

## Early Dropout of Japanese Patients Undergoing Anti-sclerostin Antibody Treatment for Osteoporosis

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### Abstract

**Aim:** This clinical study involved antisclerostin antibody therapy for Japanese diagnosed with severe osteoporosis.

**Subject and Methods:** Patients received romosozumab for severe osteoporosis at three affiliated hospitals of the Kinki University 10-year Graduate Association, the data was extracted from those patients who discontinued treatment.

**Results:** Among the 69 patients, 10 discontinued treatment. The reasons for discontinuation included feeling sick (n = 4), fluctuating blood pressure (n = 2), eczema (n = 1) concomitant pneumonia (n = 1), injection site reaction (n = 1) and cost increase (n = 1). In all 10 patients, romosozumab was discontinued between the first and third administration (month).

**Conclusions:** In this small study, the dropout rate for romosozumab was relatively low (14.4%) against our PTH treatment.

**Keywords:** Dropout; Osteoporosis; Anti-Sclerostin Antibodies

### Abbreviations

PTH: Parathyroid Hormone; Romo: Romosozumab; BMI: Bone Mass Index; YAM: Young Adult Mean; BKP: Balloon Kyphoplasty; RANKL: Receptor Activator of NF-κB Ligand

### Introduction

Japan has reached an era wherein its people live up to 100 years of age. Accordingly, there is an ongoing effort to protect against inevitable osteoporotic fractures in this patient subset. Patients with advanced age and compromised with multiple comorbidities need to be more carefully examined and evaluated [1-3]. With the advent of N-terminal fragment 1-34 parathyroid hormone (Teriparatide, PTH) and anti-sclerostin antibodies (Romosozumab, [Romo]. Evenity®. Astellas and AMGEN Biopharma. Japan), bone mass in osteoporotic patients can be restored to normal levels within 2 years (recommended by the National Osteoporosis Foundation (NOF)- Osteoporosis International 2019 [4]. The health insurance coverage of Romo in Japan began in March 2019. Unlike PTH preparations, the use of Romo resulted in an increase in bone mass at the proximal end of the femur [5]. Within this clinical setting, many elderly patients had significant comorbidities and Romo can act as an additional problem [6].

### Materials and Methods

The Osteoporotic patients were identified. Patients subsequently received Romo at three affiliated hospitals of the Kinki University 10-year Graduate Association (Departments of Orthopedic Surgery, Sakai Sakibana Hospital, Sumoto Itsuki Hospital, and Hara Hospital).

**Results**

There were 69 patients in total (62 - 94 [mean 81.1 ± 8.5] years; 11 men and 58 women; BMI, 12.6 - 33.3 [mean 22.1 ± 4.7]; bone mineral young adult mean (YAM) before treatment, 30 - 86 [mean 58.3 ± 12.6]). Comorbidities included cardiovascular disease (n = 30), renal impairment (n = 19), osteoporotic surgery (n = 13) (including patients who underwent vertebroplasty [Balloon Kyphoplasty, Teijin-Nakashima incorporated, Japan], bipolar type femoral head replacement [Peterbrähm and Colin incorporated. Germany and England], or osteosynthesis [ME system and others. Japan]), diabetes mellitus (n = 11), dementia (n = 9), rheumatoid arthritis (RA. n = 5) and cancer (n = 3). Prior medications were bisphosphonates in 30 patients, PTH in 19, anti-receptor activator of NF-κB ligand (RANKL) antibody (Pralia®). Every 6month subcutaneous injection. Daiichi-Sankyo Pharma. Japan) in 11, and others in 9. Patients with a history of cerebral infarction or a cardiovascular event within 1 year were excluded. All patients received Romo within 1 year; bone mass was not assessed during this period. Among patients transferred to another institution, only those who could be followed up ≥ 3 times (6 patients) were included, but those who were followed up ≤ 2 times (5 patients) were excluded. Among the 69 patients, 10 discontinued treatment (14.4%; 70 - 92 [mean 80.2 ± 6.6] years; 1 man and 9 women; BMI, 17.1 - 26.8 [mean 20.3 ± 2.4]; YAM, 38 - 69 [mean 56.8 ± 14.4]). The reasons for discontinuation included feeling sick (n = 4), fluctuating blood pressure (n = 2) and eczema, concomitant pneumonia, injection site reaction, and cost increase (to approximately 500 USD/month in Japan). In all 10 patients, Romo was discontinued between the first and third administration (month); it was not re-administered after the resolution of adverse reactions. During the study period, a 73-year-old woman with RA fell, resulting in a fractured olecranon, and treated with JS pin [Jseed incorporated. Japan] tension band wiring. However, there were no new evident vertebral and hip fractures, fragility fractures, or serious cardiovascular adverse drug reactions.

**Discussion**

We reported the comparison of therapeutic results for osteoporosis between two PTH preparations at the WCO-IOF-ESCEO 2016 (H Kikuchi, *et al.* P:250 - A comparative study of the effects of parathyroid hormone formulations on Japanese patients with osteoporosis). The treatment continuation rate was 76.3% (29/38 patients) for daily PTH (Forteo®, Eli Lilly and Company. USA) and 56.1% (23/41 patients) for once-weekly PTH (Teribone®, Asahikasei Pharma. Japan). The dropout rates for the two drugs in Japanese real-world were observed 23.7% for daily PTH and 43.9% for once-weekly PTH. The main reasons for dropout were gastrointestinal symptoms, such as transitional functional dyspepsia (mainly nausea and vomiting) in this series. To increase bone mineral density to the normal level may protect fractures and prolong life span from patients with osteoporosis all over the world [7]. In this small study, the dropout rate for Romo was relatively low (14.4%); dropout patients had no symptoms of nausea or vomiting, and the reasons for dropout differed from those for PTH. During the 6-month post-marketing Romo surveillance in Japan [8], the incidence of all adverse reactions was 3.9% (1,626/about 42,000 patients) and severe adverse reaction was 11.7% (190/1,626 patients). The adverse reactions were mainly injection site reactions (44.6%. 726/1,626 patients); serious cardiovascular events were frequently observed in patients in their 80s (53.8%. 21/39 patients). Indicate their adverse reaction rate for 3 medications in table 1 [8-10], but not comparative trial each. The persistency (180 Day) of Romo was not published, but in our data nearly same to daily PTH. December 2019, twice weekly PTH (Teribone®) can released to decrease adverse reactions and maintain their persistency [10]. Although no serious adverse reactions were observed in our small number Romo patients, it may be difficult for slim, low YAM and/or female patients to continue Romo therapy in Japan, where the aging population is increasing.

	<b>Romosozumab</b>	<b>Daily PTH</b>	<b>Weekly PTH</b>
Number	42,000 kits	1,847 patients	3,573 patients
Adverse reaction	1,626 (3.9%)	140 (7.6%)	898 (25.1%)
Dyspepsia	226 (13.9%)	31 (1.7%)	508 (14.2%)
Our data	10/69 (14.4%)	7/38 (18.4%)	12/41 (29.2%)
Persistency (Day)	No data (180)	76.3% (180)	56.1% (180)
Our data	84.6% (128)	82.3% (135)	64.0% (133)

**Table 1:** Three medications: Post-marketing surveillance in Japan.

## Conclusion

In this small Japanese real-world study, the dropout rate for Romo was relatively low (14.4%); dropout patients had no symptoms of functional dyspepsia (nausea and/or vomiting), and the reasons for dropout differed from those for PTHs.

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## Conflict of Interest

No potential conflict of interest to this article was reported.

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