Clinical features associated with fragility fracture after discontinuation of treatment with denosumab: A case-control study

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on behalf of AIRE-MB group

Picture taking is ALLOWED during my presentation (including presented slides)

DISCLOSURES

- José Miguel Senabre-Gallego Speakers bureau: Abbvie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche and UCB
- Jose Rosas: None declared
- Ana Pons: None declared
- Gregorio Santos Soler: None declared
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Background

- Discontinuation of denosumab treatment causes an increase in bone resorption that has been linked to the emergence of vertebral fractures

Objective

- To evaluate the association of **clinical features** and **demographic characteristics** with the emergence of new **fragility fractures** in patients with osteoporosis who **interrupt treatment with denosumab**

Methods

- Retrospective case-control study
- Patients: osteoporosis (local densitometry database) treated with denosumab (at least one dose) and discontinue the treatment
- Data collection:
  - Demographic variables (age, sex)
  - Risk factors for osteoporosis (alcohol and tobacco consumption, personal history of fragility fracture and history of maternal hip fracture)
  - Secondary osteoporosis (early menopause, osteopenizing disease or treatment)
  - Previous treatment for osteoporosis, start and end date of denosumab treatment and subsequent treatments

Statistical analysis

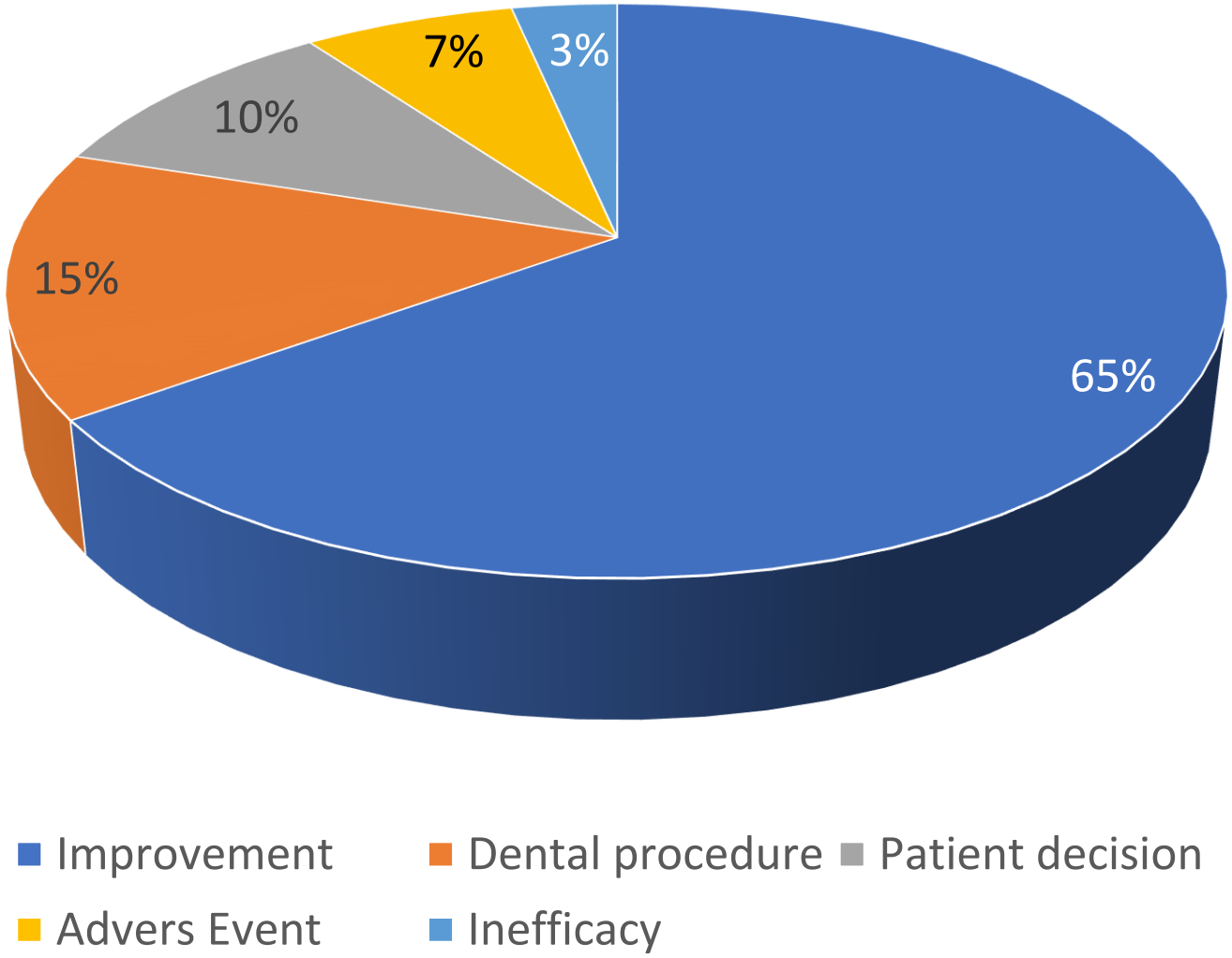
- Mean (SD) for quantitative variables
- Percentage for qualitative variables
- Chi-squared
- Fisher exact test when necessary

