Tohoku J. Exp. Med., 2025, **266**, 99-106

Comparison of the Continuation Rates of Romosozumab and Teriparatide Administrations in a Rural Area

Hiroyuki Tsuchie,[1] Hidekazu Abe,[2] Norimitsu Masutani[2] and Naohisa Miyakoshi[1]

[1]Department of Orthopedic Surgery, Akita University Graduate School of Medicine, Hondo, Akita, Japan
[2]Department of Orthopedic Surgery, Ugo Municipal Hospital, Ogatsu-gun, Akita, Japan

Romosozumab has a dual effect on bones; it promotes bone formation and inhibits bone resorption and has a strong bone density-increasing effect. There have been various reports on the continuation rates of teriparatide, another drug used for osteoporosis treatment; however, there are few reports on the continuation rate of romosozumab. Therefore, this study aimed to examine the continuation rate of romosozumab and the factors affecting it, and to compare the continuation rates of romosozumab and teriparatide in a rural area. We retrospectively reviewed 199 patients with osteoporosis who were administered romosozumab monthly and teriparatide acetate preparation weekly or twice-weekly in an outpatient clinic. Patient information included age, sex, distance by road to the hospital, reason for the start of treatment, history of osteoporosis treatment and fracture, serum levels of some parameters, bone mineral density, adverse events, and a continuation period within one year. We compared differences in patient backgrounds and continuation rates among the romosozumab (ROM), twice-weekly teriparatide (TW), and weekly teriparatide (W) groups. Furthermore, we examined the factors influencing discontinuation in all patients. The continuation rate of the ROM group (88.9%) was significantly higher than that of the W group (70.2%) (P = 0.0358). In the Kaplan-Meier curves for treatment continuation, the ROM group showed a significantly higher continuation rate than the W group (P = 0.0202). Univariate analyses of all patients showed that romosozumab administration reduced the risk of discontinuation (P = 0.0450). Romosozumab has a considerably higher continuation rate than weekly teriparatide.

Keywords: continuation rate; discontinuation; osteoporosis; romosozumab; teriparatide
Tohoku J. Exp. Med., 2025 June, **266** (2), 99-106.
doi: 10.1620/tjem.2024.J102

Introduction

Osteoporosis is characterized by a low bone mass and microarchitectural deterioration of the bone structure, resulting in bone fragility. Patients with osteoporosis are prone to fractures that lead to lower limb muscle weakness and a decline in activities of daily living. In addition, approximately 30% of all postmenopausal women have osteoporosis (Melton et al. 1992), and there are approximately 13 million osteoporosis patients in Japan (Japan Osteoporosis Society, The Japanese Society for Bone and Mineral Research, Japan Osteoporosis Foundation 2015). Therefore, osteoporosis is considered a serious public health concern, and various new drugs are becoming available for its treatment.

Romosozumab is a humanized anti-sclerostin monoclonal antibody and is the only medicine used to treat osteoporosis that has a dual effect on bones, promoting bone formation and inhibiting bone resorption. Romosozumab is a subcutaneous injection administered monthly at a hospital and is used continuously for one year. Each dose requires 210 mg; however, because each vial contains 105 mg, it is necessary to receive two subcutaneous injections during one visit. Romosozumab is one of the few osteoporosis treatments, such as teriparatide, that promote bone formation; it has a strong bone density-increasing effect and plays an important role in patients with severe osteoporosis. However, regardless of the strength of the therapeutic agent used for osteoporosis, it is meaningless unless the patient continues to use it. There have been various reports on the continuation rates of teriparatide (Arden et al. 2006; Adachi et al. 2007; Ziller et al. 2010; Foster et al. 2011;

Received May 3, 2024; revised and accepted September 9, 2024; J-STAGE Advance online publication September 19, 2024
Correspondence: Hiroyuki Tsuchie, M.D., Akita University Graduate School of Medicine, Department of Orthopedic Surgery, 1-1-1 Hondo, Akita 010-8543, Japan.
e-mail: e-mail: tuchikiti@yahoo.co.jp

Kyvernitakis et al. 2014; Rajzbaum et al. 2014; Oishi et al. 2018; Usui et al. 2018; Tsuchie et al. 2020, 2023; Fujita et al. 2022; Mochizuki et al. 2023), but only few reports on the continuation rate of romosozumab are available (Cosman et al. 2016; Saag et al. 2017; Tominaga et al. 2021). Romosozumab has been available in Japan for approximately five years. However, factors affecting its continuation rate have not been adequately investigated.

