META-ANALYSIS

Evaluating the Clinical Efficacy of Teriparatide and Denosumab Combination Therapy in Postmenopausal Osteoporosis: A Systematic Review and Meta-Analysis

Yanqun Liu, MD; Yajun Xu, MM; Xiaopeng Zhang, MM; Jiadan Li, MM; YuanSheng Xia, MD; Haikun Chu, MM

ABSTRACT

Objective • This meta-analysis aims to assess the clinical effectiveness of the combination therapy involving Teriparatide (TPTD) and Denosumab (DEN) in managing postmenopausal osteoporosis (PMO). The findings provide valuable insights into clinical treatment decisions.

Methods • We conducted a comprehensive search of PubMed, the Cochrane Library, Embase, and other relevant databases to gather literature concerning the treatment of PMO with TPTD and DEN. After a thorough screening, we selected and analyzed the final literature set. Information relevant to the study was extracted, and a quality assessment was carried out. The meta-analysis utilized RevMan 5.3 software to evaluate the impact of DEN combined with TPTD on parameters such as bone mineral density (BMD), tartrate-resistant acid phosphatase-5b (TRACP-5b), fracture incidence, and adverse reactions in PMO patients.

Results • After the screening process, a total of 513 patients were studied across 8 studies. Among these, 259 patients received treatment involving DEN combined with TPTD (the research group), while 254 patients were subjected to different treatment regimens (the control group). As per the Cochrane Handbook's quality assessment, all included literature exhibited high overall quality. The meta-analysis demonstrated that the research group exhibited significantly higher BMD than the control group, lower TRACP-5b levels and fracture incidence ($P < .05$). However, the two groups had no evident difference in adverse reaction incidence ($P > .05$).

Conclusions • The combined treatment of DEN and TPTD exhibits notable efficacy in managing PMO, warranting its promotion and use in clinical practice. (*Altern Ther Health Med.* 2024;30(6):270-275).

Yanqun Liu, MD, Department of Orthopedics, Yanbian University Hospital, Yanji City, Jilin Province, China. **YaJun Xu,** MM, Department of Pharmacy, Daqing Oilfield General Hospital, Daqing, China. **Xiaopeng Zhang,** MM, Department of Oral and Maxillofacial Surgery, Daqing Oilfield General Hospital, Daqing, China. **Jiadan Li,** MM, Department of Laboratory Medicine, Daqing Oilfield General Hospital, Daqing, China. **YuanSheng Xia,** MD; **Haikun Chu,** MM; Department of Orthopedics, Daqing Oilfield General Hospital, Daqing, China.

Corresponding author: Yanqun Liu, MD
E-mail: 13844312816@163.com

INTRODUCTION

Postmenopausal osteoporosis (PMO) is a prevalent age-related condition primarily affecting women after menopause.[1] The deficiency of estrogen reduces bone mass and alters bone tissue structure, rendering bones more susceptible to fragility and fractures.[2] Consequently, PMO can result in pain, bone deformities, complications, and potentially reduced lifespan, significantly impacting the physical well-being and quality of life among elderly individuals.[1-2]

It is estimated that there are currently approximately 200 million PMO patients worldwide, and 30-40% of newly added fracture patients each year are attributed to PMO.[3] Projections suggest that by 2050, the number of fractures associated with PMO will surpass 6 million, with corresponding medical expenses reaching 160 billion yuan.[4] Therefore, the management strategy for PMO warrants significant attention due to its potential health risks and burden on patients and clinical practice.

Denosumab (DEN) is a common treatment choice for PMO, designed to selectively target the receptor activator of NF-kB ligand (RANKL). This action inhibits the activation and maturation of osteoclasts, thereby reducing bone resorption and enhancing bone density.[5] Due to its cost-effectiveness, substantial efficacy, and robust safety profile, Denosumab is extensively used in clinical practice.[6-7]

Teriparatide (TPTD), also referred to as recombinant human parathyroid hormone, is an analogue of the first 34 amino acids at the N-terminus of human parathyroid hormone. Its primary function involves stimulating osteoblast activity, fostering bone formation, enhancing bone density, and decreasing the risk of vertebral fractures.[8] Despite its

distinct mechanism of action from DEN, both TPTD and DEN share similar indications and have demonstrated beneficial effects in the treatment of PMO.

