

## Case Report

# Remarkable response to abiraterone acetate in castration-resistant prostate cancer patient with aggressive liver metastasis

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### Abbreviations & Acronyms

ABI = abiraterone  
 ADT = androgen deprivation therapy  
 ALT = alanine aminotransferase  
 AST = aspartate aminotransferase  
 CRPC = castration-resistant prostate cancer  
 CT = computed tomography  
 ENZ = enzalutamide  
 mCRPC = metastatic castration-resistant prostate cancer  
 PSA = prostate-specific antigen

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Received 17 August 2018;  
 accepted 15 October 2018.  
 Online publication 12 November 2018

**Introduction:** The number of treatment options for metastatic castration-resistant prostate cancer has increased in recent years. Abiraterone, which selectively inhibits CYP17 in the androgen synthesis pathway, is widely used. Liver metastasis is one of the worst prognostic factors in metastatic castration-resistant prostate cancer. Only a few case reports have shown abiraterone successfully treated the liver metastasis of metastatic castration-resistant prostate cancer.

**Case presentation:** A 62-year-old man with prostate-specific antigen of 16.69 ng/mL was diagnosed with Gleason 8 (3 + 5) poorly differentiated prostate adenocarcinoma. Androgen deprivation therapy and sequential anti-androgen replacement were performed; however, the disease advanced to castration-resistant prostate cancer with liver metastasis. Prior to docetaxel, abiraterone achieved marked improvements in liver metastasis and prostate-specific antigen.

**Conclusion:** Metastatic castration-resistant prostate cancer patients with visceral metastasis were excluded from COU-AA-302, which is phase III trial on abiraterone prior to docetaxel. Although docetaxel is the recommended treatment for the visceral metastasis of castration-resistant prostate cancer according to the European Association of Urology guidelines, abiraterone also has potential as a treatment option.

**Key words:** abiraterone acetate, before chemotherapy, castration-resistant prostate cancer, liver metastasis, lung metastasis.

## Keynote message

Only a few cases reports have shown that abiraterone acetate successfully treated the liver metastasis of CRPC. There is currently no evidence for the benefits of administering abiraterone acetate to mCRPC patients with visceral metastasis before docetaxel. We herein report a case of mCRPC with aggressive liver metastasis that exhibited a strong response to abiraterone acetate. Although docetaxel is recommended for the visceral metastasis of CRPC according to the European Association of Urology guidelines, abiraterone acetate has potential as a treatment option.

## Introduction

Although prostate cancer generally has a good clinical course, patients with visceral metastasis have a poor prognosis. The recommended treatment for mCRPC with visceral metastasis is chemotherapy with docetaxel. Only a few case reports have shown that abiraterone acetate successfully treated the liver metastasis of mCRPC. We herein report a case of mCRPC with aggressive liver metastasis that exhibited strong responses to abiraterone acetate.

## Case presentation

A 62-year-old man with PSA of 16.69 ng/mL was diagnosed with prostate cancer in a previous hospital in March 2011. The pathology of biopsy specimens was Gleason 8 (3 + 5)

poorly differentiated prostate adenocarcinoma. A whole body examination revealed multiple bone metastasis, including the 12th thoracic vertebra, sacrum, left sacroiliac joint, and left shoulder blade, as well as left obturator lymph node metastasis. ADT with goserelin acetate (10.8 mg every 3 months) and bicalutamide (80 mg/day) was initiated. PSA reached a nadir at 0.75 ng/mL in April 2012, and increased thereafter. Anti-androgen replacement had no effect. His serum testosterone level at that time was 9.0 ng/dL, and he was diagnosed with CRPC. Chemotherapy with docetaxel was recommended, but the patient refused. He was aware of the implications of his refusal of chemotherapy and was transferred to a specialized radiotherapy facility by his own request. Systemic therapy was stopped by the radiotherapist based on the judgment that it was not successful. In January 2013, he received radiation therapy for bone metastases and discontinued ADT. After radiation, PSA decreased temporarily, but increased to 59.70 ng/mL in February 2014 when multiple liver metastases were found. In March 2014, he came to our hospital and ADT with flutamide (375 mg/day) and degarelix acetate (initially 120 mg and 80 mg every month thereafter) was reinitiated. After 1 month, his serum testosterone level was 21.0 ng/dL, and PSA decreased to 10.59 ng/mL, but increased thereafter. In July 2014, PSA increased to 54.07 ng/mL and the patient abandoned all medical treatment against his physician's recommendation. In October 2014, he came back to our hospital for fatigue and a loss of appetite. A blood examination showed elevated PSA of 626.43 ng/mL and severe liver dysfunction (AST/ALT 249/106); however, his serum testosterone level was 35.8 ng/dL. A CT examination revealed a markedly enlarged liver with aggressive metastasis, pleural effusion, mediastinal lymph node metastasis, ascites, and multiple bone metastases (Fig. 1). He accepted treatment with abiraterone acetate (1000 mg/day) and prednisone (10 mg/day) combined with a luteinizing hormone-releasing hormone agonist.