This study aimed to examine the continuation rate of romosozumab and the factors affecting it and to compare the continuation rates of romosozumab and weekly and twice-weekly teriparatide preparations in a rural area.

Materials and Methods

Subjects

This study retrospectively reviewed the medical records of 255 Japanese patients who were administered either romosozumab monthly, weekly teriparatide acetate, or twice-weekly teriparatide acetate at Ugo Municipal Hospital, located in a rural northeastern area of Japan, between September 2012 and December 2023. Subcutaneous injection of two 105 mg vials of romosozumab (total of 210 mg) (Evenity®, Amgen K.K., Tokyo, Japan) was administered monthly in a hospital. However, subcutaneous injection of teriparatide was administered at a dose of 56.5 μg weekly in the hospital or 28.2 μg self-injection with an auto-injector twice-weekly at home (Teribone®, Asahi Kasei Pharma Co., Ltd., Tokyo, Japan). We included patients with osteoporosis with a bone mineral density (BMD) of the lumbar spine or femoral neck lower than −2.5 S.D. of the T-score or patients with histories of fragile-bone fractures. Since teriparatide administration after hospitalization has a negative effect on the continuation rate (Tsuchie et al. 2020), only patients who started using the drugs at an outpatient clinic were included in this study. Patients with a history of metabolic bone diseases other than osteoporosis or malignancy were excluded from the study. Among the cases in which romosozumab or teriparatide was used to promote bone fusion, those in which these drugs were discontinued at the discretion of the attending physician after achieving bone fusion were also excluded. Patients living in elderly care facilities were also excluded because their living environment affected their continuation rate. Finally, 186 consecutive patients, with a mean age of 76.7 years (59-92), were included in this study, 54 of whom used romosozumab (ROM group), 98 used twice-weekly teriparatide administration (TW group), and 47 used weekly teriparatide administration (W group). A total of 13 out of 186 patients received both romosozumab and twice-weekly teriparatide administration. In this study, the timing of romosozumab administration was assigned to patients in the ROM group, and the timing of twice-weekly teriparatide administration was assigned to patients in the TW group.

Patient information included age; sex; distance by road between the hospital and home; reason for the start of administration (fracture or examination of osteoporosis); history of osteoporosis treatment; history of fracture; presence of rheumatoid arthritis; regular visits to our hospital for other illnesses, including orthopedic diseases other than osteoporosis; serum levels of intact procollagen 1 N-terminal propeptide, tartrate-resistant acid phosphatase 5b, and 25(OH)D; BMD of the lumbar spine and femoral neck before and one year after administration; adverse events leading to discontinuation; and continuation period. We performed BMD measurements within two months of starting treatment in all patients, and measured the anteroposterior views of the lumbar spine from L2 to L4 and the femoral neck. As the maximum continuous administration period for romosozumab is one year, we also evaluated the one-year continuation rate of teriparatide. Patients who reached the one-year period were considered to have completed the treatment. To exclude cases in which treatment was ongoing, only those in which the first treatment was started by January 2023 were included.

We compared differences in patient backgrounds and continuation rates among the ROM, TW, and W groups. Furthermore, we examined the factors influencing discontinuation in all patients. In the absence of any events, the date of the last follow-up was considered the endpoint.

Ethical statement

Our study was conducted in accordance with the ethical standards of the Declaration of Helsinki of 1975, revised in 1983 and was approved by the Institutional Review Board for Clinical Research at Ugo Municipal Hospital (approval number: 2401). Informed consent was obtained from all patients enrolled in the study.

Statistical analysis

All continuous variables were expressed as means ± standard deviation (SD). One-way analysis of variance, Scheffe's multiple comparison procedure, and Chi-squared (χ^2) tests were used to compare the characteristics between the groups. Romosozumab and teriparatide continuation curves were drawn using the Kaplan-Meier method, and the differences between the two groups were analyzed using the generalized Wilcoxon test. A Cox proportional hazards model was used to identify the factors associated with the discontinuation of romosozumab or teriparatide. Statistical significance was set at $P < 0.05$.

Results

The patient demographics and clinicopathological information are presented in Table 1. The distance by road between the hospital and home in all patients was 8.3 ± 7.1 km (0.1-27.7). Thirty-nine patients started romosozumab or teriparatide after the following fractures: the vertebral body in 29 patients; pelvis in six, and femur, humerus, rib, and distal radius in one each. Osteoporosis treatment was prescribed to 105 patients before the initiation of romosozumab or teriparatide treatment. Alendronate (Fosamac®;

Table 1. Comparison of the clinical characteristics of patients in the romosozumab and twice-weekly and weekly teriparatide groups.

