

Peer Review File

Article Information: <https://dx.doi.org/10.21037/tp-22-276>

Review Comments (Round 1)

Reviewer A

Comment 1: The use of the abbreviation Dmab is not widely accepted and indeed confusing while it is used in many othe contexts and should be replaced by Denosumab.

Reply 1. All abbreviation Dmab have been replaced by Denosumab in the article.

Changes in the text: We have modified our text as advised (see all pages).

Comment 2: In the introduction there should be written more regarding the complications of Denosumab, and especially when combined with other drugs like steroids and VEGF inhibitors. The complications of MRONJ should be mentioned.

Reply 2: We added some contents in the introduction about the complications of Denosumab as reviewer mentioned.

Changes in the text: we have modified our text as advised (see page 3, line63-65)

Comment 3: In line 460, there is a referral to CGCG that is allready discussed before, please remove all duplication or change scentence.

Reply 3: We changed the sentence as Reviewer suggested in line 479.

Changes in the text: We have modified our text as advised (see page 23, line479)

Comment 4: The article can profit from further improvement of the English language

Reply 4: We have revised and polished the language according to the suggestions of the editor and Reviewer, and selected the extensive language editing service to further improve the language expression.

Changes in the text: We have modified our text as advised. (see all revised mark)

Reviewer B

Comment 5: Spelling out denosumab and bisphosphonates (no abbreviations for these).

Reply 5: All abbreviation Dmab and BP have been changed in the article.

Changes in the text: We have modified our text as advised (see all pages revised mark).

Comment 6: Breaking down supplementary table 1 into several tables with references and effects in these tables. Then when a parent or physician wants summary information on a particular condition they don't need to hunt for it in a supplementary table- it is in the appropriate section of your article.

Reply 6: We have broken down supplementary table 1 into five tables and put them in the appropriate section in the article.

Changes in the text: We inserted 5 tables in the article (see lines 233, 295, 380, 433, 520).

Comment 7: Further comments please see the file attached.

Reply 1: I would like to thank Reviewer B for his detailed advice and practical suggestions attached in the file, 44 comments attached in the PDF were modified in the text.

Changes in the text: We have modified 44 places in our text as advised (see all pages revised marks).

Review Comments (Round 2)

Reviewer A

Thank you for the significant improvements. To my knowledge and compared to the literature, the paper does not cover all the indications for the use of Denosumab in children. Osteoporosis, Bone Metastases, and Hypercalcemia and others are not discussed. Possibly a table with all the indications as found in the literature should be included. Line 51. stating that MRONJ is a rare complication in adults is incorrect.

Reply 1: Thanks for the reviewer's advice. Because the prevalence rate of Hypercalcemia and Bone Metastases in children is too low, this study was not included and summarized. For children's Osteoporosis, the current research mainly focuses on hormone-related Osteoporosis, and pediatric endocrinology department has carried out phase II clinical trials. This study focused on orthopedic diseases related to children and was not included. After the relevant literature research is updated, it is expected that the research results of Hypercalcemia, Bone Metastases and Osteoporosis can be included in the next research.

We changed that MRONJ is not a rare complication in adults.

Changes in the text: We have modified our text as advised. (see line 88)

Reviewer B

It is now a HIGH quality and very useful paper!

For your information, denosumab should be without the capital D (unless at beginning of a sentence- it is a generic name)

The authors have done an admirable job of review and now having tables that accompany the text of specific sections.

Reply 2: We agreed with reviewer. We changed the capital D which is incorrect.

Changes in the text: We have modified our text as advised. (see all pages)