Reviewer's report

Title: Tibolone inhibits bone resorption without secondary positive effects on cartilage degradation - suggestion of uncoupling of bone and cartilage effects

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Reviewer: Graeme Jones

Reviewer's report:

I am of the opinion that the authors have satisfactorily dealt with most comments. There are two exceptions

1. The magnitude of the difference in CTX2 is similar to many other interventions eg risedronate or strontium. It would help to have a comparison of the size of effect from these other treatments to further the discussion on power issues. In addition, the authors currently state that the difference will become significant with a greater sample size. One cannot be certain that this will happen. The word ‘may’ should be used instead of ‘will’.

2. It is foreseeable that the use of the term uncoupling will be controversial. While I would accept that the magnitude of change is different for bone versus cartilage this can imply many things eg sensitivity to change, measurement error, individual variation. I would only accept the use of the term uncoupling if the ratio of the bone to cartilage markers is significantly different between tibolone and placebo. Please provide this data or modify the title even more.

3. Lastly, some discussion on where CTX2 is derived from would be useful eg discs, peripheral cartilage and bone.

Declaration of competing interests:

I have no competing interests