	Romosozumab	Twice-weekly teriparatide	Weekly teriparatide	*P* value All	*P* value ROM vs. TW	*P* value ROM vs. W
Number	54	98	47	-	-	-
Age, years	77.6 ± 6.3	76.1 ± 6.9	77.0 ± 6.6	0.3649	-	-
Sex - Male/Female	0/54	1/97	5/42	-	0.7616	0.0456
Distance between hospital and home (km)	7.7 ± 6.6	8.9 ± 7.7	7.8 ± 6.1	0.4871	-	-
Reason for the start of administration - Fracture/Examination	8/46	18/80	13/34	-	0.7402	0.1800
Past osteoporosis treatment - Present/None	34/20	53/45	18/29	-	0.3746	0.0229
Past fractures - Present/None	18/36	38/60	16/31	-	0.6241	0.1394
Rheumatoid arthritis - Present/None	1/53	4/94	1/46	-	0.7929	0.5374
Visiting the hospital for other illnesses - Present/None	12/42	25/73	14/33		0.7990	0.5227
25 (OH) D	17.7 ± 7.4	16.9 ± 6.0	17.6 ± 6.9	0.7939	-	-
P1NP	58.2 ± 39.9	45.8 ± 29.3	47.9 ± 18.6	0.1052	-	-
TRACP-5b	410 ± 201	396 ± 204	491 ± 190	0.0769	-	-
BMD (g/cm2) of the lumbar spine						
Before treatment	0.712 ± 0.169	0.708 ± 0.180	0.678 ± 0.172	0.6191	-	-
One year after starting treatment	0.799 ± 0.154	0.747 ± 0.208	0.670 ± 0.147	0.0272	0.4209	0.0284
BMD of the proximal femur (g/cm^2)						
Before treatment	0.477 ± 0.077	0.481 ± 0.094	0.482 ± 0.112	0.9507	-	-
One year after starting treatment	0.501 ± 0.069	0.478 ± 0.092	0.474 ± 0.097	0.3821	-	-
Adverse event leading to discontinuation - Present/None	2/52	14/84	7/40	-	0.0787	0.1055
Treatment - Completed/Discontinued	48/6 (88.9)	75/23 (76.5)	33/14 (70.2)	-	0.1010	0.0358
Duration of treatment (months)	10.9 ± 3.2	10.2 ± 3.6	9.3 ± 4.5	0.0645	-	-

Values are expressed as the number of patients or mean ± standard deviation, with ranges.
PINP, intact procollagen 1 N-terminal propeptide; TRACP-5b, tartrate-resistant acid phosphatase 5b; BMD, bone mineral density; ROM, romosozumab, TW, twice weekly teriparatide; W, weekly teriparatide.

Table 2. Details of past osteoporosis treatment.

	Romosozumab	Twice-weekly teriparatide	Weekly teriparatide
Number	34	53	18
Bisphosphonate	9	24	13
Alendronate - 35 mg/week	3	7	4
Risedronate - 17.5 mg/week	3	9	8
Minodronate - 50 mg/4 weeks	1	3	1
Ibandronate - 1 mg/4 weeks	1	3	0
Zoledronic acid - 5 mg/year	1	2	0
Eldecalcitol - 0.75 mg/day	7	23	7
Combination of other osteoporosis drugs	5	14	4
Bazedoxifene - 20 mg/day	3	12	1
Denosumab - 60 mg/6 months	2	4	0
Romosozumab - 210 mg/months	0	4	0
Teriparatide	18	0	0
Daily - 20 µg	9	0	0
Twice-weekly - 28.2 µg	9	0	0
Elcatonin - 20 µg/week	0	0	1

Values expressed represent the number of patients.

MSD, Tokyo, Japan), risedronate (Actonel®; Eisai, Tokyo, Japan, or Benet®; Takeda Pharmaceutical, Tokyo, Japan), minodronate (Recarbon®; Ono Pharmaceutical, Osaka, Japan), ibandronate (Bonviva®, Taisyo Toyama Pharmaceutical, Tokyo, Japan), zoledronic acid (Reclast®, Asahi Kasei Pharma Co., Ltd., Tokyo, Japan), eldecalcitol

