

# Ostenonecrosis of the jaw (ONJ) after denosumab in patients with giant cell tumor of bone (GCTB): a single institution analysis of a prospective, international study 20062004

Emanuela Palmerini<sup>1</sup>, Elisa Carretta<sup>1</sup>, Alberto Bazzocchi<sup>1</sup>, Marilena Cesari<sup>1</sup>, anna paioli<sup>1</sup>, rossella hakim<sup>1</sup>, Massimo Eraldo Abate, Antonio Carella<sup>1</sup>, Michela Pierini<sup>1</sup>, Tommaso Frisoni<sup>1</sup>, Davide Maria Donati<sup>1</sup>, Claudio Marchetti<sup>2</sup>

<sup>1</sup> Istituto Ortopedico Rizzoli

<sup>2</sup> University of Bologna

**Funding:** The author(s) received no specific funding for this work.

**Potential competing interests:** The author(s) declared that no potential competing interests exist.

## Abstract

### Background

Giant cell tumor of bone (GCTB) is a progressive osteolytic tumor with proven response to denosumab when unresectable or at high surgical risk. We report on incidence of suspected (sONJ) and adjudicated (aONJ) osteonecrosis of the jaw cases, from a single institution series of patients treated with denosumab within a phase 2 study

### Methods

Patients were enrolled with unresectable GCTB (Cohort 1), resectable GCTB with planned high morbidity surgery (Cohort 2). Denosumab was given 120 mg SC every 4 weeks with loading doses on days 8 and 15. The primary endpoint was safety: aONJ and s ONJ rate; efficacy endpoints included proportion of Cohort 2 patients without surgery, and progression-free survival for all patients

### Results

Baseline characteristics and ONJ results for 52 patients are shown in the Table 1. Median follow-up was 103 months (95%CI 55-126) in Cohort 1 and 105 months (95%CI 94-116) in Cohort 2. Overall response rate was 20% in all sample. Of 9 Cohort 1 patients, 1 ended denosumab for GCTB progression after 70 months of follow-up. Overall Kaplan Meier (KM) estimates (95% CI) for GCTB progression-free in these patients were 88% (39-98%). 23 Cohort 2 pts (53%) ended denosumab without GCTB progression, and 20 (47%) recurred with a KM estimate of 67% (51-79) at 24 months, and 52% (36-66%) at 60 months. Median time of denosumab therapy was 80 months in Cohort 1 and 14 months in Cohort 2. Within Cohort 2 patients with planned surgery, 88% underwent surgery and 12% continued with denosumab only.

Following surgery, recurrence occurs higher after curettage than resection (47% vs 5%). ONJ rate is reported in Table 1.

### Conclusions

Denosumab was generally well tolerated with excellent long-term disease control in unresectable patients. A 47% recurrence rate following surgery was seen in this high-risk, selected, resectable population. Denosumab has major, long-lasting antitumor activity in unresectable or metastatic GCTB, with an aONJ and sONJ rate of 4% and 8%, respectively, in this series.

Table 1. Demography and osteonecrosis of the jaw (ONJ) in 52 patients with giant cell tumor of bone (GCTB)

	<b>N = 52 n (%)</b>
Women	30 (58)
Median age (range)	39 (17-76)
Stage local	50 (96)
Site:	
Pelvis/sacrum	15 (29)
Radius	12 (23)
Tibia	11 (21)
Other	14 (27)
<u>Osteonecrosis of jaw<sup>a</sup></u>	6 (11.5)
<u>aONJ</u>	2 (4)
<u>sONJ</u>	4 (8)

<sup>a</sup>Considered by investigator to be possibly related to denosumab

---

## Reference

Chawla S, Blay JY, Rutkowski P, Le Cesne A, Reichardt P, Gelderblom H, Grimer RJ, Choy E, Skubitz K, Seeger L, Schuetze SM, Henshaw R, Dai T, Jandial D, Palmerini E. Denosumab in patients with giant-cell tumour of bone: a multicentre, open-label, phase 2 study. *Lancet Oncol.* 2019; 20(12):1719-1729

NCT00396279

Sponsor Amgen Inc.

E. Palmerini: Amgen advisory board.

