Paired biopsy study shows strontium ranelate's biological effectiveness

Strontium ranelate (Protelos) was shown to be significantly more effective in helping osteoporosis patients rebuild bone than the current standard of care bisphosphonate alendronate, reported a study presented at the European Congress on Osteoporosis and Osteoarthritis in Valencia, Spain (23–26 March).

The research – representing the largest paired bone biopsy study ever performed – showed that the bone-forming activity seen in patients given strontium was 14 times greater at 6 months than that seen in patients treated with alendronate and 17 times greater at 1 year.

Strontium ranelate, an orally active agent licensed since 2004, consists of two atoms of stable strontium and an organic moiety (ranelic acid). Efficacy has been evaluated in patients according to reductions in subsequent fracture rates, with in-vitro studies and experiments in animals showing that strontium stimulates the formation of new bone and decreases bone resorption.

'Paired bone biopsy is the technique that allows us to truly understand the mechanism of action of drugs and evaluate the dynamic bone cell activity. It offers a useful approach to compare the, effectiveness of different medications,' explained Professor Jean-Yves Reginster from the University of Liege, Belgium, president of the European Society for Clinical and Economic Aspects of Osteoporosis.

Paired bone biopsy involves taking two samples of bone from the iliac crest with a large bore needle, with samples taken 6–12 months apart to allow investigators to estimate bone growth. The procedure is undertaken in tandem with sequential tetracycline labelling: 2–3 weeks before biopsy patients are given two doses of tetracycline for 2 days, with the administration spaced 10 days apart. Tetracycline binds to calcium within newly formed bone producing a fluorescent line, the length of which reflects active bone forming surfaces and cellular activity. The second dose of tetracycline produces a second fluorescent line, allowing investigators to measure the amount of bone produced during the window between the tetracycline doses.

In the current double-blind multicentre study 268 women aged over 50 years with postmenopausal osteoporosis, low mineral density and fragility fractures were randomized 2:1 to receive strontium ranelate (n=179) at the standard dose of 2 g/day or alendronate 70 mg/week (n=89). Transiliac bone biopsies to assess bone formation were carried out at baseline and after 6 and 12 months, with the primary end point being the cancellous mineralizing surface. Patients were allocated to have their second biopsy either at 6 months (n=90 strontium; n=43 alendronate) or 12 months (n=98 strontium; n=46 alendronate).

Results showed that the mineralizing surface expressed as a percentage of bone surface was 3% in strontium ranelate patients at 6 months, compared to 0.20% in patients receiving alendronate (P<0.001). The difference was further amplified at 12 months, with the mineralizing surface being 4.91% for strontium *vs* 0.28% for alendronate (P<0.001).

'Even greater bone formation was seen with strontium at 12 months than 6 months,' said the study's presenter Professor Roland Chapurlat from the Université de Lyon, France.

Additional data presented at the congress supported strontium's efficacy over 10 years in an extension of the SOTI and TROPOS trials, and also showed that consistent results were obtained in a male study population. On the basis of these data Servier are seeking marketing authorization to use strontium in men.

In a press conference Professor Reginster provided insights into the future potential of strontium ranelate. Ongoing studies, he said, are currently exploring use in osteoarthritis, fracture healing and pseudoarthosis. 'When we looked at the spinal X-rays of patients who'd been given strontium for osteoporosis we discovered they had a 45% decrease in the progression of spinal osteoarthritis,' he said, adding that studies have suggested that strontium may stimulate chrondrocytes to produce cartilage.

Janet Fricker

Novel biomarkers linked to asthma and COPD

Four novel biomarkers have been identified which may aid in the diagnosis and management of asthma and chronic obstructive pulmonary disease (COPD), according to a study conducted by researchers in Australia (Verrills et al, 2011).

The biomarkers identified are predominantly liver-synthesized proteins that can have important anti-inflammatory activity through the inhibition of oxidative stress and may be used in different combinations to successfully identify patients with either of the airway diseases.

In conducting the study, the researchers relied on proteomics, an emerging field of science that focuses on the structure and functions of an organism's proteins.

'Using a proteomics approach, we have identified a panel of four blood-based biomarkers that, when used in combination, can discriminate between healthy controls, asthmatics and individuals with COPD, and has the potential to be a valuable tool in the clinical diagnosis of respiratory disease,' said Professor Peter G Gibson, conjoint professor at the University of Newcastle's School of Medicine and Public Health.

He added: 'These results were confirmed in a second clinical population of older adults with airflow obstruction.'

Professor Peter G Gibson, University of Newcastle's School of Medicine and Public Health, Australia

Verrills NM, Irwin JA, He XY et al (2011) Identification of novel diagnostic biomarkers for asthma and chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* [epub before press]