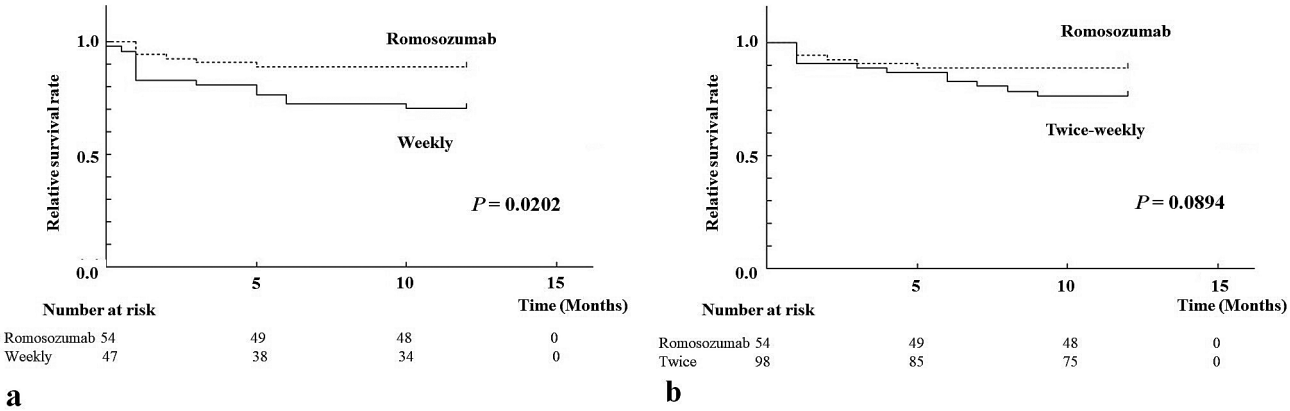

Fig. 1. The Kaplan-Meier curves showing the difference in treatment continuation between the romosozumab group and each teriparatide group (weekly [a] and twice-weekly [b]).
The romosozumab group shows a significantly higher continuation rate than the weekly teriparatide group ($P = 0.0202$).

Table 3. Reasons for discontinuation of the three osteoporosis treatment drugs.

	Romosozumab (%)	Twice-weekly teriparatide (%)	Weekly teriparatide (%)
Number patients who discontinued the treatment	6	23	14
Adverse events	2 (33.3)	14 (60.9)	7 (50)
Nausea	0	7	3
Dizziness	1	2	0
Malaise	1	3	1
Itching	0	1	0
Body pain	0	0	1
Hypertension	0	0	1
Palpitation	0	1	0
Numbness in the lower limbs	0	0	1
Dropout from outpatient treatment	2 (33.3)	4 (17.4)	1 (7.1)
Financial burden	0 (0)	2 (8.7)	0 (0)
Difficult to continue going to the hospital	0 (0)	0 (0)	6 (42.9)
Self-inject problems	-	2 (8.7)	-
Death from other illness	1 (16.7)	0 (0)	0 (0)
Anxiety	1 (16.7)	1 (4.3)	0 (0)

Values are expressed as number of patients.

(Edirol®; Chugai Pharmaceutical, Tokyo, Japan), bazedoxifene (Viviant®; Pfizer Japan Inc., Tokyo, Japan), denosumab (Pralia®, Daiichi Sankyo, Tokyo, Japan), romosozumab (Evenity®, Amgen K.K., Tokyo, Japan), daily 20-μg teriparatide injection (Forteo®, Eli Lilly Japan Co., Ltd., Kobe, Japan), twice per week 28.2-μg teriparatide injection (Teribone®, Asahi Kasei Pharma Co., Ltd., Tokyo, Japan), and elcatonin (Elcitonin®; Asahi Kasei Pharma, Tokyo, Japan) were prescribed to these patients. Details of the past osteoporosis treatment are shown in Table 2. Twenty-two of 37 patients received eldecalcitol and a combination of other osteoporotic drugs (alendronate, risedronate, minodronate, ibandronate, and bazedoxifene). Excluding the present fracture that triggered the introduction of teriparatide, 72 patients had a history of previous fractures as follows: the vertebral body in 26 patients; distal radius in 19; femur in 11; proximal tibia in four; ankle joint in three; pelvis, patella, and tibial shaft in two each; and sternum, rib, humerus, ulna, calcaneus, and metatarsus in one each. Three of the 72 patients had a history of two fractures.

The number of male patients were significantly more in the W group than in the ROM group (5 vs. 0, $P = 0.0456$). History of past osteoporosis was significantly higher in the ROM group than in the W group (63% vs. 37.3%, $P = 0.0229$). The BMD of the lumbar spine at the end of one year of treatment was significantly higher in the ROM group than in the W group ($P = 0.0284$). The continuation rate in the ROM group was significantly higher than

Table 4. Univariate analysis of factors affecting discontinuation in patients administered romosozumab and weekly or twice weekly teriparatide.

