Treating mCRPC in the post-chemotherapy setting with abiraterone acetate

The landmark COU-AA-301* trial demonstrated that abiraterone acetate (AA) prolonged overall survival (OS) among patients with metastatic castration-resistant prostate cancer (mCRPC) who previously received chemotherapy.[1] During the PROSPECT (Prostate Cancer Patient Case Exchange Taskforce) Series 2 experts' discussion organised by Johnson & Johnson, Assistant Professor Dr Worapat Attawettayanon shared a case study that highlighted the role of AA in prolonging OS in a patient with progressive mCRPC in the post-chemotherapy setting. Other distinguished speakers present in the meeting were Dr Takashi Kawahara, Prof Dr Rainy Umbas and Dr Jason Letran.

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Case presentation and clinical examination

A 62-year-old male patient presented to the hospital with:

- Back pain
- Lower extremity weakness
- Urinary retention
- An initial prostate-specific antigen (PSA) level of >1,000 ng/mL

Findings of clinical examination are as follows:

- Reduced lower-limb strength (3/5)
- Decreased sensation at the T12 level suggestive of spinal cord compression
- Digital rectal examination found that his prostate had a hard consistency
- A bone scan revealed widespread bone metastases without visceral metastasis

The patient was started on a gonadotropin-releasing hormone antagonist. Subsequently, he experienced clinical improvement – spontaneous voiding and return of muscle power – but defaulted his follow-up appointments.

Progression of bone metastases and chemotherapy initiation

After 2 years, he presented to the emergency department with:

- Left hip pain
- Loss of muscle power (2/5) in the lower extremity
- Decreased sensation at the T10 level
- PSA level was 4,722 ng/mL
- Bone scan indicated multiple progressive bone metastases

The patient was then started on docetaxel 75 mg/m^2. However, owing to adverse effects such as fever, nausea, and vomiting, the dose was reduced to 60 mg/m^2 in the next six cycles. He tolerated the adjusted dose well and experienced good PSA response (PSA nadir of 112 mg/dL).

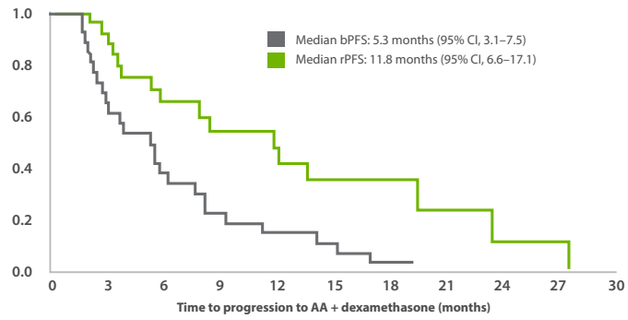
AA is more favourable compared with ENZ in terms of cognition and fatigue outcomes

After 6 months of loss to follow-up, the patient complained of back pain and fatigue. His PSA level was >5000 ng/dL. Novel hormonal therapy was the recommended next-line treatment, and the patient chose enzalutamide (ENZ) therapy owing to the benefits afforded by its Patient Assistance Programme. However, after 2 weeks of treatment with ENZ 160 mg once daily (OD), the patient experienced intolerable fatigue, which persisted even when the dose was reduced to 120 mg OD. He was switched to AA 1,000 mg OD plus prednisolone 5 mg twice daily (BD) and tolerated the treatment well. This was consistent with the results of the AQUARiUS study, which showed that patients treated with AA experienced significantly less fatigue compared with those treated with ENZ.[2] The patient achieved good PSA response in the beginning (PSA nadir of 5.76 ng/dL) but after three cycles of treatment, a steady increase in PSA level was observed.

Steroid switching is safe and effective in docetaxel-treated patients with mCRPC

According to the SWITCH study, a steroid switch from prednisolone to dexamethasone in patients with clinically stable mCRPC progressing on AA can lead to PSA and radiological responses (**Figure**).[3] In this case study, the patient was switched to dexamethasone 0.5 mg BD and his PSA level decreased to 0.48 ng/dL after seven more cycles of AA therapy. The patient remained clinically stable until his most recent follow-up on 1 October 2021.

Figure. Biochemical progression-free survival (PFS) and radiographic PFS of patients with progessive mCRPC after steroid switch[3]



bPFS, biochemical progression-free survival; **CI**, confidence interval; **rPFS**, radiographic progression-free survival

1 What is the prostate biopsy technique used in your clinical practice?

Insight from Dr Letran

In my current practice, urologists frequently conduct transrectal ultrasound (TRUS)-guided biopsy. However, I usually refrain from performing TRUS-guided biopsy as it is associated with an increased risk of urosepsis. Instead, I prefer the transperineal biopsy technique.

Insight from Asst Prof Dr Worapat

I agree with Dr Letran that the transperineal route of biopsy is associated with a lower risk of complications as compared with TRUS-guided biopsy. Additionally, a study by Simsir, et al., found that patients with urethral catheters, diabetes mellitus and those who undergo core biopsy from more than 10 sites were predictive risk factors for urosepsis and should be monitored closely after TRUS-guided biopsy.[4]

2 What would be your preferred next-line treatment after the second disease progression (post-docetaxel) in this case?

Insights from Dr Letran and Prof Dr Umbas

The preferred second-line therapy would be AA treatment as it has been shown to be efficacious post-docetaxel chemotherapy. However, owing to the aggressive nature of the patient's disease, his response to AA may be short-lived. Thus, the patient should be made aware of subsequent treatment choices such as cabazitaxel chemotherapy and lutetium-177 therapy.

KEY TAKEAWAYS

- AA prolonged OS among patients with mCRPC who previously received chemotherapy.[1]
- Patients treated with AA experienced significantly less fatigue compared with those treated with ENZ.[2]
- A steroid switch from prednisolone to dexamethasone in patients with clinically stable mCRPC progressing on AA can lead to PSA and radiological responses.[3]

***COU-AA-301**, AA in Castration-Resistant Prostate Cancer Previously Treated with Docetaxel-Based Chemotherapy

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