Clinical and Economic Benefits of Early Romosozumab Initiation in Patients with Recent Osteoporotic Hip Fractures in Japan

EE132

Saeko Fujiwara [1], Eric Yeh [2], Etsuro Hamaya [3], Yoshito Bushita [3], Satoru Tanaka[3], Sudhanshu Ranjan [4], Geetika Khatri [4], Sakshi Garg [4], John R. Cook [4]

[1] Yasuda Women's University, 6-13-1 Yasuhigashi, Asaminami-ku, Hiroshima 731-0153, Japan; [2] Amgen Inc., Thousand Oaks, California 91320, USA; [3] Amgen K.K., 9-7-1 Akasaka, Minato-ku, Tokyo 107-6239, Japan; [4] Peritia, Morrisville, NC, USA

INTRODUCTION

- In Japan, approximately 193,000 hip fractures were experienced among 15.9 million individuals with osteoporosis in 2017.[1]
- Japanese guidelines for prevention and treatment of osteoporosis (2025) recommend osteoanabolic agents such as romosozumab be used first, followed by antiresorptive agents like bisphosphonates for very-high fracture-risk and recent hip fracture patients.
- However, the per diem system often disincentivizes use of osteoanabolic agents at Diagnosis Procedure Combination hospitals despite guideline recommendations.

OBJECTIVES

This study assesses the cost-effectiveness, return on investment (ROI) and budget impact (BI) of early romosozumab initiation versus late initiation in patients aged ≥ 50 years with recent osteoporotic hip fracture in Japan.

METHODS

- A patient-level simulation model was developed with five health states, using a 3-month cycle and a 2% annual discount rate over a 10-year horizon from the payer perspective (Figure 1).
- For the patients experiencing a hip fracture, a decision-tree model was used to calculate fracture care costs for patients experiencing first or subsequent fracture, by simulating their pathway of care (Figure 2).
- Three types of fractures outcomes are recorded: hip, vertebral and non-hip non-vertebral.
- The model compared the following sequences over a 5-year treatment period:
  - Sequence 1 (early romosozumab initiation): romosozumab (1 year) → alendronate (4 years)
  - Sequence 2 (late romosozumab initiation): alendronate (9 months) → romosozumab (1 year) → alendronate (3 years 3 months)
- Age-specific baseline fracture risk was derived using risk equations from Moriwaki et al. 2017 and adjusted for treatment effects via relative risk (RR) estimates.[2, 3-7]
- For sequence 1, RR estimates were derived by multiplying RR of romosozumab/alendronate vs alendronate (Hagino et al. 2021) with RR of alendronate vs placebo (Willems et al. 2022).[3,4]
- Sequence 2 RR estimates were derived from Willems et al. 2022 for first course of alendronate. Due to lack of data, RR for romosozumab at 12 months post 9-month alendronate was derived by multiplying ARCH bone mineral density (BMD) change with the ratio of treatment naïve versus experienced Romosozumab BMD change by Tominaga et al, 2022.[4-6] BMD changes during later romosozumab cycles (15–21 months) were estimated from the calculated 12-month BMD change and STRUCTURE trial data on romosozumab after 3 years of alendronate.[7] For second course of alendronate, 0.4% BMD increase was assumed as the residual effect after romosozumab discontinued.
- The relationships of BMD changes and fracture risk reduction were modification ofBouxsein et al. 2019.[8]
- Quality-adjusted life years (QALYs) were calculated using general population utilities and fracture-specific utility decrements.[9]
- Costs (2024 Japanese Yen) included drug acquisition, administration, disease management and fracture care costs.[10,11]
- Per patient ROI was calculated using the average cost outcomes over a 10-year time horizon by calculating the net benefit as return (decrease in disease management and fracture care costs) minus the investment (increase in drug acquisition and administration costs).
- BI was evaluated where the uptake of sequence 1 was increased from 2% in the reference scenario to 10% in the new scenario, using the average cost outcomes over a 10-year time horizon.
- Cost-effectiveness of sequence 1 was also evaluated against active vitamin D_3 and alendronate as scenario analyses.

