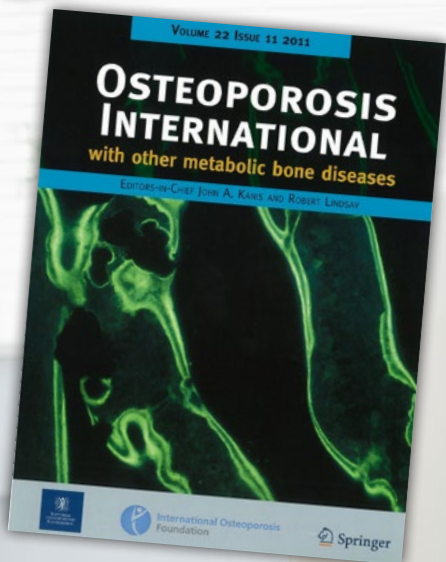
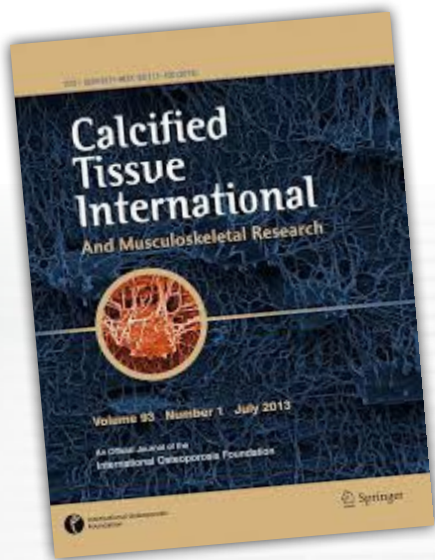


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Osteoporosis International è una rivista medica peer-reviewed pubblicata da Springer Nature con la collaborazione della International Osteoporosis Foundation e della National Osteoporosis Foundation. Lanciata nel 1990, è pubblicata mensilmente e costituisce un forum per la comunicazione e lo scambio di idee sulle più recenti ricerche riguardanti la diagnosi, la prevenzione, il trattamento e la gestione dell'osteoporosi e di altre malattie metaboliche delle ossa, nonché articoli didattici e case reports. Pubblica ricerche cliniche e documenti originali che indicano i progressi e i risultati raggiunti.

I condirettori sono J.A. Kanis e F. Cosman. Il Journal of Citation Reports ha assegnato alla rivista un **impact factor di 3,819** (dato 2018).

## Calcified Tissue International and Musculoskeletal Research

Calcified Tissue International è una rivista medica peer-reviewed pubblicata da Springer Nature con la collaborazione dell'International Osteoporosis Foundation. Dal 1967 al 1978 la rivista è stata pubblicata con il nome Calcified Tissue Research.

A partire dal volume 93 la rivista ha cambiato il titolo in Calcified Tissue International Musculoskeletal Research, condirettori S.H. Ralston and R. Rizzoli.

Viene pubblicata mensilmente e include ricerche e recensioni originali sulla struttura e la funzione delle ossa e di altri sistemi mineralizzati negli organismi viventi, nonché studi clinici di rilevanza sulle malattie ossee, il metabolismo minerale, la funzione muscolare e le interazioni muscolo-scheletriche.

I coeditori sono Roberto Civitelli e Stuart H. Ralston. Il Journal of Citation Reports ha assegnato alla rivista un **impact factor di 3,265** (dato 2018).

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July 2019, Volume 105, Issue 1, pp 107–108 | Cite as

### Effect of Zoledronate on Bone Loss After Romosozumab/Denosumab: 2-Year Follow-up

Authors Authors and affiliations

Anne M. Horne, Borislav Mihov, Ian R. Reid

Letter to the Editor

First Online: 17 April 2019

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About this article

Romosozumab and denosumab are monoclonal antibodies for the treatment of osteoporosis. Both have a rapid offset of effect, resulting in loss of bone density (BMD) gained on-treatment and, in some cases, multiple vertebral fractures following treatment cessation [1]. We found that in women discontinuing long-term treatment with denosumab, zoledronate infusions 6 months after the last dose of denosumab were ineffective in preserving hip BMD and only partially effective at the spine [2]. We hypothesized that this lack of efficacy was contributed to by the very low bone turnover after denosumab treatment, resulting in low skeletal uptake of the bisphosphonate. More recently, we reported data from women followed up for 1 year after the FRAME trial [3]. In that study, osteoporotic women were randomized to romosozumab or placebo for 1 year, and then both groups were provided with open-label denosumab for the subsequent 2 years. Our report demonstrated that zoledronate infusions given to 11 women after a median delay of 65 days from trial-end (i.e., 245 days after the last denosumab injection) substantially preserved BMD, whereas those declining post-trial treatment lost 80–90% of the BMD gained during treatment with romosozumab–denosumab [4]. We have now followed up

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LETTER TO THE EDITOR



### Effect of Zoledronate on Bone Loss After Romosozumab/Denosumab: 2-Year Follow-up

Anne M. Horne<sup>1</sup> · Borislav Mihov<sup>1</sup> · Ian R. Reid<sup>1,2</sup>

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Romosozumab and denosumab are monoclonal antibodies for the treatment of osteoporosis. Both have a rapid offset of effect, resulting in loss of bone density (BMD) gained on-treatment and, in some cases, multiple vertebral fractures following treatment cessation [1]. We found that in women discontinuing long-term treatment with denosumab, zoledronate infusions 6 months after the last dose of denosumab were ineffective in preserving hip BMD and only partially effective at the spine [2]. We hypothesized that this lack of efficacy was contributed to by the very low bone turnover after denosumab treatment, resulting in low skeletal uptake of the bisphosphonate. More recently, we reported data from women followed up for 1 year after the FRAME trial [3]. In that study, osteoporotic women were randomized to romosozumab or placebo for 1 year, and then both groups were provided with open-label denosumab for the subsequent 2 years. Our report demonstrated that zoledronate infusions given to 11 women after a median delay of 65 days from trial-end (i.e., 245 days after the last denosumab injection) substantially preserved BMD, whereas those declining post-trial treatment lost 80–90% of the BMD gained during treatment with romosozumab–denosumab [4]. We have now followed up nine of those zoledronate-treated women for a further year, during which time no further interventions were provided.

Figure 1 shows the evolution of BMD over the 2 years from the end of the FRAME study. In the second year, there was minimal further BMD loss at any of the three skeletal sites assessed, such that at the end of follow-up BMD was 10.2% above FRAME baseline at the lumbar spine, 7.6% above baseline at the total hip, and 4.3% at the femoral neck. PINP levels at the end of follow-up were 20–60 µg/L, mean 41 µg/L, slightly lower than levels at 12 months in these women [4] and similar to those seen 18 months post-zoledronate in osteopenic women not previously treated with bone-active drugs [5]. Of the five women taking risedronate in our earlier report, one declined further follow-up, two discontinued risedronate, and two continued that drug. In the latter pair, total hip BMDs 2 years post-FRAME were 6.2% and 8.1% above pre-FRAME values, suggesting satisfactory maintenance of treatment effects.

These data suggest that zoledronate administered 7–8 months after the last denosumab injection provides sustained protection against rebound bone resorption and the resulting bone loss. Whether efficacy would be similar after more long-term denosumab treatment and whether zoledronate also protects against rebound fractures now needs to be explored in systematic prospective studies.

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