Reviewer’s report

Title: Systemic alendronate prevents resorption of necrotic bone during revascularization. A bone chamber study in rats.

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Version: 1 Date: 1 May 2002

Reviewer: Prof Geoff Nicholson

Level of interest: A paper of considerable general medical or scientific interest

Advice on publication: Accept after discretionary revisions

Discretionary revisions

1. Agarwala S et al (Rheumatology 2002;41:346-347) have reported an uncontrolled study in 16 patients with avascular necrosis of the hip (AVN) who were treated with oral alendronate 10 mg per day for 12-36 weeks. Although they did not include a placebo control group, there was significant improvement in pain, disability and function, whereas historically 85% of patients with AVN progress to "end-stage" disease over 2 yrs. Thus, although this study is not conclusive, it does provide some tantalising evidence that the dramatic anti-resorptive effect of alendronate demonstrated in the current study may be translated to the effective treatment of AVN in humans. The authors should reference the report of Agarwala et al and discuss its relevance to their own work. Clearly, there is need for a randomised, placebo-controlled clinical trial.

2. It has been correctly stated that "In humans, the alendronate dose recommended for use against osteoporosis would correspond to an injection of 1 microgram/kg/day". Readers who are not aware that only approx 0.6% of the usual oral dose of 10 mg/day is absorbed may have difficulty confirming this calculation. Suggest adding "oral" to this sentence. In addition, it could be pointed out that alendronate 40 mg/day is usually well tolerated in patients with Paget's disease of bone. Intravenous alendronate is not generally available but other potent bisphosphonates are

Competing interests:
I have received clinical trial funding and speakers honoraria from MSD, which markets alendronate.