Pre-chemo treatment of mCRPC with abiraterone acetate afforded survival benefit

The pivotal COU-AA-302* study showed that treatment with abiraterone acetate (AA) delayed disease progression in chemotherapy-naive (CN) metastatic castration-resistant prostate cancer (mCRPC) regardless of baseline pain, prostate-specific antigen (PSA) level, and Gleason Score (GS).[1,2] During the PROSPECT (Prostate Cancer Patient Case Exchange Taskforce) Series 2 experts' discussion organised by Johnson & Johnson, Prof Dr Rainy Umbas shared a case study that highlighted the role of AA in prolonging overall survival (OS) in a patient with progressive CN mCRPC.

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Patient history and timeline of events

A 56-year-old male patient was diagnosed with stage IVA prostate cancer (pT2, N1, M0) and he had a GS of 7 (3+4). The timeline of events is as follows:

February 2010 - Underwent an open radical prostatectomy. Postoperative PSA level was 0.13 ng/dL. Started on a luteinising hormone-releasing hormone (LHRH) analogue, given every 3 months.

April 2014 - PSA levels started to rise and bicalutamide 50 mg once daily (OD) was added to his LHRH analogue regimen.

August 2014 - Bicalutamide was discontinued when PSA level reached 11.73 ng/dL, and testosterone level dropped to 0.5 ng/dL (castrate level).

October 2014 - He presented with:
- Bone pain
- PSA level of 103 ng/dL

Findings of clinical examination confirms the diagnosis of mCRPC:
- A bone scan revealed eight lesions in the lumbar, humerus and costae bones
- Magnetic resonance imaging showed that the patient had multiple pelvic lymph node metastases

Treatment and management

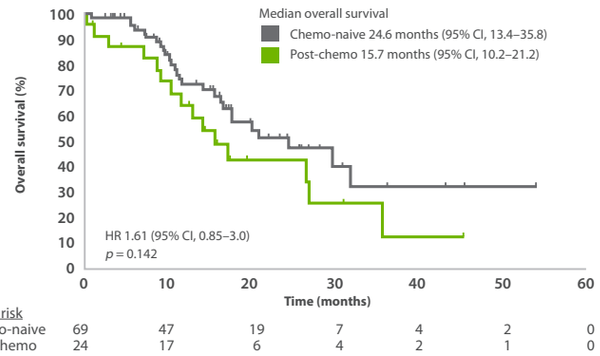
The patient was started on AA 1,000 mg OD in combination with LHRH analogue, which resulted in good PSA response; adverse events were mild (e.g. hypertension, fatigue, oedema) and well tolerated. However, owing to issues with his insurance coverage, AA was discontinued between July and August 2015. When AA was restarted in September, the patient's response was unsatisfactory and PSA levels rose to 581 ng/dL in February 2016. The patient was then switched to chemotherapy (docetaxel 75 mg/m^2 every 3 weeks) and he responded well for eight cycles before his cancer started to progress again. He passed away in March 2017.

AA provides survival benefit in real-world clinical setting among CN patients

In this case study, the patient was on AA treatment for a total of 14 months and it delayed chemotherapy for 16 months. The patient had an OS of 29 months, as well as PSA and radiographic progression-free survival (rPFS) of 11 months.

The clinical outcome of this case study was consistent with that of various real-world studies. In a retrospective analysis (N=200) carried out in Singapore, treatment with AA in the CN mCRPC setting resulted in a median OS, rPFS and biochemical PFS (bPFS) of 20 (95% confidence interval [CI], 18.3–22.9), 10.3 (95% CI, 7.8–11.7) and 9.6 months (95% CI, 7.8–11.1), respectively. A subset analysis also showed that CN patients who had prior androgen deprivation therapy (ADT) for more than 12 months had significantly longer OS.[3] In another real-world study (N=93), the median OS of patients with CN mCRPC (from Malaysia and Thailand) who were treated with AA was 24.6 months (**Figure**). The median duration of AA treatment was 10 months; however, patients with longer AA treatment duration (>10 months) had lower risk of death and longer bPFS, compared to those with shorter AA treatment duration.[4]

Figure. OS for CN and post-chemo patients with mCRPC treated with AA[4]



CI, confidence interval; **HR,** hazard ratio

1 Do you continue prednisolone after stopping AA or switching to a different therapy?

Insight from Prof Dr Umbas

It is not recommended to stop prednisolone abruptly after long-term use as it is associated with prednisolone withdrawal symptoms. Therefore, prednisolone should be tapered gradually before being discontinued among patients treated with AA plus prednisolone. In my current practice, we taper the dose of prednisolone over the span of at least 2 weeks if AA is to be discontinued or switched to a different treatment (e.g. enzalutamide).

2 Do you have any experience with using low-dose AA among patients with cost constraints?

Insight from Prof Dr Umbas

A prospective international randomised phase II study showed that low-dose AA (250 mg) with a low-fat meal was noninferior to standard dosing (1,000 mg, fasting) with regard to PSA response rate among patients with mCRPC. However, additional studies are required to assess the long-term efficacy of this approach.[5]

In my experience, I have only reduced the dose of AA to 500 mg (with a meal) among patients who cannot tolerate the standard 1,000 mg regimen.

KEY TAKEAWAYS

- The COU-AA-302* trial, as well as real-world clinical studies, have shown that treatment with AA was associated with survival benefit among patients with CN mCRPC regardless of baseline pain, PSA level and GS.[1,2]
- Patients who had prior ADT for more than 12 months had significantly longer OS.[3]
- Patients with longer AA treatment duration had lower risk of death and longer bPFS.[4]

***COU-AA-302,** AA plus prednisone versus placebo plus prednisone in chemotherapy-naive men with mCRPC

References: 1. Rathkopf DE, et al. *Eur Urol* 2014;66:815–825. 2. Miller K, et al. *Eur Urol* 2018;74:17–23. 3. Chan J, et al. *Asia Pac J Clin Oncol* 2020;16:75–79. 4. Lim J, et al. *Cancer Med* 2020;9:4613–4621. 5. Szmulewitz RZ, et al. *J Clin Oncol* 2018;36:1389–1395.

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