Reviewer's report

Title: Bone turnover is adequately suppressed in osteoporotic Patients treated with Bisphosphonates in daily Practice

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Reviewer: Michael McClung

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This study attempts to assess the utility of bone turnover markers in monitoring bisphosphonate therapy in a daily practice setting. Two groups of patients are studied. A small group of individuals are begun on bisphosphonate therapy and both baseline and 3-month values are measured. The majority of the patients have a decrease in both a formation and resorption marker that was statistically significant (greater than the Least Significant Change (LSC)). For those who did not have significant decrease, a clinical explanation was noted. The other larger cohort consists of patients who had been on bisphosphonate therapy. Samples were collected and majority of the values were in the lower portion of a premenopausal reference range.

These data are not surprising and simply restate what is well known from data in clinical trials. The unique part of the study is that subjects were simply being followed in a clinical setting rather than in a clinical trial setting.

Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

1. In the Background section, it is stated that the goal of treatment is to reduce BTM levels to be within the premenopausal range. Does this mean that patients with osteoporosis who have values within the premenopausal range are not candidates for therapy?

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

2. Zoledronic acid is the correct name for the intravenous bisphosphonate, not zoledronate

Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

1. In the Background Section, least significant change (LSC) is defined as a difference that represents a relevant change. The correct definition is that LSC is a difference that is statistically significant, irrespective of whether the change is clinically relevant.

2. Were the LSC values for the two markers determined in your laboratory or were these derived from the literature?
3. Single values for analytical variation (AV) and LSC were used for each of the two markers. Is this appropriate? Was the analytical variance for CTX and P1NP constant over the range of values measured? Usually, the AV is greater when values are higher. If one uses the LSC for CTX of 29%, quite small absolute change would meet that criteria if a patient began with a relatively low level of serum CTX. When LSC is used in bone density evaluation, an absolute rather than a percent decrease is considered to be the appropriate metric.

4. The values in the cross sectional cohort were compared to the premenopausal reference range. Was this range determined in your laboratory? If so, describe the population in which it was derived, What is the range and what is the median value? How do these values compare with the premenopausal ranges of bone turnover markers published by Garnero, Eastell, and DePapp? If not derived in your laboratory, which reference range did you use?

5. What proportion of patients had baseline marker values in the lower half of the premenopausal reference range, the upper half of the premenopausal reference range, or above the premenopausal reference range?

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.