

Denosumab related osteonecrosis of the jaw: an emergent and potentially complex bone and joint infection

R. Bricca¹, F. Valour²⁻⁵, A. Conrad²⁻⁵, E. Braun², P. Jaby², J. T. Bachelet², P. Breton², A. Gleizat², F. Laurent²⁻⁵, C. Chidiac²⁻⁵, T. Ferry²⁻⁵ on behalf of the Lyon BJI Study group

¹ Hôpital de Villefranche sur Saône, ² Hospices Civils de Lyon, ³ UCBL1, ⁴ CRIOAc Lyon, ⁵ CIRI, Lyon, FRANCE

Aim

Osteonecrosis of the jaw is a known complication of antiresorptive treatment, like bisphosphonate. More recently, denosumab was validated as a treatment in the osteoporosis and bone metastasis. Its mechanism is different from bisphosphonate but induces also a decrease of bone resorption and a risk of osteonecrosis of the jaw. In case of treatment failure by a dental surgeon or in complex cases, patients may be addressed to a bone and joint infection reference center.

The aim of this study is to analyze microbiology, as well as surgical and medical care of patients who present denosumab related osteonecrosis of the jaw (DRONJ) and who were treated in a bone and joint reference center.

Method

All patients managed in our reference center between January 2013 and December 2018 for a DRONJ were included in our retrospective observational monocentric cohort.

Results

Twelve patients (median age 71; ratio W/M 0.71) with a DRONJ (metastatic cancer, n=10 (83%)) in grade 3 (n=5), 2 (n=4), 1 (n=3) were included. Only 3 patients (25%) had a dental health control before initiating the treatment by denosumab and 7 patients (58%) had a dental surgical procedure done before the DRONJ. Eleven patients had a bone exposure (including 5 with a multiple exposure), treated at least with a scaling and mucosal closure at the same time. The median follow-up was 6 months. Eight patients were cured after a medico-surgical care and a median duration of antibiotics of 97 days (including 28.5 days in intravenous). One patient required a suppressive antibiotic treatment, 1 relapsed at distance of the treatment and 2 were still under curative treatment.

Population	
Number of patients	12
Age (median)	71
Ratio W/M	0,7
Osteosynthesis	1
Dénosumab	
Accumulated dose (mg)	1350
Duration (month)	12,5
Indication for neoplasia	11

Table 1 : Population's characteristics

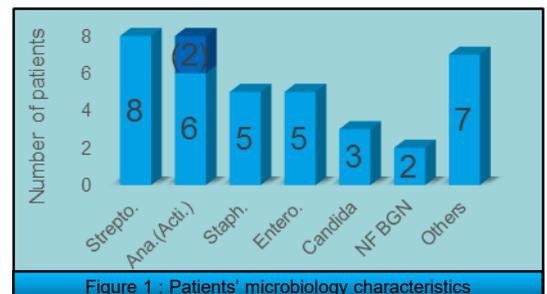


Figure 1 : Patients' microbiology characteristics
Strepto.: Streptococcus spp., Ana.: anaerobia, Acti.: Actinomyces, Staph.: Staphylococcus spp., Entero.: Enterobacteria, NF BGN : non fermentative bacille gram negative

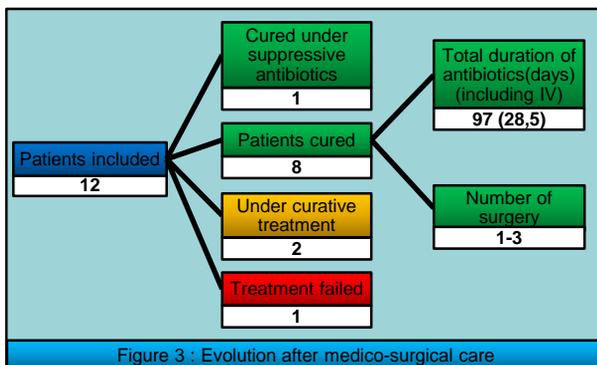


Figure 3 : Evolution after medico-surgical care

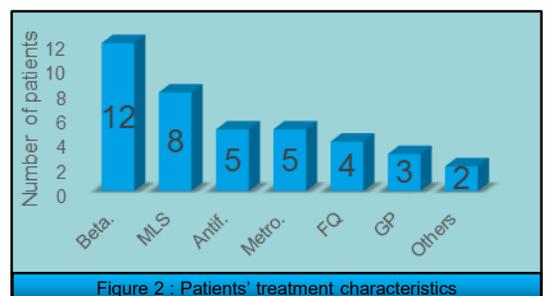


Figure 2 : Patients' treatment characteristics
Beta.: Betalactamine, MLS: Macrolide, Lincosamide, Synergistine, Antif.: Antifongal, Metro.: Metronidazole, FQ: Fluoroquinolone, GP: Glycopeptide

Conclusion

DRONJ is a potential complex bone and joint infection, for which some patients could benefit from medical care in a reference center.

Author email : rbricca@hopitalnordouest.fr

Lyon BJI Study group

Lyon Bone and Joint Infection Study Group:
Coordinator: Tristan Ferry; **Infectious Diseases Specialists** – Tristan Ferry, Florent Valour, Thomas Perpoint, Patrick Mailhes, Florence Ader, Sandrine Roux, Agathe Becker, Claire Triffault-Fillit, Anne Conrad, Cécile Poudroux, Marie-Elodie Langlois, Marielle Perry, Fatma Daoud, Johanna Lippman, Evelyne Braun, Christian Chidiac; **Surgeons** – Sébastien Lustig, Elvire Servien, Cécile Batailler, Romain Gaillard, Stanislas Gunst, Julien Roger, Charles Fiquet, Michel Henri Fessy, Anthony Viste, Philippe Chaudier, Jean Luc Besse, Lucie Louboutin, Gail Gaudin, Tanguy Ledru, Adrien Van Haecke, Quentin Ode, Marcelle Mercier, Florie Alexch-Tournier, Sébastien Martres, Franck Trouillet, Cécile Barrey, Emmanuel Jouanneau, Timothée Jacquesson, Ali Mojalali, Fabien Boucher, Hristo Shipkov, Joseph Chateau, Philippe Cérouse, Carine Fuchsman, Arnaud Gleizat; **Anesthesiologists** – Frédéric Aubrun, Mikhail Dzadzko, Caroline Macabéo; **Microbiologists** – Frederic Laurent, Laetitia Beraut, Céline Dupieux, Camille Kolenda, Jérôme Josse, Claude-Alexandre Gustave; **Imaging** – Fabien Craighero, Loïc Bousset, Jean-Baptiste Piat; **Nuclear Medicine** – Isabelle Morelec, Marc Janier, Francesco Giannarini; **PK/PD specialists** – Michel Tod, Marie-Claude Gagnieu, Sylvain Goutelle; **Clinical research assistant and database manager**– Eugénie Habrout