Variable	OR	95% CI	*P*
Romosozumab			
Age	1.140	0.985-1.320	0.0795
Distance between hospital and home	0.925	0.788-1.086	0.3426
Reason for the start of administration - Fracture	1.188	0.139-10.171	0.8750
Past osteoporosis treatment	0.592	0.119-2.933	0.5207
Past fractures	1.000	0.183-5.461	0.9999
Visiting the hospital for other illnesses	1.420	0.166-12.152	0.7491
25 (OH) D	0.934	0.795-1.096	0.4017
P1NP	1.001	0.978-1.025	0.9107
TRACP-5b	1.002	0.998-1.006	0.3243
BMD of the lumbar spine	1.615	0.017-156.012	0.8373
BMD of the proximal femur	0.059	0.00-1715.39	0.5898
Twice-weekly			
Age	1.002	0.946-1.062	0.9397
Distance between hospital and home	0.965	0.909-1.024	0.2411
Reason for the start of administration - Fracture	1.651	0.651-4.190	0.2909
Past osteoporosis treatment	0.785	0.346-1.778	0.5612
Past fractures	1.329	0.582-3.032	0.4998
Visiting the hospital for other illnesses	0.621	0.263-1.464	0.2761
25 (OH) D	0.981	0.911-1.057	0.6111
P1NP	0.991	0.972-1.009	0.3161
TRACP-5b	1.000	0.998-1.002	0.7548
BMD of the lumbar spine	0.533	0.048-5.873	0.6075
BMD of the proximal femur	1.747	0.018-171.538	0.8115
Weekly			
Age	1.049	0.960-1.145	0.2900
Distance between hospital and home	1.004	0.923-1.093	0.9176
Reason for the start of administration - Fracture	1.389	0.465-4.147	0.5556
Past osteoporosis treatment	0.640	0.201-2.042	0.4511
Past fractures	0.739	0.232-2.358	0.6100
Visiting the hospital for other illnesses	1.134	0.356-3.616	0.8318
25 (OH) D	0.963	0.856-1.083	0.5306
P1NP	1.025	0.981-1.051	0.3908
TRACP-5b	1.001	0.998-1.005	0.4624
BMD of the lumbar spine	0.531	0.010-28.578	0.7557
BMD of the proximal femur	18.361	0.07-5078.12	0.3103

OR, odds ratio; 95% CI, 95% confidence interval; P1NP, intact procollagen 1 N-terminal propeptide; TRACP-5b, tartrate-resistant acid phosphatase 5b; BMD, bone mineral density.

that in the W group ($P = 0.0358$) (Table 1). In the Kaplan-Meier curves comparing the treatment continuation in the ROM group and each teriparatide groups, the ROM group showed a significantly higher continuation rate than the W group ($P = 0.0202$) (Fig. 1).

The rate and reasons for the discontinuation of osteoporosis treatment are shown in Table 3.

Univariate analysis revealed no obvious factors associated with discontinuation in the ROM, TW, and W groups (Table 4). However, univariate analyses of all patients showed that romosozumab administration reduced the risk of discontinuation ($P = 0.0450$) (Table 5).

Discussion

Although it was a short period of one year, our study showed that romosozumab had a very high continuation rate of 88.9%. Additionally, the use of romosozumab reduces the risk of treatment discontinuation. Teriparatide has various dosage forms, such as daily, weekly, and twice-weekly, and the one-year continuation rate has been reported to be 43.1-87% for daily, 23.2-66.7% for weekly, and 47.5-79.5% for twice-weekly administrations (Arden et

Table 5. Univariate analyses of factors affecting discontinuation of all treatments in all patients.

Variables	OR	95% CI	*P*
Age	1.027	0.981-1.076	0.2524
Distance between hospital and home	0.973	0.930-1.019	0.2452
Reason for the start of administration - Fracture	1.629	0.836-3.171	0.1515
Past osteoporosis treatment	0.634	0.346-1.163	0.1410
Past fractures	1.076	0.579-1.996	0.8176
Visiting the hospital for other illnesses	0.801	0.418-1.536	0.5048
25 (OH) D	0.968	0.915-1.025	0.2636
P1NP	0.995	0.983-1.008	0.4605
TRACP-5b	1.001	0.999-1.002	0.2755
BMD of the lumbar spine	0.593	0.089-3.946	0.5886
BMD of the proximal femur	3.292	0.099-109.753	0.5054
Romosozumab	0.414	0.175-0.981	0.0450
Twice-weekly teriparatide	1.165	0.640-2.121	0.6174
Weekly teriparatide	1.694	0.895-3.207	0.1052

