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Pharmacokinetic and Pharmacodynamic Characteristics of Ibandronate in Healthy Subjects

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Background: Ibandronate is a nitrogen-containing bisphosphonate and used for the treatment of hypercalcemia of malignancy and postmenopausal osteoporosis as a potent inhibitor of osteoclast- mediated bone resorption. This study was performed to evaluate pharmacokinetic (PK) and pharmacodynamic (PD) characteristics of ibandronate after a single intravenous (iv) infusion in healthy subjects.

Methods: The study was conducted as a double blinded, randomized, placebo controlled, parallel group study in twenty-six healthy Korean subjects (13 male and 13 female). Subjects were randomized into one of three treatment groups of 2 mg, 6 mg, or placebo, with 10, 10, 6 subjects in each group, respectively. Blood and urine samples for PK assessments were collected till 24 hours after start of 60 minutes iv infusion. For PD assessments, serum CTX (Type I Collagen-linked C-telopeptide), NTX (Type I Collagen-linked N-telopeptide) and urinary CTX, NTX were measured.

Results: The area under the concentration-time curves from time zero to infinity (AUC0-∞) were 333.4$\pm$46.0 (Mean$\pm$SD) ng · h/mL for the 2 mg group, and 939.1$\pm$267.1 ng · h/mL for the 6 mg group. The values of mean clearance were 6.1 L/h and 6.9 L/h in the 2 mg and 6 mg group, respectively. Urinary CTX was decreased by 71.5% (2 mg) and 93.5% (6 mg group) from baseline (both $P<.001$). Other PD parameters were also significantly decreased in active treatment groups compared with the placebo group.

Conclusions: Pharmacokinetic parameters exhibited linear properties regarding dose. Pharmacodynamic parameters as markers of bone turnover were significantly decreased from baseline in the active treatment groups.