SAT0453

DELAYED DENOSUMAB INJECTIONS AND FRACTURES RISK AMONG SUBJECTS WITH OSTEOPOROSIS: A POPULATION-BASED COHORT STUDY

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Background: Denosumab is effective for osteoporosis, but discontinuation leads to rapid reversal of its therapeutic effect^[1].

Objectives: To estimate the risk for fracture among users of denosumab who delayed subsequent dosages compared with users who received dosages on time.

Methods: Population-based cohort study. We included patients aged over 45 years who initiated denosumab for osteoporosis from UK THIN database, 2010 to 2019. Observational data were used to "emulate a hypothetical trial"^[2, 3] with three dosing intervals: subsequent denosumab injection 24-28 weeks after prior dose ("on time"), delay by 4-16 weeks ("short delay"), and delay by over 16 weeks ("long delay"). The primary outcome was a composite of all fracture types. Secondary outcomes included major osteoporotic fracture, vertebral fracture, and hip fracture.

Results: The rate of composite fracture per 1000 person-years was 58.9 for on-time, 61.7 for short delay, and 85.4 for long delay of subsequent denosumab injections. Compared to on-time injections, short delay had a hazard ratio (HR) for composite fracture 1.03 (95% CI 0.63-1.69) and long delay HR 1.44 (95% CI 0.96-2.17; p for trend 0.093). For major osteoporotic fractures, short delay had an HR 0.94 (95% CI 0.57-1.55) and long delay an HR of 1.69 (95% CI 1.01-2.83; p for trend 0.056). For vertebral fractures, short delay had an HR 1.48 (95% CI 0.58-3.79) and long delay 3.91 (95% CI 1.62-9.45; p for trend 0.005).

Conclusion: While delayed subsequent denosumab dosages over 16 weeks was associated with an increased risk of vertebral and major osteoporotic fracture compared to no delay, composite fracture risk was not increased with longer delays.

References:

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- [2] Hernán MA. How to estimate the effect of treatment duration on survival outcomes using observational data. *BMJ* 2018.
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Table. Rates and Adjusted Hazard Ratios of Fracture

	On-time	Short delay	Long delay	P for linear trend
Composite Fracture				
Rate (per 1000 person-years)	59	61.7	85.4	-
Unadjusted HR (95 %)	Ref	1.05 (0.62, 1.76)	1.45 (0.95, 2.21)	0.097
Adjusted HR (95% CI) †	Ref	1.03 (0.63, 1.69)	1.44 (0.96, 2.17)	0.093
Major Osteoporotic Fracture				
Rate (per 1000 person-years)	34.8	31.9	58	-
Unadjusted HR (95 %)	Ref	0.92 (0.55, 1.53)	1.67 (0.98, 2.84)	0.074
Adjusted HR (95% CI) †	Ref	0.94 (0.57, 1.55)	1.69 (1.01, 2.83)	0.056
Vertebral Fracture				
Rate (per 1000 person-years)	4.9	7.3	19.4	-
Unadjusted HR (95 %)	Ref	1.47 (0.58, 3.71)	3.93 (1.59, 9.72)	0.006
Adjusted HR (95% CI) †	Ref	1.48 (0.58, 3.79)	3.91 (1.62, 9.45)	0.005
Hip Fracture				
Rate (per 1000 person-years)	10.2	9.6	18.3	-
Unadjusted HR (95 %)	Ref	0.94 (0.43, 2.04)	1.78 (0.80, 3.97)	0.18
Adjusted HR (95% CI) †	Ref	0.97 (0.44, 2.12)	1.75 (0.81, 3.79)	0.173

† Adjusted model: adjusted by age, sex, baseline CCI index, major osteoporotic fracture, oral BP duration (years), 10-year risk of major osteoporotic fracture, prior denosumab doses.

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SAT0454

EARLY CLINICAL EFFICACY OF ROMOSUZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PRIMARY OSTEOPOROSIS

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Background: Romosozumab (ROM), a monoclonal antibody that binds sclerostin, increases bone formation and decreases bone resorption. And although it is a novel therapeutic agent for osteoporosis, which has shown high effects of increasing bone density and inhibiting fragile fracture in overseas clinical trials. However the clinical efficacy in daily clinical practice is unknown.

Objectives: To evaluate the early clinical efficacy of ROM in patients with osteoporosis between rheumatoid arthritis (RA-OP) and primary osteoporosis (P-OP) for 6 months.

Methods: RA patients diagnosed according to the 2010 ACR/EULAR criteria. RA-OP and P-OP patients met at least one of the following criteria were eligible; a bone mineral density T score of -2.5 or less at the lumbar spine or total hip and either one or more moderate or severe vertebral fractures or two or more mild vertebral fractures. All patients were initiated ROM from between March and June, 2019. The total number of patients was 15 cases, including 8 RA-OP and 7 P-OP. All patients received continuous ROM therapy more than 6 months. The DMB dose was 210mg at once every 1 months. In all cases native or activated vitamin D has been used. We reviewed the results for 6 months about the increase and decrease of bone mineral density (BMD) of lumbar spine (LS) and total hip (TH) by DEXA and bone turnover markers, intact n-terminal propeptide type I procollagen (PINP) and tartrate-resistant acid phosphatase form 5b (TRACP-5b).

Results: The gender was all female. The mean age was 71.8 ± 8.7; disease duration of RA-OP patients was 23.0 ± 15.1 years; the body mass index was 19.9 ± 3.2 and the FRAX was 32.5 ± 14.9. Clinical findings related to RA-OP at baseline were as follows; CRP 0.97 ± 0.77; DAS-CRP 3.22 ± 0.41; HAQ 1.41 ± 0.94 in RA-OP patients and in the all patients, bone turnover markers and bone mineral density at baseline were as follows; PINP 72.2 ± 39.8; TRACP-5b 539 ± 212; LS-BMD and T-score 0.80 ± 0.20 g/cm² and -2.75 ± 1.36 and TH-BMD 0.55 ± 0.07 g/cm² and -3.18 ± 0.55 g/cm². The rate of increased PINP from baseline to 1, 3 and 6 months were each -96.8 ± 80.8% at 1 month, 106.8 ± 115.6% at 3 month and 90.7 ± 115.7% at 6 month and decreased TRACP-5b were -20.4 ± 20.6% at 1 month, -80.8 ± 19.6% at 3 month and -1.8 ± 50.8% at 6 month. The rate of increased LS-BMD from baseline to 6 months were 11.0 ± 8.0% and TH-BMD were 5.3 ± 3.8% (Fig. 1, 2).

Conclusion: Early clinical efficacy of ROM for RA-OP and P-OP was extremely effective and has the high potential to be an important option in the treatment of osteoporosis.

Fig.1: The rate of increased LS-BMD from baseline to 6 month