Clinical Characterization Might Help in Preventing Osteonecrosis of the Jaw

To the Editors: We read with considerable interest the article by Raje et al. (1) shedding light on clinical, radiographic, and biochemical markers concerning bisphosphonate osteonecrosis of the jaw (ONJ). The investigators highlight that most information regarding ONJ has been from case series and case reports (1). This was correct until recently as we reported the first pair-matched case-control study addressing potential risk factors for ONJ development in breast cancer patients under zoledronic acid medication (2).

Raje et al. (1) report that 7 of 11 patients did undergo tooth extraction. They do not, however, comment on tooth extractions as a potential risk factor. In our study, we report tooth extraction as the most potent ONJ predictor. Moreover, a recent article provides evidence that mucosal wound healing following tooth extractions could be actually defective, also showing that apoptosis is unlikely to be the key mechanism for keratinocyte damage caused by bisphosphonates (3).

Another issue pointed out by Raje et al. (1) concerns ONJ incidence differences in the Greek and US populations. This could hardly be attributable to more tooth extractions in the Greek population probably because of poor hygiene (4); thus, it could be an issue of differential susceptibility to ONJ in the Greek population. Susceptibility differences could exist, given that we reported decreased susceptibility to adenocarcinoma among Greek patients with Barrett’s esophagus and inflammatory bowel disease, perhaps attributable to Bax-protein overexpression (5).

Raje et al. (1) point out that two studies from Greece suggest zoledronic acid medication might be an independent risk factor for ONJ development. Zoledronic acid is considered the most potent osteoclast inhibitor (2), and in our institution, we have witnessed more ONJ in patients receiving zoledronic acid rather than other bisphosphonate treatment. Hitherto, we are monitoring this variable in a cohort study (2). Pharmacogenomics is a promising field in cancer treatment and the investigators conclude (3) that clinical and laboratory end points will be validated in future prospective clinical trials (1). This is very true, but to our point of view, more attention should be paid in prevention of ONJ, if possible via simple risk predictors. In this regard, we have shown that ONJ is associated with tooth extraction and use of overdentures, currently updating the American Society of Clinical Oncology’s level of evidence from V to III (2). We therefore concluded, based on evidence, that oncologists should refer their patients for baseline dental evaluation and potential pretreatment before engaging bisphosphonate therapy (2). Evidence provided by Raje et al. (1) shedding light on the pathophysiologic basis of the above association strengthens our point.

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Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

References
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