Past studies have demonstrated the effectiveness and safety of DEN and TPTD in managing PMO. However, there exists a lack of comprehensive summaries relating to these research findings. Therefore, this study conducted a meta-analysis on the application of DEN and TPTD to support the value of their combined administration in the context of PMO. This analysis aims to serve as a theoretical reference for future clinical medical decisions.

METHODS

Literature Search Strategy

A computerized search was conducted across multiple English-language literature databases, including PubMed, the Cochrane Library, and Embase, utilizing the following search terms: "osteoporosis," "postmenopausal," "teriparatide," and "denosumab." The literature search was confined to studies published from the inception of the databases till 2023.

Inclusion and Exclusion Criteria

Inclusion criteria were as follows: (1) studies involving PMO patients; (2) randomized controlled trials or cohort studies examining the combination of DEN and TPTD for PMO treatment; (3) studies comparing the efficacy of DEN and TPTD combination therapy with alternative treatment strategies. Exclusion criteria were as follows: (1) studies with fewer than 20 cases; (2) studies involving patients with different types of osteoporosis; (3) literature lacking complete original data; (4) duplicate publications; (5) literature with treatment duration of less than 2 months.

Data Extraction

Literature management was conducted using EndNote X9 software. Initially, two researchers independently reviewed the titles and abstracts of the retrieved literature with the aim of eliminating duplicates. Subsequently, following full-text examination, the literature underwent a secondary review in alignment with the inclusion and exclusion criteria. Studies meeting this thorough process were included in this meta-analysis.

The two researchers performed quality assessment and data extraction, and the gathered data were subsequently collated and verified. In cases where discrepancies arose in the data extraction results between the two researchers, a third independent researcher was engaged for review and discussion. The results were established through consensus. If required, we reached out to the corresponding author to secure complete original data, and subsequently, all gathered information was translated into English for further analysis.

Literature Quality Assessment

The quality assessment of the final selected literature was conducted independently, following the guidelines outlined in the Cochrane Handbook. This assessment encompassed various aspects, including (1) random allocation sequence generation; (2) allocation scheme concealment; (3) use of blinding for investigators and subjects; (4) blinded evaluation of study endpoints; (5) completeness of outcome data; (6) selective reporting of study results; and (7) evaluation of other potential sources of bias.

A quality assessment diagram was created to represent the outcomes visually. The criteria for rating literature quality were as follows: 5 points or above (indicating a low risk of bias), 3-4 points (reflecting a moderate risk of bias), and 1-2 points (indicating a high risk of bias). In case of conflicting opinions, a third researcher was consulted to facilitate discussion and arrive at a consensus judgment.

Outcome Measures

The study considered the following outcome measures: (1) Bone mineral density (BMD); (2) Tartrate-resistant acid phosphatase-5b (TRACP-5b); (3) Incidence of fractures; (4) Adverse reactions, including symptoms such as nausea, vomiting, and dizziness.

Statistical Analysis

We conducted the meta-analysis using RevMan 5.3 software from the Cochrane Collaboration, United Kingdom. Count data were expressed as risk ratios (RR), and all selected study parameters were continuous data. The effect size was calculated using the mean difference (MD) under the condition of consistent measurement methods and tools. Confidence intervals (95% CI) were provided for all effect indicators. Heterogeneity was assessed using I^2: $I^2 < 50\%$ employed the fixed-effect model, while $I^2 \geq 50\%$ imposed the use of the random-effect model for analysis. To examine publication bias, we employed funnel plots. The statistical significance level for all analyses was set at $P < .05$.

RESULTS

Literature Screening Results

Initially, a total of 229 articles were identified during the preliminary screening. After a thorough screening process, eight reference articles[9-16] were finally included for analysis. The literature screening process is illustrated in Figure 1.

