Complete clinical and biological response to zoledronic acid in castrate-resistant prostate cancer metastatic to bone

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Zoledronic acid has been the standard of care for the prevention of skeletal-related events in patients with bone metastases from prostate cancer for the past 10 years. However, its potent antitumor activity has been questioned. We report the occurrence of a complete clinical and biological response to zoledronic acid in a patient with bone metastases from castrate-resistant prostate cancer. ***Anti-Cancer Drugs*** **23:141–142 © 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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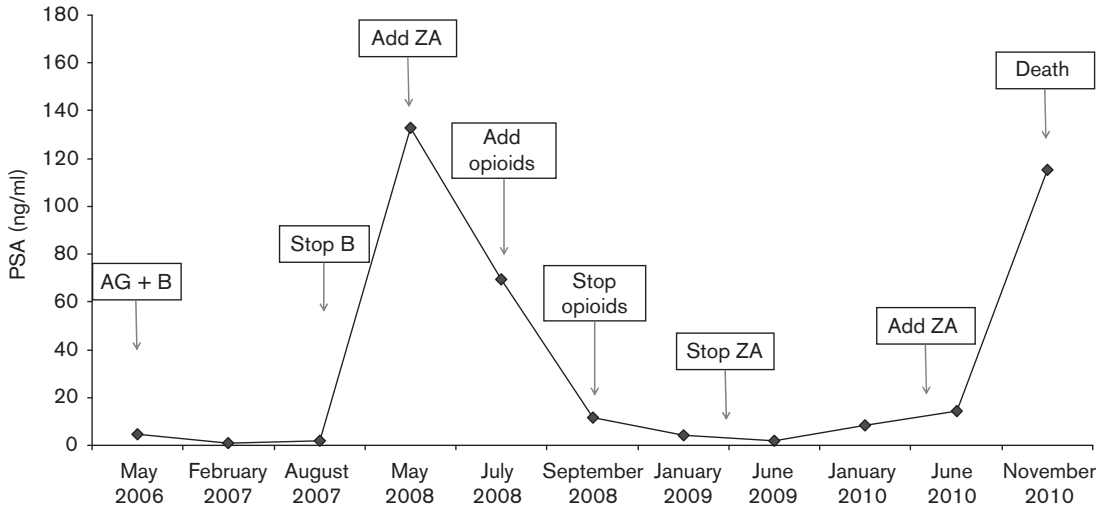
Introduction

Zoledronic acid (ZA), an inhibitor of osteoclast-mediated bone resorption, has been the standard of care for the prevention of skeletal-related events (SRE) in patients with bone metastases from prostate cancer since the past 10 years [1]. In the only phase III trial ever reported, ZA significantly reduced the incidence of SRE by 36% and delayed the first SRE by more than 5 months compared with placebo [2]. In a recently published exploratory analysis, the efficacy of ZA was superior when initiated before the onset of pain [3]. However, no difference in the percentage of change from baseline serum prostate-specific antigen (PSA) and time to progression was observed, thus questioning the antitumor activity of ZA. Here, we report the occurrence of a complete clinical and biological response to ZA in a patient with bone metastases from castrate-resistant prostate cancer.

Case report

A 74-year-old patient underwent radical prostatectomy for a pT2 pN0 prostate adenocarcinoma of Gleason score 7 (3+4) in March 1994. He developed a biochemical recurrence in 2000 and received intermittent androgen deprivation therapy with agonist luteinizing hormone–releasing hormone until May 2006, when continuous combined androgen blockade with bicalutamide was initiated. As PSA values were increasing in 2007 (from 0.76 ng/ml in February to 2.01 ng/ml 6 months later),

Fig. 1



Prostate-specific antigen (PSA) over time. 'AG,' agoniste luteinizing hormone–releasing hormone; 'B,' bicalutamide; 'ZA,' zoledronic acid.

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bicalutamide was stopped in September 2007. In May 2008, PSA reached 133 ng/ml, and symptomatic bone metastases required nonopioid analgesics. Chemotherapy with docetaxel in combination with ZA was planned. However, the patient refused chemotherapy and received ZA alone (3.5 mg every 4 weeks; creatinine clearance = 55 ml/min) from July 2008. After two ZA infusions, PSA had decreased to 69.27 ng/ml, but increasing bone pain required opioid analgesics. From then on, PSA values continued to decrease (from 11.59 ng/ml in September 2008 to 4.07 ng/ml in January 2009 to 2.06 ng/ml in June 2009), reaching as low as 1.77 ng/ml in January 2010. Alkaline phosphatases decreased from 4.5 N in July 2008 to the normal value in September 2009. Opioid analgesics were stopped in September 2008, and nonopioid analgesics were stopped in June 2009. ZA infusions were stopped in March 2009 after the ninth infusion on the patient's request. During follow-up in May 2010, bone pain occurred, whereas PSA increased. The reintroduction of ZA infusions did not alter the progression of the disease and the patient died in November 2010 (Fig. 1).

Discussion

The unique structure of ZA, specifically the presence of a second nitrogen atom, may account for its markedly increased in-vitro and in-vivo potency compared with all other biphosphonates, including other nitrogen-containing biphosphonates. The potent antitumor activity of ZA in prostate cancer has been questioned. Preliminary evidence of in-vitro antitumor effects [4] was supported by data from tumor xenograft models in animals, suggesting that biphosphonates can reduce tumor-induced osteolysis, inhibit the establishment and progression of bone lesions, and reduce skeletal tumor burden [5]. Mechanisms whereby biphosphonates exert these effects remain unclear but could go through inhibition of tumor cell adhesion and invasion of the extracellular bone matrix and/or antiangiogenic effects. However, no evidence of clinical or biological activity has been reported with ZA alone in randomized clinical trials reported so far in prostate cancer [2,5,6]. In addition, the frequent combination of ZA with hormone therapy and/or chemotherapy precludes any conclusion regarding the self-efficacy of ZA. To the best of our knowledge, this case report provides the first clinical evidence of the potent antitumor activity of ZA in prostate cancer.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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