

## **Phase II Study of Zoledronic Acid Concomitant with Androgen Deprivation Therapy for Patients with Treatment-Naïve Bone-Metastatic Prostate Cancer: An Interim Analysis**

**Introduction and Objectives:** We conducted a phase II study in which zoledronic acid was introduced from the beginning of the androgen deprivation therapy (ADT) for prostate cancer patients with bone metastasis who had not been treated before. The primary endpoint was the skeleton-related event (SRE)-free survival at 24 month after the introduction of treatment. Secondary endpoints included progression-free survival (PFS), time to first SRE, overall survival (OS), decrease of the extent of bone diseases, improvement of pain, and safety. As more than half of the patients enrolled in this study progressed or died, an interim analysis was performed. Here we report the result of evaluation of PFS and the impact of baseline patient characteristics on PFS.

**Materials and methods:** Treatment-naïve male patients with histologically confirmed adenocarcinoma of the prostate and radiologic evidence of bone metastasis were eligible. Patients were treated with the combination of zoledronic acid, bicalutamide, and goserelin acetate until disease progression. Zoledronic acid was administered at 4 mg IV every 4 weeks with bicalutamide 80mg PO every day and goserelin acetate 10.8mg SC every 12 weeks. PFS as one of secondary endpoints was estimated by Kaplan-Meier method and the impact of baseline patient characteristics on PFS was evaluated by Cox regression analysis.

**Results:** A total of fifty-three men with treatment-naïve bone-metastatic prostate cancer were enrolled. Twenty-eight patients experienced disease progression or death after treatment and the interim analysis to evaluate PFS was performed for 50 patients in whom all baseline laboratory data were evaluable. Median age was 72 years. Median primary PSA was 249.4 ng/ml. Median follow-up period was 24.6 months. Median PFS was 23.8 months (95% confidence interval 14.0-33.6 months). Higher baseline bone metabolism markers were significantly associated with shorter PFS.

**Conclusions:** ADT with concomitant zoledronic acid used in the current study may prolong PFS of treatment-naïve prostate cancer patients with bone metastases compared with ADT alone. The addition of zoledronic acid from the beginning of ADT may lead to sustention of sensitivity of prostate cancer cells to ADT.