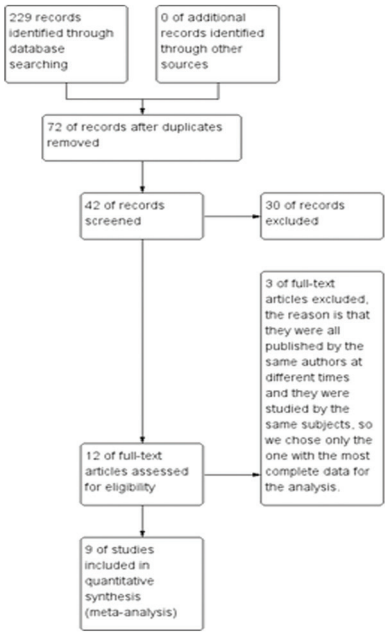
Basic Patient Characteristics

The study included eight studies comprising a total of 513 patients. Among these, 259 patients received DEN combined with TPTD treatment, forming the research group. The remaining 254 patients were under alternative treatment regimens and constituted the control group. Complete patient characteristics and outcome measures are presented in Table 1.

Results of Literature Quality Evaluation

We employed RevMan 5.3 software to assess the quality of the selected literature. As illustrated in Figure 2, all included articles achieved scores of 5 or higher. Figure 3 displays that the percentage of items related to selective reporting of study results was 100%, while the percentages of

Figure 1. Flow Chart of Literature Screening



Note: This flow chart visually illustrates the screening process employed to select relevant literature for the meta-analysis. It outlines the steps involved in identifying and filtering research articles, ultimately leading to the inclusion of pertinent studies in the analysis.

items pertaining to random sequence generation, completeness of outcome data, and other potential sources of bias all exceeded 75%. These findings indicate that the overall quality of the literature was notably high.

Comparison of Bone Mineral Density (BMD)

Among the included eight studies, changes in patients' BMD were reported, as illustrated in Figure 4. The variations among these studies exhibited heterogeneity and were therefore analyzed utilizing a random-effects model. The outcomes indicated that post-treatment, BMD in the research group exceeded that in the control group, with statistical significance ($P < .05$). This finding suggests that patients with PMO can expect an increase of approximately 0.11 in BMD after treatment with DEN combined with TPTD.

Comparison of Tartrate Resistant Acid Phosphatase-5b (TRACP-5b)

Among the included studies, six discussed the changes in TRACP-5b levels, as illustrated in Figure 5. Analysis using a random-effects model revealed that TRACP-5b levels were lower in the research group after treatment compared to the control group, with statistical significance ($P < .05$). This finding suggests that PMO patients could anticipate a reduction of approximately 7.14 in TRACP-5b levels after treatment with DEN combined with TPTD.

Comparison of Adverse Effects

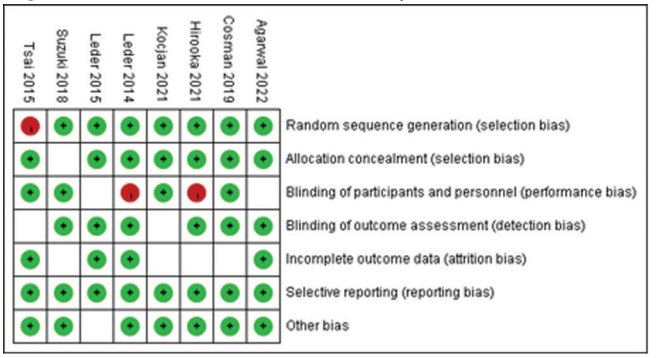
Eight studies reported adverse reactions observed during patient treatment, as illustrated in Figure 6. The results of the analysis, conducted using a fixed-effect model, indicated no

Table 1. Basic Characteristics of Patients

Author/Years of Research	Group		Regimen Of Control Treatment	Outcome Measures
	Research Group	Control Group		
Agarwal et al. (2022)[9]	28	28	Placebo-Controlled Study	①③④
Cosman et al. (2019)[10]	35	35	DEN	①②③④
Hirooka et al. (2021)[11]	18	6	DEN	①②③④
Kocjan et al. (2021)[12]	70	70	TPTD+BPs	①②③④
Leder et al. (2014)[13]	30	33	DEN	①②③
Leder et al. (2015)[14]	23	27	DEN	①②③
Suzuki et al. (2018)[15]	25	22	DEN	①②③④
Tsai et al. (2015)[16]	30	33	DEN	①③④

