ONJ UPDATE 2024
Torino, 24 febbraio 2024

Abstract Submission FORM

WASHOUT OF BISPHOSPHONATES FROM THE JAWS AFTER PHARMACOLOGICAL TREATMENT WITH PENTOXIFYLLINE AND TOCAFEROL IN OSTEOPOROSIS PATIENTS WITH ONJ CANDIDATES FOR SURGERY

SECTION: *5C*

Gianluca Colapinto [1,2] *, Funda Goker [2], Riccardo Nocini [1], Aldo Bruno Giannì [2,3], Angelo Vacca [4], Roberto Scirpo[1], Massimo del Fabbro [2,3*], Massimo Albanese[1]

AFFILIATION:
[1] UNIVERSITA' DI VERONA, [2] UNIVERSITA' degli Studi di MILANO, [3] Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, MILANO, [4] UNIVERSITA degli Studi di BARI

Background and Rationale of the study: Medication-related osteonecrosis of the jaws (MRONJ) is a complication related to the use of drugs in the treatment of bone oncological, metabolic diseases and bone metastases. Various therapeutic protocols have been proposed for the management of osteonecrosis, to control the disease and prevent its extension, but there is currently no unanimous consensus on which approach is the most effective. Resective surgery today is still considered the gold standard in the management of this pathology, but the high rate of recurrence makes it ineffective, and due to its demolitive character with the impossibility of associating it with reconstructive and / or rehabilitative surgery, it considerably compromises the patient quality of life, with a drastic reduction in the life expectancy of cancer patients. Hence the need to develop a therapeutic protocol capable of reducing the relapse rate, and transforming the surgical approach from extremely destructive to minimally invasive. In the scientific literature no randomized controlled clinical trials exist for this purpose.
Objective and Aims: Compare the therapeutic impact of two-months pharmacological preparation with Pentoxifylline and Tocaferol in a group of ONJ subjects candidate to surgical treatment, as compared to a group undergoing preparation with placebo (sodium bicarbonate rinses).
Study Design: Prospective Randomized Controlled Clinical Trial (RCT).
Materials & Methods: Inclusion criteria: Patients suffering from ONJ Stage IA (osteonecrosis extending only to the alveolar process of the jaw), taking amino-bisphosphonate (aBPs) for over 3 years for the treatment of osteoporosis. Exclusion criteria: Patients with ONJ of any stage after taking aBPs, non-aBPs, and anti-Rank-L drugs (Denosumab), in combination or not with antiangiogenics or other ONJ-related drugs for the treatment of other dysmetabolic, oncological, and metastatic bone diseases. Based on sample size calculation, it is planned to include at least 80 patients per group. After collection of demographic data, anamnesis, clinical signs of ONJ, laboratory data, CBCT imaging, all patients will initially undergo a bone biopsy with the technique of coring to obtain a bone sample to estimate the aBPs quantity using liquid chromatography. Subsequently, patients will be randomly divided into two groups using an online tool for random sequence generation: surgery after pharmacological preparation for two months with pentoxifylline and tocaferol, 600 mg x 2/day and 800 I.U. x2/day, (test group), and surgery after pharmacological preparation with placebo, ie rinses with sodium bicarbonate 1.5 g in 20 ml of physiological solution 2/day (control group). After two months for both groups, new CBCT imaging diagnostic information will be collected, and patients will undergo resective surgery, harvesting a second bone sample with coring technique, to evaluate the quantity of aBPs by liquid chromatography. The same surgeon will perform all the interventions. Patients will be recalled at 7 days, 15 days, 1, 3, 6, and 12 months, for clinical and radiographic evaluation. Any intra and post-surgical complications, any relapses, non-healing, or changes in the staging of the ONJ will be recorded. Statistical analysis will be performed to evaluate the significance of within- and between-group differences in outcomes.
Expected Results: The expected results are that in the test group there will be a washout of bisphosphonates from the jaws and a significantly better clinical outcome than control group.
Conclusion and clinical relevance: This study will test the efficacy of pharmacological preparation to produce bisphosphonate washout from the jaws and will lay the groundwork for the absence of relapse, the possibility of minimally invasive surgery with the association of reconstructive and rehabilitative surgery, and therefore the formulation of a novel therapeutic protocol that could establish a new gold standard treatment.

REFERENCES:

1. *Ruggiero S.L. et al. American Association of Oral and Maxillofacial Surgeons' Position Paper on Medication-Related Osteonecrosis of the Jaws-2022 Update. Review J Oral Maxillofac Surg 2022 May;80(5):920-943. doi: 10.1016/j.joms.2022.02.008. Epub 2022 Feb 21.*
2. *Petrovici AR, et al. Quantification of Low Amounts of Zoledronic Acid by HPLC-ESI-MS Analysis: MethodDevelopment and Validation. Int J Mol Sci. 2022 May 25;23(11):5944. doi: 10.3390/ijms23115944. PMID: 35682618; PMCID: PMC9180824.*
3. *Colapinto G. et al. Outcomes of a Pharmacological Protocol with Pentoxifylline and Tocopherol for the Management of Medication-Related Osteonecrosis of the Jaws (MRONJ): A Randomized Study on 202 Osteoporosis Patients J. Clin. Med. 2023,12,4662. https://doi.org/10.3390/jcm12144662*

Il titolo non deve essere superiore a 130 caratteri (spazi inclusi); l'abstract deve essere scritto in Times New Roman carattere 10. Numero minimo di parole: 400 inclusi titoli, autori e affiliazioni; numero massimo di parole: 600 inclusi titoli, autori e affiliazioni. Inserire al massimo 3 note bibliografiche. L'abstract (tutto in inglese titolo e testo) deve essere contenuto all'interno della prima pagina del form.