Figure 1: Model structure

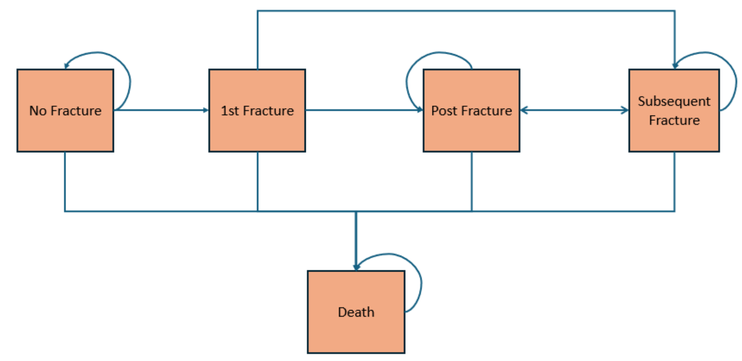
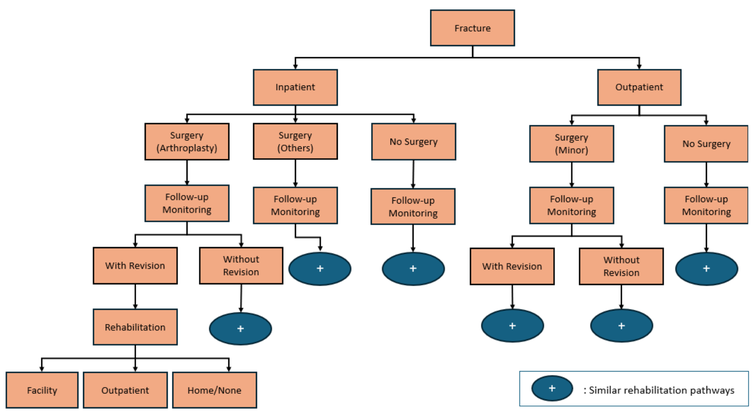


Figure 2: Decision-tree for fracture care



RESULTS

- For 100,000 patients, treatment sequence 1 yielded fewer fractures (11,800), additional life-years (7,908) and QALYs (6,533), and saved ¥15.9 billion versus sequence 2 over a 10-year horizon, making early initiation of romosozumab dominant (Figure 3, Figure 4, Table 1).
- While drug acquisition costs were higher for sequence 1, the projected reduction in fractures would lead to lower fracture care costs and a reduction in total costs compared with sequence 2 (Table 1).
- ROI analysis indicated a strong benefit of 607% per patient.
- BI decreased approximately ¥1.2 billion among 100,000 patients with an increased uptake of romosozumab (Table 2).
- One-way sensitivity analysis indicated that the results were most sensitive to RR of death and utility inputs after experiencing hip fracture.
- Probabilistic sensitivity analysis results were consistent with the base case, with sequence 1 dominating sequence 2.
- In the scenario analyses, sequence 1 was cost-effective against other sequences explored (at a willingness-to-pay threshold of ¥5,000,000):
  - Incremental cost-effectiveness ratio (ICER) vs active vitamin D_3 (5-years): ¥1,589,356 per QALY gained
  - ICER vs alendronate (5-years): ¥4,442,132 per QALY gained

Figure 3: Cumulative number of fractures outcomes - Base case

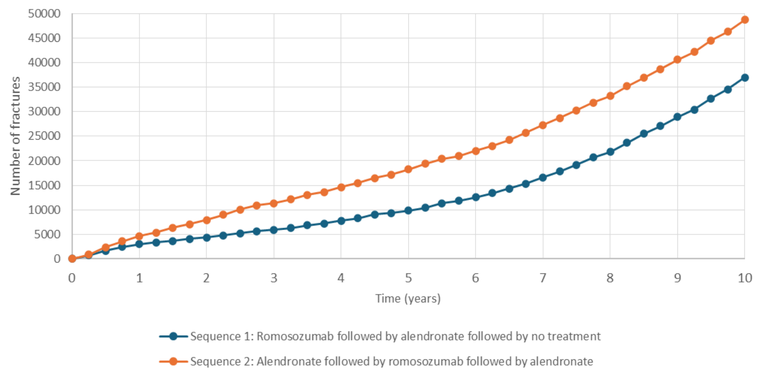


Figure 4: Number of fracture outcomes by fracture type (for 100,000 patients) - Base case

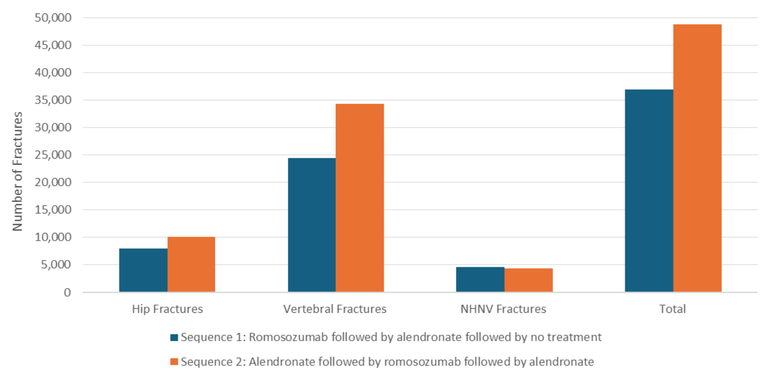


Table 1: Results (for 100,000 patients) - Base case

Outcome	Sequence 1	Sequence 2	Difference
Life years	688,323	680,415	7,908
QALYs	471,667	465,135	6,533
Costs (¥)	**529,919,174,825**	**545,863,415,199**	**-15,944,240,374**
Drug acquisition	57,713,759,031	55,735,199,355	1,978,559,676
Drug administration	288,588,887	269,763,734	18,825,153
Disease management	10,608,463,561	10,426,739,244	181,724,317
Fracture care	459,518,291,917	479,416,307,763	-19,898,015,846
ICER (¥/QALY)	**Sequence 1 dominates**		

