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Intravenous Ibandronate in the Treatment of Osteoporosis

A Viewpoint by Silvano Adami

University Hospital of Valeggio, University of Verona, Verona, Italy

Bisphosphonates are considered the first-line option for the treatment of postmenopausal osteoporosis. However, the available oral formulations cannot be taken by patients with a number of conditions, such as those with oesophageal abnormalities, cognitive difficulties or inability to follow dose administration instructions (e.g. bedridden) or those taking multiple oral medications.

In a well conducted randomised clinical trial (DIVA) it was shown that intravenous (IV) injections of the aminobisphosphonate ibandronate 3mg every 3 months were associated with bone mineral density (BMD) increases that were statistically noninferior, and actually statistically greater, than those observed in patients receiving treatment with oral ibandronate 2.5 mg/day. In the BONE study, this oral ibandronate dosage was shown to decrease vertebral fracture risk by 62% over 3 years, but was associated with a nonsignificant decrease in nonvertebral fracture risk. The results of the DIVA study led to the registration by both the European Agency for the Evaluation of Medicinal Products and the US FDA of the IV preparation of ibandronate for the treatment of postmenopausal osteoporosis. This new formulation covers the previously mentioned therapeutic gap and it also offers a new treatment option for patients who are not able to tolerate oral aminobisphosphonates, broadening the treatment choice for both patients and physicians.

The results of the DIVA study raise a couple of points for consideration. In the view of a number of osteoporosis experts, the antifracture efficacy of antiresorptive compounds, such as bisphosphonates, is related to the BMD increase achieved with treatment. Generally, a decrease in nonvertebral fracture risk is observed only when the increase in spine BMD within the first year of treatment is >4%. In the DIVA study the increase was slightly lower than 4% with oral ibandronate 2.5 mg/day and close to 5% with the IV preparations. This might suggest that the overall antifracture efficacy of IV ibandronate could be somewhat superior to that observed in the pivotal trial of oral ibandronate 2.5 mg/day.

The safety profile of IV ibandronate appears to be acceptable. The acute phase response (or flu-like syndrome) reported by a small proportion of patients is a well known adverse event that mostly occurs after the first injection. The observation that no cases of osteonecrosis of the jaw have been reported during clinical trials with ibandronate (which included a few thousand patients given IV ibandronate) is also reassuring. The registration of an IV aminobisphosphonate preparation for an indication such as osteoporosis is going to greatly increase the number of patients treated with IV bisphosphonates, compared with the previous relatively limited experience in patients with malignant bone conditions. This might clarify whether osteonecrosis of the jaw is an aminobisphosphonate adverse effect occurring only in malignant conditions and with IV preparations. ▲