



## FC-134

### Adjuvant zoledronic acid in high-risk giant cell tumor of bone – Preliminary results of a randomized phase II study

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**Introduction:** Systemic targeted therapy has been introduced as adjuvant to surgery aiming at reducing recurrence-rate and avoiding morbid surgery in patients with advanced giant cell tumor of bone (GCTB). Based on small retrospective series, bisphosphonates are assumed to inhibit GCTB-derived osteoclast formation. This study aims to determine if adjuvant zoledronic acid improves 2-years recurrence-rate of high-risk GCTB compared with standard care. Secondary, the predictive role of bone markers will be studied.

**Methods:** In this prospective multicenter randomized open-label phase II trial ([www.clinicaltrials.gov](http://www.clinicaltrials.gov), NCT00889590), patients with high-risk GCTB were included (December 2008-October 2013). Recruitment was stopped because of low accrual. High-risk GCTB included soft tissue extension, pathologic fracture, axial localization, histological atypia, absence of local adjuvant use (i.e. phenol or polymethylmethacrylate [PMMA]) or recurrent GCTB. Patients with malignant GCTB or metastases were not included. In the intervention group, patients received adjuvant zoledronic acid (4mg) intravenously at 1, 2, 3, 6, 9 and 12 months after surgery with daily calcium (500mg) and vitamin D (400IU) supplements.

**Results:** Fifteen patients were included (intervention group n=8, control group n=7; Table 1). Surgery consisted of curettage with adjuvants (n=9), isolated curettage (n=3) or en bloc resection (n=3). Median follow-up was 41 months (range 8-80). Two-years recurrence-rate was 25% (2/8) in the intervention versus 29% (2/7) in the control group (p=0.99); after curettage with adjuvants 40% (2/5) in the intervention versus 25% (1/4) in the control group, respectively (p=0.75; Table 2). There was one recurrence after isolated curettage (control group; 1/1); no recurrence after resection. Overall estimated 5-years recurrence-free survival was 75% in the intervention versus 83% in the control group (p=0.84). Two patients in the intervention group had recurrence 3 months after start of zoledronic acid; systemic therapy was switched to denosumab. Complications included osteonecrosis of the jaw after 3 months zoledronic acid and 2 years denosumab (n=1), infection (n=2), chondromalacia (n=1), intra-articular PMMA leakage (n=1) and hospital-acquired pneumonia (n=1).

**Conclusion:** The low accrual was due to the introduction of denosumab in this patient group. Adjuvant zoledronic acid was feasible, but it did not result in a decrease in 2-years recurrence-rate in this study.

	Total (n=15)	Intervention group (n=8)	Control group (n=7)
Females	6	3	3
Age (median, range)	36 (19-73)	38 (21-55)	36 (19-73)
Follow-up (median, range)	41 (8-80)	44 (18-80)	41 (8-60)
Soft tissue extension	9	5	4
Pathologic fracture	5	2	3
Localization			
- Distal femur	5	3	2
- Sacrum	2	1	1
- Proximal femur	2	1	1
- Fibula	2	1	1
- Proximal tibia	1	1	-
- Distal tibia	1	1	-
- Proximal humerus	1	-	1
- Spine	1	-	1
Histological atypia	1	1	-
Surgical treatment			
- Curettage	3	2	1
- Curettage with local adjuvants	9	5	4
- En bloc resection	3	1	2
Local adjuvants with intralesional surgery			
- Phenol and PMMA	8	4	4
- PMMA	1	1	-
- None	3	2	1
Recurrent GCTB	6	4	2

Table 1. Patient, tumor and treatment characteristics



	Total (n=15)	Intervention group (n=8)	Control group (n=7)	p-value
2-year recurrence rate	27% (4/15)	25% (2/8)	29% (2/7)	0.99
- Curettage	33% (1/3)	0% (0/2)	100% (1/1)	<0.001
- Curettage with local adjuvants	33% (3/9)	40% (2/5)	25% (1/4)	0.75
- En bloc resection	0% (0/3)	0% (0/1)	0% (0/2)	1.0
5-year recurrence free survival	80%	75%	83%	0.84

**Table 2.** Local recurrences after adjuvant systemic therapy with zoledronic acid compared with standard care