After 2 months of treatment, his blood test results markedly improved with PSA of 2.92 ng/mL and AST/ALT of 26/15 IU/L. PSA subsequently increased, while liver function remained normal. In May 2015, a CT examination showed marked decreases in the sizes of liver metastases (Fig. 2). Although bone metastasis had progressed, liver metastases continued to diminish in September 2015. Although we changed to enzalutamide, PSA continued to increase; therefore, he was introduced to another hospital in December 2015. Eight courses of docetaxel and three courses of cabazitaxel were subsequently administered, and he died in March 2017.

## Discussion

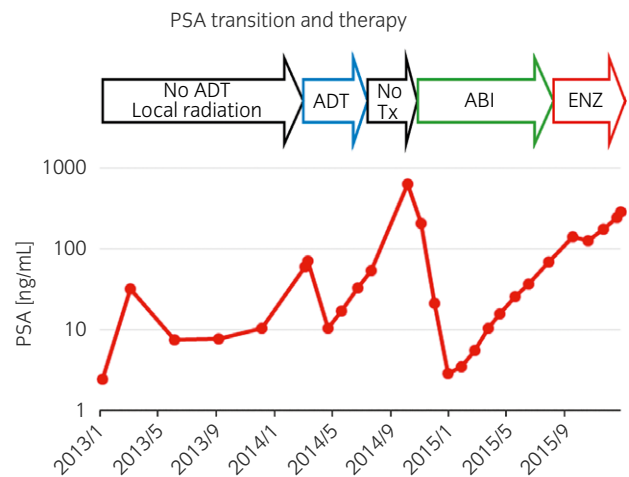
Visceral metastasis causes liver and respiratory dysfunctions, decreases the activity of daily living of patients, and ultimately is life-threatening. Visceral disease in the lungs or liver has been reported to occur in approximately 20–30% of mCRPC patients and is associated with a poor prognosis.<sup>1</sup> In the European Association of Urology guidelines, docetaxel therapy is recommended as a first-line therapy for mCRPC patients with visceral metastasis if their performance status is favorable.<sup>2</sup> However, in the present case, the patient refused



**Fig. 1** CT before the initiation of abiraterone acetate (October 2014). Multiple masses were detected in the liver.



**Fig. 2** CT after 7 months of treatment with abiraterone acetate (May 2015). Liver metastasis decreased in size after 7 months of treatment with abiraterone acetate.



**Fig. 3** PSA transition and therapy. PSA transition between January 2013 and December 2015, and therapy received by the patient.

docetaxel chemotherapy. There is no clear description on alternative treatments for mCRPC with visceral metastasis.

mCRPC patients with visceral metastasis were excluded from COU-AA-302, which is a large-scale phase III trial of abiraterone acetate prior to docetaxel chemotherapy. Therefore, there is no current evidence for the benefits of administering abiraterone acetate to mCRPC patients with visceral metastasis before docetaxel.<sup>3</sup>

In COU-AA-301, 29% of patients presented with visceral metastases at baseline, and an objective response rate of 14% was obtained.<sup>4</sup> The post hoc study of the COU-AA-301 also showed that abiraterone acetate plus prednisone produced similar absolute improvements in median overall survival in patients with (4.6 months) and without (4.8 months) visceral metastasis; hazard ratios were 0.79 and 0.69, respectively.<sup>5</sup> Therefore, abiraterone acetate after docetaxel chemotherapy appears to be effective not only for patients without, but also for those with visceral metastasis. Although the present case was treated with abiraterone acetate prior to docetaxel, abiraterone acetate itself is not ineffective for patients with visceral metastasis.

Halabi *et al.* performed a meta-analysis comparing overall survival for each metastatic site of CRPC.<sup>6</sup> The median overall survival periods of men with liver metastases, lung metastases, non-visceral bone metastases, and lymph node-only disease were 13.5, 19.4, 21.3, and 31.6 months, respectively. Thus, liver metastasis was the worst prognostic factor in mCRPC patients. Dupuy *et al.* reported two mCRPC patients with visceral metastasis who were successfully treated by the administration of abiraterone acetate. In one patient, abiraterone acetate was started at a dose of 1000 mg/day together with prednisone at 10 mg/day for chemoresistant CRPC with multiple visceral metastases, including liver lesions. A 3-month treatment achieved radiological improvements and decreases in PSA.<sup>7</sup> However, the improvement in liver metastasis was only limited, and not as prominent as that in the present case.

Marech *et al.* reported that the administration of abiraterone acetate to a 65-year-old male patient after chemotherapy with docetaxel resulted in a partial response by liver metastasis.<sup>8</sup> After the treatment with abiraterone acetate (1000 mg/day), liver metastasis decreased in diameter from 3 to 1.8 cm.

In the present case of mCRPC with aggressive liver metastasis before chemotherapy, abiraterone acetate sustained

improvements in liver metastatic lesions despite decreases in PSA for a brief time. A recent study reported that the number of prior regimens is a predictive factor of a low response to abiraterone acetate.<sup>9</sup> The present case suggests the potential of abiraterone acetate as an initial treatment option for CRPC with liver metastasis.

## Acknowledgments

The authors thank the staff at the Department of Urology, Keio University for their inpatient treatment of chemotherapy.

## Conflict of interest

The authors declare no conflict of interest.

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