

## Review of: "Bisphosphonate-Related Osteonecrosis of the Jaws Treated with Platelet-Rich Plasma: Preliminary Results from a Case Series"

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Potential competing interests: No potential competing interests to declare.

The manuscript reports data and proposes for the BPS-induced osteonecrosis of the jaw a novel platelet-rich plasma administration that needs to be tested in a long-term study and in large populations. A dose-response curve to the MTD, the maximal tolerated dose, is also necessary, in my opinion, to further support the use of this novel formulation; if not, please explain why.

Introduction: The epidemiological data on the osteonecrosis of the jaw are known and are reported in the pharmacovigilance databases; for instance, the most frequently observed A.D.R. of zoledronic acid, reported per System Organ Class (S.O.C.), were musculoskeletal and connective tissue disorders, general disorders and administration site conditions, and gastrointestinal disorders. Among the musculoskeletal and connective tissue disorders, the osteonecrosis of the jaw was the most frequently reported A.D.R., representing 47.9% of the total A.D.R. and affecting 4792 females and 3184 males of all ages. Arthralgia and myalgia were also frequently reported, representing 16% and 10% of the A.D.R., respectively, with several unresolved cases. Muscular weakness was 2.7% of the A.D.R. per S.O.C., and some cases of atrophy and rhabdomyolysis with blood creatine phosphokinase increased were reported. See <u>Fatima Maqoud et al.</u>. <u>Pharmaceutics</u>. 2021 Sep; 13(9): 1350. doi: 10.3390/pharmaceutics13091350. Zoledronic Acid as a Novel Dual Blocker of KIR6.1/2-SUR2 Subunits of ATP-Sensitive K+ Channels: Role in the Adverse Drug Reactions.

Furthermore, the action of zoledronic acid can be mediated by irreversible inhibition of Kir6.1/2-SUR2B channel subunits expressed in osteoblasts and in vascular smooth muscles, respectively, regulating osteoblastogenesis and vasodilation. See <u>Fatima Maqoud et al., Pharmaceutics.</u> 2021 Sep; 13(9): 1350. doi: 10.3390/pharmaceutics13091350. Zoledronic Acid as a Novel Dual Blocker of KIR6.1/2-SUR2 Subunits of ATP-Sensitive K<sup>+</sup> Channels: Role in the Adverse Drug Reactions.

Functional characterization of the inward-rectifier potassium (Kir) channel family in bone cells. Rosa Scala, Lidia Ibanez, Isabelle Rubera, Christophe Duranton, Samuel Guilbault, Julia Halper, Matthieu Rouleau, Claudine Blin-Wakkach, Domenico Tricarico, Said Bendahhou. Bone Reports Volume 16, Supplement, May 2022, 101386.

Qeios ID: G7AQ59 · https://doi.org/10.32388/G7AQ59