Further Section

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Reply

J.-Y.

Reginster

Centre Universitaire d'Investigation du Métabolisme Osseux et du Cartilage
Articulaire, Policliniques L. Bull, Liège, Belgium

Prof. Jean-Yves Reginster, MD, PhD, Centre Universitaire d'Investigation du Métabolisme, Osseux et du Cartilage
Articulaire, Policliniques L. Bull, CHU Centre Ville, 45, Quai Godefroid Kurth (9e étage), B-4020 Liège (Belgium)

We agree with our colleagues from the Merck Sharp & Dohme company that bisphosphonates should not be classified on the basis of their time of discovery. However, we do not favor a classification made on the basis of their relative potencies which may considerably vary as a function of the models used to evaluate their antiosteoclastic properties. For example, in vitro, alendronate was reported to inhibit bone resorption at doses 700 times lower than those needed to obtain a similar effect with etidronate [1], while in osteoporotic postmenopausal women, a similar reduction in biochemical markers reflecting bone resorption was obtained with an oral administration of alendronate, 20 mg daily, or etidronate, 400 mg daily [2]. It seems more realistic to classify bisphosphonates on the basis of their chemical structure, and more precisely on the nature of their side chain. This choice also allows one to isolate some clinical characteristics common to particular groups of bisphosphonates like the gastrointestinal intolerance specific to amino-bisphosphonates and reported with pamidronate and alendronate at doses currently used in osteoporosis [3] or Paget's disease of bone [4]. These effects appear to be related to the chemical nature of the bisphosphonates since they are not or much less described with compounds exhibiting a cyclic ring on the side chain, like tiludronate [5] or risedronate [6].

We do not want to enter into an argument about the paper of Apseloff et al. [7] published and discussed in a peer-reviewed journal. We agree that the subsequent data published by the Merck Sharp & Dohme scientists and quoted in their letter are convincing of an osseous safety of their bisphosphonate. However, as a clinician, and taking into account the chronic nature of osteoporosis and the long osseous half-life of bisphosphonates, we consider it essential for all

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compounds of this class to clearly demonstrate an anti-fracture efficacy and a long-term local and general safety, at the dose chosen to be administered, on a long-term basis, to postmenopausal women, in agreement with the new recommendations for registration of drugs in the prevention and treatment of osteoporosis in Europe [8].

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Correspondence
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