Methods

Results

Demographic and osteoporosis clinical data	
n	63
Fragility fractures (%)	10 (15.9)
Women (%)	61 (96.83)
Age, years, mean (SD)	70.2 (8.95)
Denosumab treatment duration, Months, mean (SD)	42.3 (17.32)
Denosumab doses, mean (SD) [range]	7.9 (2.8) [2 – 14]
Patients with ≥ 6 denosumab doses	52 (82.54)

Reasons for denosumab discontinuation



Fragility fractures

- 6 vertebral fractures
- 3 forearm fractures
- 1 hip fracture

- Mean time to fracture: 12,67 months

Demographic and clinical features by fragility fracture

	No fracture	Fracture	Total	P
Age, mean (SD)	70.2 (9.5)	70.5 (5.5)	70.2 (8.9)	0.956
BMI, mean (SD)	25.0 (4.8)	25.3 (3.2)	25.1 (4.6)	0.844
Secondary OP (%)	26 (49.1)	0 (0.0)	26 (41.3)	**0.004**
Tobacco (%)	17 (32.1)	2 (25.0)	19 (31.1)	0.687
Alcohol (%)	3 (5.7)	0 (0.0)	3 (4.9)	0.490
Previous facture (%)	20 (37.7)	6 (66.7)	26 (41.9)	0.104
Mother hip (%)	6 (11.3)	0 (0.0)	6 (9.8)	0.316
Previous BP (%)	30 (57.7)	2 (28.6)	32 (54.2)	0.229
Denosumab dose, mean (SD)	7.9 (2.8)	7.5 (3.0)	7.9 (2.8)	0.676
Follow-on BP (%)	21 (42.9)	1 (10.0)	22 (37.3)	**0.050**

BMI: body mass index; BP: bisphosphonate; OP: osteoporosis; SD: standard deviation.

Odds ratio

- **Follow-on bisphosphonate**
  - Odds ratio estimate: **0.15 (95% CI: 0.02 – 1.26; p-value = 0.052)**
- **Secondary osteoporosis**
  - Odds ratio estimate: **0.05 (95% CI: 0.00 – 0.89; p-value = 0.007)**

Discussion

- **Prior exposure to BP** does not seem to protect from fracture
- **Secondary osteoporosis** seem to protect from this type of fractures (regardless of age)
- **Previous fractures** were more common in group with event (although we have not found statistically significant differences)
- **Denosumab doses** does not seem to be related to fractures (although most of our patients have received ≥ 6 doses)
- **Follow-on treatment with BP** seems to protect from fractures (although we have one case, and other cases reported in literature)

Limitations

- Small **number** of patients
- **Retrospective** case – control study
  - Unable to estimate **incidence** rate
  - **Temporal sequence** between exposure and event difficult to determine
  - Effect of **bias** (recall bias, observer bias, selection – control group bias…)

Conclusion

- Sequential treatment with bisphosphonates and diagnosis of secondary osteoporosis are related to the absence of fractures after discontinuation of denosumab treatment

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Thanks for your attention!!