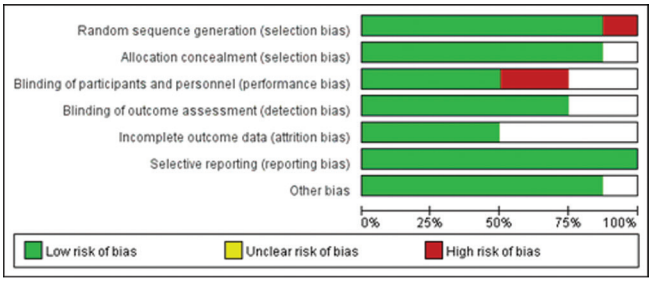
Note: BPs refer to Bisphosphonates. Outcome measures include: ① BMD (Bone Mineral Density), ② TRACP-5b (Tartrate Resistant Acid Phosphatase-5b), ③ Fracture Incidence, and ④ Adverse Reactions.

Figure 2. Results of Literature Quality Evaluation



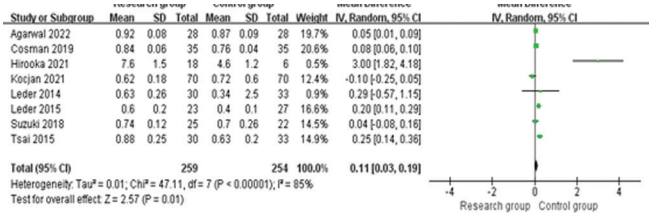
Note: This figure presents the outcomes of the quality assessment of the selected literature. It summarizes the evaluation of various criteria, such as random allocation, blinding, completeness of outcome data, and other potential sources of bias. The results affirm the overall quality of the included literature for the meta-analysis.

Figure 3. Percentage of Quality Evaluation Results in the Literature



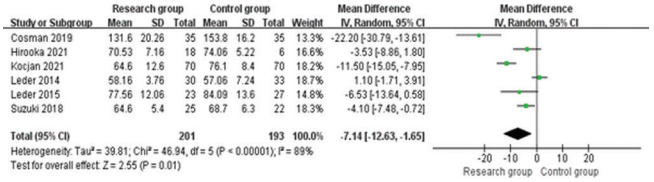
Note: This figure displays the distribution of quality assessment results for the included literature as percentages. This figure employs a color-coded scheme to represent the outcomes of the literature quality assessment. Green signifies a low risk of bias, yellow indicates unclear risk, and red designates a high risk of bias.

Figure 4. Comparison of BMD



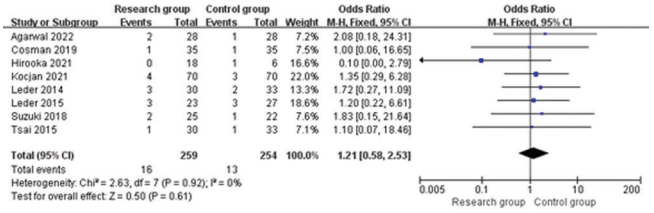
Note: This forest plot illustrates the comparison of Bone Mineral Density (BMD) between the research group and the control group. The results of the analysis demonstrate a higher BMD in the research group compared to the control group. This plot provides a graphical representation of the effect size and confidence intervals, enhancing the understanding of the BMD outcomes.

Figure 5. Comparison of TRACP-5b



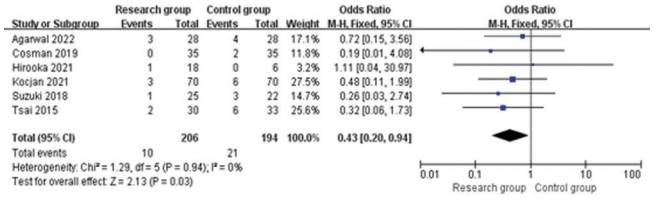
Note: This forest plot presents the comparison of Tartrate Resistant Acid Phosphatase-5b (TRACP-5b) levels between the research group and the control group. The analysis reveals that TRACP-5b levels were lower in the research group compared to the control group. Squares represent the effect size (e.g., mean difference or risk ratio); Horizontal lines extending from the squares represent the confidence intervals; The diamond at the bottom represents the overall effect size, incorporating all individual study results.

