First-line abiraterone and the role of PSA kinetics in the management of mCRPC

During the PROSPECT (Prostate Cancer Patient Case Exchange Taskforce) Series 2 experts' discussion organised by Johnson & Johnson, Dr Takashi Kawahara shared his experience in managing several cases of metastatic prostate cancer (PCa) in his clinical practice.

Dr Takashi Kawahara
Consultant Urological Surgeon
Yokahama City University Medical Centre, Japan

Case 1: First-line AA therapy in the management of high-risk metastatic PCa

In January 2020, a 65-year-old male patient presented with cervical lymph node metastasis. A core needle biopsy confirmed the diagnosis of metastatic PCa. He had a Gleason Score (GS) of 8 (4+4) and an initial prostate-specific antigen (PSA) level of 85 ng/mL. Computed tomography (CT) scan revealed the presence of lung metastasis. He was given upfront abiraterone acetate (AA) owing to the high-risk feature of his disease. This is supported by the LATITUDE* trial, which demonstrated that combination of AA plus prednisone with androgen deprivation therapy (ADT) was associated with significantly longer overall survival (OS) compared with placebo plus ADT in men with newly diagnosed high-risk metastatic castration-sensitive PCa.[1]

Case 2: Low PSA level in a case of metastatic bone progression

In June 2016, an 81-year-old male patient presented with lymph node and bone metastases. His initial PSA level was 85 ng/mL. The patient was then initiated on ADT and he maintained good PSA response for the next 2 years. In March 2019, new metastatic bone lesions were found, and he was switched to radium-223 plus enzalutamide (ENZ) combination therapy. Despite having a low PSA level (0.11 ng/mL) during his follow-up visit a year later, a new metastatic brain lesion was found. According to Karzai, et al., the evaluation of cancer progression should not be based solely on PSA levels alone, but be assessed along with other clinical data.[2]

Case 3: AA is the preferred first-line NHT for patients who are docetaxel-ineligible

In September 2017, a 74-year-old male patient presented with lymph node metastasis, bone metastasis and a GS of 9 (5+4). He responded well to ADT and achieved a PSA nadir of 0.15 ng/mL. In June 2019, a new metastatic bone lesion was discovered, and he was then initiated on AA. His PSA level increased further to 5.38 mg/mL 2 months later, but the patient remained on AA since bone and CT scan did not reveal any new metastatic lesions. In October, his PSA level had reduced to 0.69 mg/mL. The transient rise in the PSA level was most likely a case of PSA flare induced by AA treatment.

Based on a study conducted by Khalaf, et al., ENZ demonstrated activity as a second-line novel hormonal therapy (NHT), whereas AA did not. Thus, using a sequencing strategy of AA followed by ENZ provides the greatest clinical benefit.[3]

Case 4: AA provides survival benefit in docetaxel-naive patients and prolongs chemo-free period

In December 2007, a 68-year-old male patient was given ADT when he presented with an initial PSA level of 223 ng/mL and was found to have bone metastasis. He developed mCRPC 8 years later and was then initiated on AA. In February 2018, a bone scan revealed a new metastatic bone lesion, and chemotherapy was started. After completing 10 courses of docetaxel therapy, the patient was switched to ENZ treatment. However, his cancer started to progress again after 2 years, and the patient passed away in November 2020.

Based on the pivotal COU-AA-302† trial, AA treatment in patients with chemotherapy-naive mCRPC improved OS and delayed disease progression as well as chemotherapy use. In this case study, AA treatment delayed chemotherapy for 2 years and 10 months.[4]

Insights from Dr Kawahara

1 What is the commonly used dose of cabazitaxel (20 or 25 mg/m²) in patients with castration-resistant PCa in Japan?

In our institute, the 20 mg/m² dose of cabazitaxel is more commonly used. According to a Japanese post-marketing surveillance study, adverse effects (AEs) such as neutropenia and febrile neutropenia occurred more frequently among patients receiving the 25 mg/m² dose compared with those receiving the 20 mg/m² dose of cabazitaxel. Therefore, patients who are unfit or at high risk of AEs may benefit from a lower starting dose of 20 mg/m², whereas fit patients may be candidates for a starting dose of 25 mg/m².[5]

2 Why is the dose of docetaxel in Japan lower than the standard 75 mg/m² dose?

Currently, the commonly used dose of docetaxel in our institute is 70 mg/m². A study showed that Japanese patients treated with docetaxel 60 mg/m² experienced more frequent haematological toxicities compared with US/European patients receiving 75 mg/m². Therefore, the standard dose of docetaxel in Japan is lower because the Japanese population is more susceptible to the toxicity of docetaxel.[6]

KEY TAKEAWAYS

- For patients with mCRPC who are ineligible for docetaxel therapy, using a sequencing strategy of AA followed by ENZ provides the greatest clinical benefit.[3]
- For patients who are eligible for docetaxel therapy, sequencing strategy of AA followed by docetaxel improves OS and prolongs chemotherapy-free period.[4]
- PSA levels do not always accurately reflect patient's disease state and should be evaluated in combination with other clinical data.[2]

*__LATITUDE__, AA plus prednisone in patients with newly diagnosed high-risk metastatic castration-sensitive PCa; †__COU-AA-302,__ AA plus prednisone versus placebo plus prednisone in chemotherapy-naive men with mCRPC

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