemohormonal therapy. The other (40%) urology experts thought that ADT provides benefit in terms of delaying disease progression in HSPC patients by 5–10 years. Treatment with ADT of patients with metastatic HSPC continues to have a major role in most hospitals in Thailand (Fig. 1).

The Chemohormonal Therapy Versus Androgen Ablation Randomized Trial for Extensive Disease trial[1] and the Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy trial[2] enrolled mainly Caucasian patients. Hence, a query about the docetaxel dose used in the Asian (especially Thai) population was discussed. Most urology experts (81.8%) recommended the same dose of docetaxel as that given to Caucasian patients (75 mg/m^2 every 3 weeks for 6 cycles) in both trials (Fig. 2).

Subsequent therapy was also discussed. If chemohormonal therapy failed and patients progressed to mCRPC, the next treatment option preferred by experts was novel IARP (7 of 12 experts). One urology expert thought that patients should undergo rechallenge with chemohormonal therapy (Fig. 3).

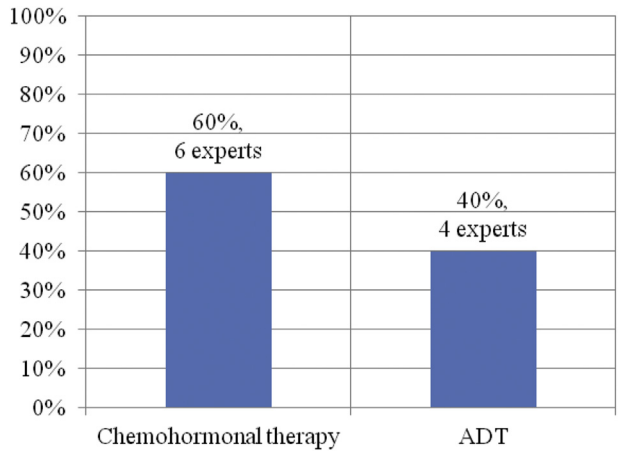

Fig. 1. Urology experts based in Thailand considered the role of chemohormonal therapy in high-tumor volume metastatic hormone-sensitive prostate cancer (HSPC). Sixty percent of urology experts voted to treat HSPC with chemohormonal therapy. The other 40% preferred to treat metastatic HSPC with androgen-deprivation therapy only. ADT, androgen-deprivation therapy.

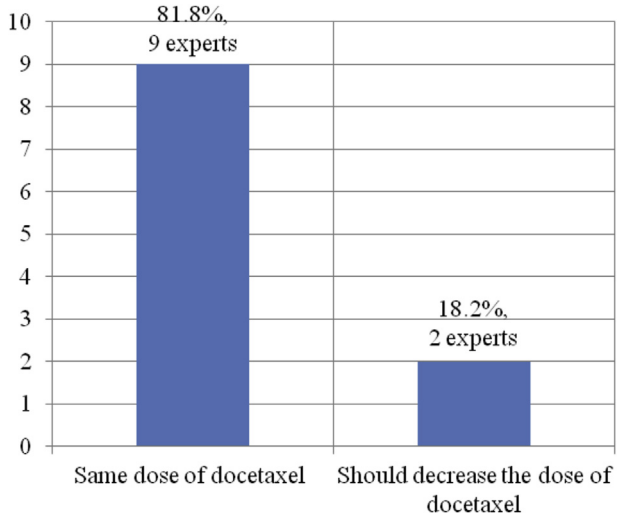

Fig. 2. Urology experts based in Thailand agreed to treat Thai patients with the same dose of docetaxel in chemohormonal therapy stated in the CHAARTED trial and STAMPEDE trials. CHAARTED, Chemohormonal Therapy Versus Androgen Ablation Randomized Trial for Extensive Disease; STAMPEDE, Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy.

2.2. Urology experts identified CRPC patients by the following guidelines set by the European Association of Urology in 2015

The definition of CRPC status was identified as stated in the European Association of Urology (EAU) guidelines in 2015[3] (Fig. 4).

The urology experts thought that some of the parameters stated in EAU guidelines cannot be followed up in a practical manner in their real-life practice, especially the timeline of PSA measurement. Most urology experts measured PSA levels twice (and not thrice, as stated in EAU guidelines[3]). The time interval between each PSA measurement varied depending on the experts' experience. Most urology experts measured the PSA levels twice at 2- to 3-week intervals.

The measurement of serum levels of testosterone to identify castration status was discussed. Most urology experts defined medical castration as a testosterone level in serum of <50 ng/dL (1.7 nmol/L). If surgical castration was undertaken, then the testosterone level did not need to be measured to confirm CRPC.

In real-life practice, 41.7% of urology experts identified mCRPC patients as individuals with a serum level of testosterone <50 ng/dL, who show increases in PSA level, and who show radiographic progression (Fig. 5).

2.3. Patient factors prior to choosing treatment

2.3.1. Choice of chemotherapy or novel IARP

Chemotherapy is not the only treatment option for mCRPC patients. Novel IARP such as abiraterone acetate and enzalutamide have shown positive outcomes in terms of OS, radiographic progression-free survival, and other QoL benefits to mCRPC patients in COU-AA-302[4,5,6] and Primary Outcomes by Site and Extent of Baseline Disease for Enzalutamide-treated Men with Chemotherapy-naïve Metastatic Castration-resistant Prostate Cancer studies.[7] Factors considered when choosing chemotherapy or novel IARP pathway inhibitors are used are discussed below.

2.3.1.1. Duration of response to ADT and symptomatic disease. All urology experts chose novel IARP in mCRPC patients if the duration of response to initial ADT ≥12 months. If patients had