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LETTER

Possible protective effect of switching from denosumab to zoledronic acid on vertebral fractures

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To the editor,

Cases have recently been published about rebound-associated vertebral fractures (RAVFs) after discontinuation of denosumab in patients with postmenopausal osteoporosis [1]. Denosumab therapy lasted between 6 and 42 months, and clinical spontaneous fractures occurred 9–16 months after the last denosumab injection. No evidence of concomitant diseases, other than osteoporosis, was found in vertebral biopsies of such patients [1, 2]. Lamy et al. reported that bone turnover after discontinuation of denosumab may be suppressed by administering bisphosphonates (BPs) prior to initiating or after discontinuation of denosumab [2]. However, so far, data on the effect of switching from denosumab to BPs on bone mineral density (BMD) and vertebral fractures is not available.

Here, we report 22 cases of women with postmenopausal osteoporosis under the care of a resident rheumatologist between May 2010 and March 2017 (Table 1). Patients, either previously treated with BPs (n = 13) or without BPs (n = 9), were started on subcutaneous denosumab (60 mg every 6 months) either due to insufficient efficacy of BPs or occurrence of fractures. All women received five injections and were then given a single dose of zoledronic acid 6 months after the fifth injection of denosumab. BMD was measured before starting denosumab, when switching to zoledronic acid, and 5 years after the baseline dual-energy X-ray absorptiometry (DXA). Changes in BMD were compared with previous measurements and vertebral fractures were evaluated by vertebral fracture analysis. Informed consent was obtained from the patients to publish the findings.

None of the postmenopausal women, with or without previous BP therapy, experienced new vertebral fractures for 5 years after the first DXA measurement and 24 months after discontinuation of denosumab. One patient developed a calcaneus fracture. Loss of BMD between discontinuation of denosumab and measurement at 5 years was more prominent at the lumbar spine (LS) and femoral neck. No difference in loss of BMD was found between patients with and without previous BP therapy.

Thus, in this small case series study, adding a single infusion of a potent intravenous BP, like zoledronic acid, after discontinuation of denosumab helped to prevent RAVFs. We found that one third of the gain in BMD at the LS provided by denosumab was eventually lost. Thus, a single infusion of zoledronic acid is not effective to sustain BMD, but is enough to avoid complete bone loss, as would be expected [4]. Until randomized controlled studies on optimal sequential management of osteoporosis in postmenopausal women are available, switching from denosumab to zoledronic acid may have a protective effect on vertebral fractures.

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Table 1 Baseline, changes, and overall data observed

Age	BP pretreatment duration	Prev Fx	RF	DXA baseline		Change BMD (%) at year 2.5			New Fx	Change BMD (%) at year 5			New Fx
Years	In years	(*n*)		T- score	FRAX (%)	LS (%)	TH (%)	FN (%)		LS (%)	TH (%)	FN (%)	
77	No	v	No	−1.1	23	na	−0.8	−3.8	No	na	−1.6	1.2	No
67	No	nv	No	−2.8	27	8.6	4.4	−0.4	No	−8.1	−2.7	−1.6	No
67	No	nv	Anti-est	−2.9	22	9.5	6.3	5.5	No	−5.6	−5.5	−5.9	No
61	5	nv (3)	FH	−2.5	30	7.0	2.4	0.4	No	−3.6	−3.4	−2.7	No
56	3	No	No	−2.6	7	2.0	0.4	1.3	No	−5.5	−5.1	−2.5	No
62	4	v (1)	No	−2.6	18	7.8	0.5	9.4	No	−4.8	4.4	−3.3	nv (1)
63	No	No	No	−2.6	12	13.3	4.5	0.9	No	−0.4	1.5	2.8	No
54	No	No	No	−3	10	5.1	5.0	4.2	No	−3.1	−2.7	−4.1	No
74	No	nv	FH	−1.5	25	8.9	2.4	4.1	No	1.4	0.5	13.4	No
66	5	No	No	−3.4	23	5.4	6.1	8.0	No	−2.4	−1.9	0.8	No
55	7	nv (1)	No	−3.9	15	9.7	9.5	1.8	No	−3.1	−0.1	3.5	No
70	4	v (1)	No	−3	33	9.9	1.3	13.1	No	−0.4	−2.2	−5.5	No
71	3	nv (1)	No	−2.7	23	9.8	5.2	1.9	No	−8.6	−5.0	−3.2	No
66	3	v (1)	FH	−2.6	26	13.1	−4.4	1.1	No	−1.9	5.9	10.3	No
65	2	No	No	−2.6	14	12.4	4.9	−2.9	No	−2.8	−2.5	−0.4	No
55	No	No	No	−3	10	5.1	5.0	4.2	No	−3.1	−2.7	−4.1	No
64	4	nv (1)	No	−3.4	36	16.3	5.4	3.3	No	−4.2	1.8	−2.4	No
56	2	v (3)	No	−2.2	22	20.8	2.8	−3.3	No	−8.8	−1.1	2.8	No
52	1	v (2)	No	−2.4	20	12.0	2.2	−10.2	No	−5.4	−5.1	−3.7	No
72	5	v (2)	No	0.6	17	9.6	1.4	2.7	No	−4.0	1.0	0.3	No
64	No	No	FH	−3	15	8.6	8.8	1.5	No	−6.3	−8.6	−7.9	No
63	No	No	Anti-est	−2	18	8.5	7.2	5.4	No	−0.1	−1.3	0.1	No
Mean of overall changes						9.8	3.9	2.3		− 3.8	− 1.7	− 0.6	

Number (*n*) of vertebral (*v*) and non-vertebral (*nv*) fractures. *TH*, *FN*, *LS*: Lowest T- score at total hip, femoral neck, and lumbar spine, respectively, according to ISCD [3]; not applicable (*na*) due to vertebroplasty. *FRAX* 10-year fracture risk for major osteoporotic fractures (FRAX tool for Switzerland). *RF* risk factors, *FH* positive family history of osteoporosis, *anti-est* positive history of anti-estrogen therapy

Compliance with ethical standards

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Conflict of interest Thomas Lehmann and Daniel Aeberli declare that they have no conflict of interest.

References

1. Popp AW, Zysset PK, Lippuner K (2016) Rebound-associated vertebral fractures after discontinuation of denosumab—from clinic and biomechanics. Osteoporos Int 27:1917–1921
2. Lamy O, Gonzalez-Rodriguez E, Stoll D, Hans D, Aubry-Rozier B (2016) Severe rebound-associated vertebral fractures after denosumab discontinuation: nine clinical cases report. J Clin Endocrinol Metab jc20163170
3. Shepherd JA, Schousboe JT, Broy SB, Engelke K, Leslie WD (2015) Executive summary of the 2015 ISCD position development conference on advanced measures from DXA and QCT: fracture prediction beyond BMD. J Clin Densitom 18:274–286
4. Bauer DC (2011) Discontinuation of odanacatib and other osteoporosis treatments: here today and gone tomorrow? J Bone Miner Res 26:239–241