Table 2: Budget impact (for 100,000 patients)

Categories	Reference Scenario	New Scenario	Budget Impact
Costs (¥)	**545,544,530,391**	**544,268,991,161**	**-1,275,539,230**
Drug acquisition	55,774,770,549	55,933,055,323	158,284,774
Drug administration	270,140,237	271,646,249	1,506,012
Disease management	10,430,373,730	10,444,911,676	14,537,945
Fracture care	479,018,347,446	477,426,506,179	-1,591,841,268

*Reference scenario: 2% uptake of sequence 1; New scenario: 10% uptake of sequence 1

CONCLUSIONS

The results suggest that early initiation of osteoanabolic agent romosozumab followed by antiresorptive agent alendronate is cost-effective with a substantial ROI and favorable BI compared to late romosozumab initiation after alendronate from the payer perspective, supporting Japanese treatment guideline recommendations. Additionally, the scenario analysis indicated that switching to sequence 1 from the commonly prescribed treatment alternatives in Japan was also cost-effective.

DISCLOSURE

This study was funded by Amgen Inc. and Amgen K.K. and conducted in collaboration with Peritia. EY, EH and YB are employees of Amgen and hold Amgen shares. ST is an employee of Amgen K.K. Peritia has received consultancy fees from Amgen.

For further clarification or support, please contact: Eric Yeh <eyeh01@@amgen.com>

REFERENCES

1. Takusari E, Sakata K, Hashimoto T, Fukushima Y, Nakamura T, Orimo H. Trends in hip fracture incidence in Japan: estimates based on nationwide hip fracture surveys from 1992 to 2017. Journal of Bone and Mineral Research Plus. 2021 Feb 1;5(2):e10428.
2. Moriwaki K, Noto S. Economic evaluation of osteoporosis liaison service for secondary fracture prevention in postmenopausal osteoporosis patients with previous hip fracture in Japan. Osteoporosis International. 2017 Feb;28(2):621-632.
3. Hagino H, Tanaka K, Silverman S, McClung M, Gandra SR, Charokopou M, Adachi K, Johnson B, Stollenwerk B. Cost effectiveness of romosozumab versus teriparatide for severe postmenopausal osteoporosis in Japan. Osteoporosis International. 2021 Oct;32(10):2011-2021.
4. D. Willems, M. Javaid, R. Pinedo-Villanueva, C. Libanati, A. Yehoshua and M. Charokopou, Importance of Time Point–Specific Indirect Treatment Comparisons of Osteoporosis Treatments: A Systematic Literature Review and Network Meta-Analyses, Clinical Therapeutics. 2022; 44(1):81-97.
5. Romosozumab. Clinical Study Report: 20110142. 26 July 2017.
6. Tominaga A, Wada K, Okazaki K, Nishi H, Terayama Y, Kodama Y, Kato Y, Effect of the duration of previous osteoporosis treatment on the effect of romosozumab treatment, Osteoporosis International, 2022; 33(6):1265-1273.
7. Romosozumab. Clinical Study Report: 20080289. 09 November 2015.
8. Bouxsein ML, Eastell R, Lui LY, Wu LA, de Papp AE, Grauer A, Marin F, Cauley JA, Bauer DC, Black DM, FNIH Bone Quality Project. Change in bone density and reduction in fracture risk: a meta-regression of published trials. Journal of Bone and Mineral Research. 2019 Apr; 34(4):632-42.
9. Svedbom A, Borgström F, Hernlund E, Ström O, Alekna V, Bianchi ML, Clark P, Curiel MD, Dimai HP, Jürisson M, Kallikorm R. Quality of life for up to 18 months after low-energy hip, vertebral, and distal forearm fractures—results from the ICUROS. Osteoporosis International. 2018 Mar; 29(3):557-66.
10. Mori T, Komiyama J, Fujii T, Sanuki M, Kume K, Kato G, Mori Y, Ueshima H, Matsui H, Tamiya N, Sugiyama T. Medical expenditures for fragility hip fracture in Japan: a study using the nationwide health insurance claims database. Archives of Osteoporosis. 2022 Dec;17(1):61.
11. DPC (Diagnosis Procedure Combination) Available at: https://bone.jp/dpc/index.html