OR, odds ratio; 95% CI, 95% confidence interval; P1NP, intact procollagen 1 N-terminal propeptide; TRACP-5b, tartrate-resistant acid phosphatase 5b; BMD, bone mineral density.

al. 2006; Adachi et al. 2007; Ziller et al. 2010; Foster et al. 2011; Kyvernitakis et al. 2014; Rajzbaum et al. 2014; Oishi et al. 2018; Usui et al. 2018; Tsuchie et al. 2020, 2023; Fujita et al. 2022; Mochizuki et al. 2023). Weekly teriparatide tends to have a lower continuation rate than the other two dosage forms (Tsuchie et al. 2023). Regarding romosozumab, while 1.2% of patients discontinued treatment in a randomized controlled trial (Cosman et al. 2016), there is also a report of treatment discontinuation in 22.52% of patients (Tominaga et al. 2021). In our study, the continuation rate of romosozumab was significantly higher than that of weekly teriparatide, even though the continuation rate of weekly teriparatide was 70.2%, which was the highest in previous reports. As the burden of hospital visits is one of the major causes of discontinuation of weekly teriparatide, it is thought that the frequency of hospital visits has a large effect in rural areas, where private cars are the main transportation method for going to the hospital. In contrast, drugs such as romanozumab, which requires monthly hospital visits, and twice-weekly teriparatide, which can be self-injected and taken home, are thought to be suitable for prescriptions in rural areas, as they are not too burdensome. As a future research project, we need to accumulate cases and compare the continuation rates of twice-weekly teriparatide and romosozumab.

In our study, the frequency of side effects leading to discontinuation, which was observed in approximately 14% of all cases with teriparatide, was extremely low at 3.7% of all cases with romosozumab, which greatly influenced the high continuation rate of romosozumab. In the past reports, the incidence of all adverse events in weekly preparations was approximately 90%, and adverse events made it difficult to continue weekly teriparatide in 9.8-19.3% (Nakamura et al. 2012; Sugimoto et al. 2019). Conversely, the incidence of all adverse events was 16.6% for romosozumab, indicating that the frequency of side effects with romosozumab tends to be very low (Cosman et al. 2016). Although it is difficult to receive two injections at an outpatient clinic, it should be easy to continue in rural areas, as it requires only monthly visits and there are few side effects.

Older age is a risk factor for failure to continue treatment (Fahrleitner-Pammer et al. 2017; Oishi et al. 2018; Tsuchie et al. 2020, 2023). Previous studies conducted at the same hospital also reported that old age is a risk factor for discontinuing treatment (Tsuchie et al. 2020, 2023). However, in the present study, which included patients from the same hospital, this was not considered a risk factor. Our previous study on patients using teriparatide included those hospitalized with fractures with a mean age of 78.0-79.5 years (Tsuchie et al. 2020, 2023). However, in this study, the participants were limited to outpatients, and the average age was 76.7 years, which is slightly younger than that reported in previous studies. It is easy to imagine that the older the patient, the less frequently they visit the hospital, and this difference may have influenced the present results.

In our study, compared with weekly teriparatide, romosozumab increased the BMD in the lumbar spine within one year of administration. Although romosozumab increases BMD after one year (Cosman et al. 2016; Saag et al. 2017; Tominaga et al. 2021), it is necessary to consider the influence of the drug used before the start of romosozumab. It has been reported that romosozumab shows the highest increase in BMD among patients with untreated osteoporosis, followed by those using teriparatide (Ebina et al. 2020). Patients in our study frequently received teriparatide before starting romosozumab, and more than two-thirds of all patients were either untreated or on teriparatide. In contrast, many patients in the teriparatide group received

bone resorption inhibitors for osteoporosis treatment. This may have further strengthened the differences in the effects of increasing BMD. Teriparatide has been proven effective against severe osteoporosis. In addition, since teriparatide is a drug that often shows effectiveness after use for more than one year, it is almost meaningless to compare the effects of increasing bone density at one year. Romosozumab and teriparatide are completely different drugs and it is not true that only one drug can be used. The choice of drug use should consider various patient situations and the combination of each drug during the course of osteoporosis treatment.

