Review of: "Long-Term Risk of Medication-Related Osteonecrosis of the Jaw (MRONJ) After Bisphosphonates and/or Denosumab in Metastatic Breast Cancer Patients"

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In this commentary, Fusco et al. highlight critical aspects of the article by Brunner et al., which investigates the long-term incidence of MRONJ associated with Denosumab and/or Bisphosphonate.
We would like to contribute additional perspectives to the commentary that may further enhance understanding and research on MRONJ.

1. Cumulative incidence rate of MRONJ

Brunner et al. report an MRONJ incidence of 11.6% for denosumab, 2.8% for bisphosphonates, and 16.3% for the combination of denosumab and bisphosphonates. Although this study spans a 20-year period beginning in 2000, it should be noted that denosumab was only introduced after 2010. Consequently, due to the shorter follow-up period for denosumab compared to the other two groups, the reported incidence of 11.6% for denosumab could be an underestimation. Additionally, our provisional analysis of the Kaplan-Meier curve in Figure 2 of the study estimates the six-year cumulative incidence of MRONJ to be 53%, 8%, and 11% for each respective group. While it is uncertain whether the denosumab group has reached the eight-year observation period, assuming it has been achieved, the cumulative incidence over eight years for each group would be 61%, 26%, and 13%, respectively. It would be advisable for the commentary of Fusco et al. to include a suggestion that Brunner et al. should emphasize the values of cumulative incidence over incidence in their study.

2. Managing the group receiving both denosumab and bisphosphonates

We fully support the viewpoint “The group of patients receiving a sequence of bisphosphonates and denosumab is very particular,” as mentioned in the commentary. The classification of this group requires meticulous consideration. The group includes: 1) patients who received bisphosphonates only a few times before subsequently starting denosumab administration, 2) patients who received BP for a prolonged period followed by a few times of denosumab treatment, and 3) patients who receive both medications concurrently; all three categories are treated as equivalent in the study. We believe that it would be more accurate to classify the first two categories as the BP-only group and the denosumab-only group, respectively. From this perspective, we agree with the suggestion that “it could be useful, in our opinion, to read the separate median time (and Q1-Q3) of the two treatments received in the study by all 77 patients receiving sequential therapy, and the duration of the two treatments in 15 patients who developed MRONJ.”

Thank you very much for referencing our paper on the incidence of MRONJ associated with long-term use of BP.