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Abstract Submission FORM

MEDICATION-INDUCED OSTEONECROSIS OF THE JAWS: RESEARCHING FOR NEW PROGNOSTIC BIOMARKERS FROM A MULTIDISCIPLINARY POINT OF VIEW

SECTION: *5A*

AUTHORS (max 8): Contrassegnare SPEAKER con "*"
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Background: Medication-induced osteonecrosis of the jaws (MRONJ) is a clinically-relevant adverse effect linked to the use of anti-resorptive drugs, such as bisphosphonates, denosumab or anti-angiogenic agents.
It is currently impossible to predict whether a patient will develop MRONJ, as there is no plasma nor osseous drug concentration predicting the toxic effect of these drugs.
Moreover, even if MRONJ is often related to recurrent oral infections, research still lacks in evidence for the role of the salivary microbiome.
Therefore, this study aims at evaluating new prognostic biomarkers, through the analysis of microbiologic, drug-related and genetical aspects which could be implied in the bioavailability of these drugs, in order to predict the development of osteonecrosis.

Patients and Methods: Sixteen patients who were suffering from oncologic or metabolic bone disorders and were treated with either denosumab or zoledronate were enrolled in the study. The patients were divided into two groups: Group A consisted of eight patients who developed MRONJ, while Group B consisted of eight patients who did not develop MRONJ.
These two groups were compared by analyzing the oral microbiome through Next-Generation Sequencing, by measuring drugs' concentrations both in plasma and bone using Liquid Chromography with Tandem Mass Spectrometry, and by evaluating the presence of polymorphisms in genes influencing the metabolism or clearance of these drugs. Risk factors, including smoke and alcohol, were assessed as well.

Results: Differences were found between the two groups, with the first group having a higher usage of alcohol and a younger median age ($p=0.003$ and $p=0.001$, respectively). In addition, mostly of the patients who experienced MRONJ were female.
Regarding the oral microbiome, group A manifested an increase in Neisseriacee ($p=0.049$). Concerning the dosage, group A patients were mostly administered high-dose drugs, which were both intravenously and subcutaneously injected.
Finally, the results suggested the role of polymorphism ABCB1 3435 C>T in the development of MRONJ, but with weaker impact ($p=0.053$).

Conclusions: this study evaluates multiple aspects playing a role in MRONJ development, such as the role of the oral microbiome, drugs' concentration and genetic polymorphisms. Further studies are required to confirm these preliminary results.

REFERENCES:

1. *Bastida-Lertxundi N, et al. Pharmacogenomics in medication-related osteonecrosis of the jaw: a systematic literature review. Eur Rev Med Pharmacol Sci. 2019 Dec;23(23):10184-10194.*
2. *Badros AZ, et al. Prospective Observational Study of Bisphosphonate-Related Osteonecrosis of the Jaw in Multiple Myeloma: Microbiota Profiling and Cytokine Expression. Front Oncol. 2021 Jun 24;11:704722.*

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