

LETTER to the EDITOR

Zoledronic Acid Administration in Aggressive Castration-Resistant Prostate Cancer

Asian Pacific J Cancer Prev, 13 (12), 6539-6540

Dear Editor

Bone metastases alone or in combination with androgen deprivation therapy-related bone loss places prostate cancer patients at great risk of skeletal morbidity, including pain and fracture. Thus patient's quality of life may be significantly impaired. One approach to control is through use of zoledronic acid (ZA), an intravenously applied bisphosphonate approved for the prevention and treatment of cancer skeletal-related events. However, ZA may also act by other mechanisms

We have experienced positive effects in a 65-year-old man who underwent retropubic radical prostatectomy with localized prostate cancer (PC) in 2004. Pathological examination revealed metastatic PC (pT3a pN1 M0, GS 4+3=7), and therefore androgen deprivation therapy (ADT) with goserelin was initiated. From October 2006 an AD agent, bicalutamide was added because of a biochemical failure. Alternative ADT including flutamide, estramustine phosphate, chlormadinone acetate, and bicalutamide was initiated according to our institutional criteria. However, PSA levels rapidly increased markedly (Figure 1A). During the switch of anti-androgen agents we checked an androgen withdrawal syndrome.

Although dexamethasone (DXM) therapy was started for aggressive castration-resistant prostate cancer (CRPC), PSA levels rose and radiological examinations revealed swelling of the para-aortic and para-inferior vena cava lymph nodes and tiny bone metastasis. Monthly administration of zoledronic acid (ZA) was then initiated

in August 2008. PSA levels decreased greatly over the next two years (see Figure 1A). ZA and goserelin administration have now maintained PSA levels below 0.2 ng/ml for 3 years. The para-aortic lymph node reduced in size and the para-inferior vena cava lymph node swelling disappeared (Figure 1B). DXM was gradually tapered off by June 2010.

ZA has been shown to block multiple steps in tumor metastases (e.g. angiogenesis, invasion, adhesion, and proliferation) in preclinical and translational studies (Gnant, 2011). A recent Austrian Breast and Colorectal Cancer Study Group trial demonstrated significantly improved in disease-free survival rates after adjuvant administration of ZA for breast cancer (Gnant et al., 2011). Several studies have suggested that the potential anticancer activity of ZA in PC. For example, ZA administration improved PSA levels in a case of CRPC with bone and lymph nodes metastases (Kikuno et al., 2007). According to Prostate Cancer Nomograms: Hormone Refractory by Memorial Sloan-Kettering Cancer Center, survival probabilities for this patient after 1 and 2 years were estimated to be 73 % and 35 % respectively (median, 18 months) (Cho et al., 2003). However, in our present case relapse-free survival with low PSA levels and reduced lymph nodes were maintained for 3 years after ZA administration.

In conclusion, ZA administration may greatly contribute to increased survival in patients with aggressive CRPC and not only through action against development of bone metastases

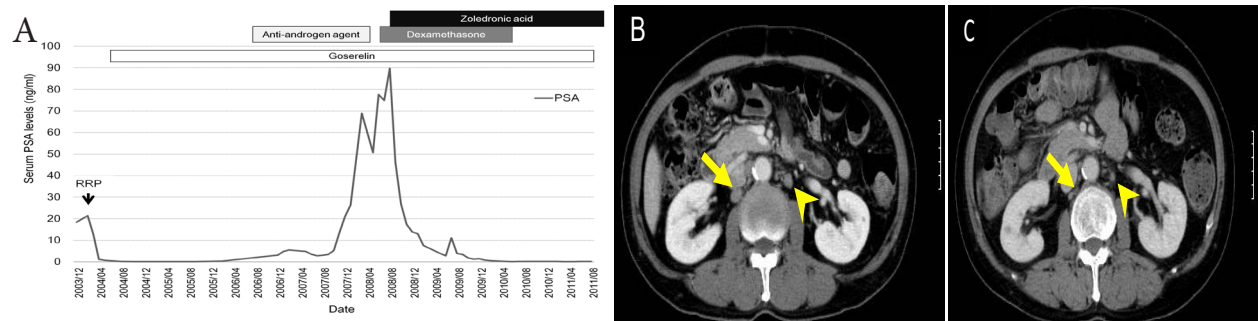


Figure 1. Therapeutic Regimen and Outcomes. A: Changes in Serum PSA. The patient underwent retropubic radical prostatectomy (RRP) with elevated serum PSA levels. After surgery, ADT (goserelin) was initiated. Due to PSA relapse AD agents was changed as follows; bicalutamide from October 2006 to December 2007, flutamide from January 2007 to February 2007, estramustine phosphate from February 2007 to October 2007), chlormadinone acetate from November 2007 to February 2008, and bicalutamide from March 2008 to June 2008. DXM and ZA had been administered from June 2008 (PSA 77.6 ng/ml) to June 2010 and from August 2008 until date, B: Computed tomography showed para-aortic (arrow head) and para-inferior vena cava lymph nodes (arrow) before ZA treatment, C: After ZA administration, the para-aortic lymph node decreased in size and the para-inferior vena cava lymph node swelling disappeared

References

- Cho D, Di Blasio CJ, Rhee AC, Kattan MW (2003) Prognostic factors for survival in patients with hormone-refractory prostate cancer (HRPC) after initial androgen deprivation therapy (ADT). *Urol Oncol*, **21**, 282-91.
- Gnant M (2011). Zoledronic acid in breast cancer: latest findings and interpretations. *Ther Adv Med Oncol*, **3**, 293-301.
- Gnant M, Mlineritsch B, Stoeger H, et al (2011). Adjuvant endocrine therapy plus zoledronic acid in premenopausal women with early-stage breast cancer: 62-month follow-up from the ABCSG-12 randomised trial. *Lancet Oncol*, **12**, 631-41.
- Kikuno N, Urakami S, Nakamura S, Shiina H, Igawa M (2007). Effect of zoledronic acid on metastatic hormone-refractory prostate cancer resistant to taxane, estramustine, carboplatin, and dexamethasone. *Int J Urol*, **14**, 82-4.

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