To the best of our knowledge, this is the first study to perform a detailed analysis of the continuation rate of romosozumab and the factors that affect it. However, this study has several limitations. The treatment periods determined from the beginning were different: one year for romosozumab and two years for teriparatide, which may psychologically affect the continuation of drug administration. If it is one year, it is easier to tolerate some side effects and continue the treatment. However, if it is two years, the patients may feel like it is too long to continue, and there is a high risk of wanting to discontinue the treatment. Another limitation is that the osteoporosis treatment status before starting each drug was not unified. Patients who have continued treatment requiring frequent hospital visits, or who have been able to continue taking drugs that carry the risk of side effects, may have a higher rate of continuation of subsequent treatments. For an accurate evaluation, it is necessary to conduct studies targeting only untreated patients, and further studies with a larger number of cases are necessary. Another limitation to consider is the differences in treating doctors. It is easy to imagine that continuation rates will be higher if the doctor is enthusiastic. This study was conducted over a long period (more than 11 years). This study facility has three full-time orthopedic surgeons on duty, but the full-time doctors are rotated.

Consequently, patient may not be seen by the same doctor throughout the study period. Therefore, it is difficult to assess the differences between the doctors who examine patients. Additionally, the decision on which medication to use in this study was made primarily at the doctor's discretion. There were multiple doctors who initiated the prescription, which may have resulted in bias. Thus, a prospective randomized study may be necessary to conduct a more accurate evaluation.

In conclusion, romosozumab has a considerably higher continuation rate than weekly teriparatide. Using romosozumab as a starting drug for osteoporosis treatment, which is easy to continue and shows effects in a short period, may be easier to increase patients' motivation for osteoporosis treatment. The possibility of improving the continuation rate of osteoporosis treatments such as teriparatide administration after romosozumab should also be investigated in the future.

Author Contributions

Tsuchie, H., Abe, H., Masutani, N., and Miyakoshi, N. were involved in the planning and revision of this research. Tsuchie, H., Abe, H., and Masutani, N. collected the clinical data. Tsuchie, H. analyzed the raw data. Tsuchie, H. wrote this manuscript. Miyakoshi, N. reviewed this manuscript.

Conflict of Interest

The authors declare no conflict of interest.

References

Adachi, J.D., Hanley, D.A., Lorraine, J.K. & Yu, M. (2007) Assessing compliance, acceptance, and tolerability of teriparatide in patients with osteoporosis who fractured while on antiresorptive treatment or were intolerant to previous antiresorptive treatment: an 18-month, multicenter, open-label, prospective study. *Clin. Ther.*, **29**, 2055-2067.

Arden, N.K., Earl, S., Fisher, D.J., Cooper, C., Carruthers, S. & Goater, M. (2006) Persistence with teriparatide in patients with osteoporosis: the UK experience. *Osteoporos. Int.*, **17**, 1626-1629.

Japan Osteoporosis Society, The Japanese Society for Bone and Mineral Research, Japan Osteoporosis Foundation (2015) Japanese 2015 guideline for prevention and treatment of osteoporosis. http://www.josteo.com/data/publications/guideline/2015_01.pdf [*Accessed*: August 17, 2024].

Cosman, F., Crittenden, D.B., Adachi, J.D., Binkley, N., Czerwinski, E., Ferrari, S., Hofbauer, L.C., Lau, E., Lewiecki, E.M., Miyauchi, A., Zerbini, C.A., Milmont, C.E., Chen, L., Maddox, J., Meisner, P.D., et al. (2016) Romosozumab Treatment in Postmenopausal Women with Osteoporosis. *N. Engl. J. Med.*, **375**, 1532-1543.

Ebina, K., Hirao, M., Tsuboi, H., Nagayama, Y., Kashii, M., Kaneshiro, S., Miyama, A., Nakaya, H., Kunugiza, Y., Okamura, G., Etani, Y., Takami, K., Goshima, A. & Nakata, K. (2020) Effects of prior osteoporosis treatment on early treatment response of romosozumab in patients with postmenopausal osteoporosis. *Bone*, **140**, 115574.

Fahrleitner-Pammer, A., Papaioannou, N., Gielen, E., Feudjo Tepie, M., Toffis, C., Frieling, I., Geusens, P., Makras, P., Boschitsch, E., Callens, J., Anastasilakis, A.D., Niedhart, C., Resch, H., Kalouche-Khalil, L. & Hadji, P. (2017) Factors associated with high 24-month persistence with denosumab: results of a real-world, non-interventional study of women with postmenopausal osteoporosis in Germany, Austria, Greece, and Belgium. *Arch. Osteoporos.*, **12**, 58.

Foster, S.A., Foley, K.A., Meadows, E.S., Johnston, J.A., Wang, S.S., Pohl, G.M. & Long, S.R. (2011) Adherence and persistence with teriparatide among patients with commercial, Medicare, and Medicaid insurance. *Osteoporos. Int.*, **22**, 551-557.

