We thank Reviewer #1 for his constructive comments.

* We agree that BV/TV often correlates with measurements of BMD. However, bone volume and bone mineral density represent different aspects of the bone, and do not necessarily have to correlate. Bone mineral density evaluates the mineral content of the bone, while bone volume is the space occupied by the bone, regardless of the mineral content. A small volume of bone can have a large mineral density. The discordance of these two parameters in our study might be due to effects of the treatment on mineral deposition, but also to the methodology used. BV was measured in the whole longitudinal section of the tibiae, while BMD was measured in the region adjacent to the growth plate. We have added a comment on this issue to the manuscript.

* Bone deposited in response to LuCaP 23.1 or, more generally, to prostate tumors is a specific type of bone -- woven bone -- that has a disorganized character in comparison to trabecular bone normally present in the bone environment. The bone present in tibiae of animals treated with zoledronic acid appears somewhat more organized, as the reviewer has pointed out. However, this might be due to larger bone volumes in the areas adjacent to the growth plate in tibiae of these animals. We agree with the reviewer that an examination of the effects of zoledronic acid and its combination with docetaxel on bone structure might yield interesting information. Unfortunately at this point we do not have the capability to perform these experiments.

* We have added the results about osteoid thickness and osteoid surface per bone surface to the results section and Table 1 as suggested.

* The reviewer has pointed out that PSA serum levels are decreased by docetaxel treatment in concordance with tumor volume in animals bearing subcutaneous tumors, while zoledronic acid decreased tumor volume in the bone environment without significantly altering serum PSA levels. It is widely accepted that serum PSA levels do not necessarily correlate with the tumor burden, especially in treatment regimens and bone metastases. Docetaxel treatment of subcutaneous tumors decreased tumor burden as well as serum PSA levels by about 10-fold. ZOL acid decreased tumor volume in the bone environment to ~30 and 50 % in groups 4 and 2 respectively with no significant decreases in serum PSA. We have reported previously that zoledronic acid lowered levels of serum PSA as well as tumor volume of LuCaP 23.1, and that the differences reported in our present manuscript may be due to the lower dosage of ZOL used in the current study. We have also reported previously that serum PSA levels did not correlate with tumor volume in the bone using a C4-2 prostate cancer intra-tibial model after zoledronic acid treatment. We hypothesize that PSA may not reflect tumor changes in response to CaP bone metastases under zoledronic acid treatment, and that regulation of tumor growth and regulation of PSA expression are affected by different signaling pathways and to different levels in the bone environment. We have added comments regarding this point to the discussion.

The minor comments:

* We used exact p values in the results section and the figure legends, and these values are in agreement in the manuscript. In the table, however, we grouped the significant differences as p lower than 0.5 for simplicity.

* We have changed the unit of tumor volume to mm3 throughout the manuscript.

* We have corrected the information about paclitaxel vs. docetaxel. The sentence now reads “Taxanes have
been shown to be effective against osteolytic experimental prostate cancer metastases [49, 50] and docetaxel has recently been approved as a standard chemotherapy for advanced prostate cancer."

* The abbreviations have been added as suggested.

We thank Reviewer #2 for his constructive comments.

* Most of the procedures in the methods sections have been reported previously and the detailed procedures are referenced in the original manuscripts. We have chosen this approach to make the article as concise as possible and report mainly the new findings. Based on the reviewer's suggestions, we have added some details to the methods section.
* We agree with the reviewer that testing of the combination of these drugs in androgen-independent bone metastasis is of great interest, and we have added a comment on this topic to the discussion section as suggested.
* The misspelled "intratibial" was corrected.

We thank Reviewer #3 for his positive review.