Fujita, R., Endo, T., Takahata, M., Haraya, K., Suzuki, H., Oda, I., Kanayama, M., Asano, T., Shigenobu, K., Iwata, A., Yamada, K., Takeuchi, H., Ohura, H., Yoneoka, D. & Iwasaki, N. (2022) Real-world persistence of twice-weekly teriparatide and factors associated with the discontinuation in patients with osteoporosis. *J. Bone Miner. Metab.*, **40**, 782-789.

Kyvernitakis, I., Kostev, K., Kurth, A., Albert, U.S. & Hadji, P. (2014) Differences in persistency with teriparatide in patients with osteoporosis according to gender and health care provider. *Osteoporos. Int.*, **25**, 2721-2728.

Melton, L.J. 3rd, Chrischilles, E.A., Cooper, C., Lane, A.W. & Riggs, B.L. (1992) Perspective. How many women have osteoporosis? *J. Bone Miner. Res.*, **7**, 1005-1010.

Mochizuki, T., Yano, K., Ikari, K. & Okazaki, K. (2023) Comparison of different parameters between daily and twice-weekly teriparatide in postmenopausal women with severe osteoporosis. *J. Bone Miner. Metab.*, **41**, 220-226.

Nakamura, T., Sugimoto, T., Nakano, T., Kishimoto, H., Ito, M., Fukunaga, M., Hagino, H., Sone, T., Yoshikawa, H., Nishizawa, Y., Fujita, T. & Shiraki, M. (2012) Randomized Teriparatide [human parathyroid hormone (PTH) 1-34] Once-Weekly Efficacy Research (TOWER) trial for examining the reduction in new vertebral fractures in subjects with primary osteoporosis and high fracture risk. *J. Clin. Endocrinol. Metab.*, **97**, 3097-3106.

Oishi, T., Fujita, T., Nishida, T., Hagiwara, K., Kurokawa, K., Yamamoto, M., Suzuki, D. & Sugiura, K. (2018) Comparison of continuation rates of osteoporosis treatment injection preparations and examination on factors involved in dropout. *Annual of Enshu Hospital*, **24**, 27-32 (in Japanese).

Rajzbaum, G., Grados, F., Evans, D., Liu-Leage, S., Petto, H. & Augendre-Ferrante, B. (2014) Treatment persistence and changes in fracture risk, back pain, and quality of life amongst patients treated with teriparatide in routine clinical care in France: results from the European Forsteo Observational Study. *Joint Bone Spine*, **81**, 69-75.

Saag, K.G., Petersen, J., Brandi, M.L., Karaplis, A.C., Lorentzon, M., Thomas, T., Maddox, J., Fan, M., Meisner, P.D. & Grauer, A. (2017) Romosozumab or Alendronate for Fracture Prevention in Women with Osteoporosis. *N. Engl. J. Med.*, **377**, 1417-1427.

Sugimoto, T., Shiraki, M., Fukunaga, M., Kishimoto, H., Hagino, H., Sone, T., Nakano, T., Ito, M., Yoshikawa, H., Minamida, T., Tsuruya, Y. & Nakamura, T. (2019) Study of twice-weekly injections of Teriparatide by comparing efficacy with once-weekly injections in osteoporosis patients: the TWICE study. *Osteoporos. Int.*, **30**, 2321-2331.

Tominaga, A., Wada, K., Okazaki, K., Nishi, H., Terayama, Y. & Kato, Y. (2021) Early clinical effects, safety, and predictors of the effects of romosozumab treatment in osteoporosis patients: one-year study. *Osteoporos. Int.*, **32**, 1999-2009.

Tsuchie, H., Abe, H., Masutani, N. & Miyakoshi, N. (2023) Comparison of the Continuation Rate of Twice-Weekly and Weekly Teriparatide Administration in a Rural Area. *Tohoku J. Exp. Med.*, **260**, 119-126.

Tsuchie, H., Miyakoshi, N., Kasukawa, Y., Abe, H., Masutani, N. & Shimada, Y. (2020) Factors affecting continuation of weekly teriparatide administration in rural areas. *J. Bone Miner. Metab.*, **38**, 248-253.

Usui, T., Funagoshi, M., Seto, K., Ide, K., Tanaka, S. & Kawakami, K. (2018) Persistence of and switches from teriparatide treatment among women and men with osteoporosis in the real world: a claims database analysis. *Arch. Osteoporos.*, **13**, 54.

Ziller, V., Zimmermann, S.P., Kalder, M., Ziller, M., Seker-Pektas, B., Hellmeyer, L. & Hadji, P. (2010) Adherence and persistence in patients with severe osteoporosis treated with teriparatide. *Curr. Med. Res. Opin.*, **26**, 675-681.