Figure 6. Comparison of Adverse Effects



Note: This is a forest plot representing the comparison of adverse effects between the research group and the control group. Squares represent the effect size (e.g., risk ratio); Horizontal lines extending from the squares represent the confidence intervals for each study; The diamond at the bottom signifies the overall effect size, which combines the results of all individual studies. The position of this diamond and its width demonstrate the collective impact of adverse effects on the research and control groups.

Figure 7. Comparison of Fracture Incidence



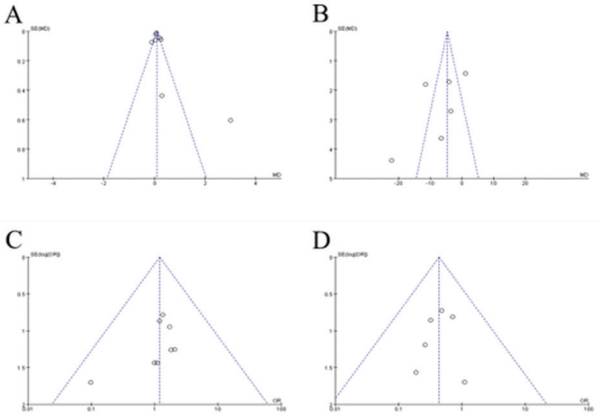
Note: This forest plot presents the comparison of fracture incidence between the research group and the control group. Squares represent the effect size (e.g., risk ratio); Horizontal lines extending from the squares represent the confidence intervals for each study; The diamond at the bottom represents the overall effect size, combining the results of all individual studies. The position of this diamond and its width indicate the collective impact of fracture incidence in the research and control groups.

significant difference in the incidence of adverse reactions between the research group and the control group ($P > .05$). This finding confirms the high safety profile of DEN combined with TPTD.

Comparison of Fracture Incidence

Six studies reported the incidence of fractures in the patient. As illustrated in Figure 7, there was no heterogeneity observed among the articles, allowing for the use of a fixed-effects model for analysis. The results indicated that the research group had a lower incidence of fractures compared to the control group ($P < .05$), with the difference being statistically significant.

Figure 8. Publication Bias Analysis



Note: This figure comprises four funnel plots labeled as (A) BMD, (B) TRACP-5b, (C) adverse effects, and (D) fracture incidence. Funnel plots are used to assess publication bias. Each point represents an individual study or data point. The vertical axis represents the precision or sample size of each study. The horizontal axis represents the effect size or outcome measure. The funnel shape of the plot helps visualize potential publication bias. Asymmetry in the plot indicates bias, while a symmetrical distribution suggests lower bias.

Publication Bias Analysis

A funnel plot was generated for the previously analyzed outcome measures, illustrated in Figure 8. The funnel plots for BMD, TRACP-5b, adverse effects, and fracture incidence exhibited a symmetrical distribution, indicating the absence of significant publication bias.

DISCUSSION

It is estimated that approximately 15% of postmenopausal women aged over 50 worldwide are affected by PMO.[17] Presently, basic supplements such as calcium and vitamin D, along with anti-resorptive drugs and drugs that promote bone synthesis metabolism, have been demonstrated to effectively enhance bone density and decrease the risk of vertebral fractures in patients.[18-19]

There are several studies focusing on the treatment of PMO in clinical practice. However, the findings across these studies lack uniformity, and there is a scarcity of comprehensive summaries. Therefore, the meta-analysis examined the impact of DEN combined with TPTD in PMO treatment, serving as a dependable reference and providing valuable guidance for the future clinical management of PMO.

At present, TPTD is the only medication capable of stimulating bone formation metabolism by inhibiting osteoblast apoptosis, activating osteoblasts, and promoting osteoblast differentiation. It diverges from bisphosphonates, which primarily function to inhibit bone resorption.[20-21] In our analysis, we observed a more substantial enhancement in BMD and a notable reduction in fracture incidence among patients treated with the combination of DEN and TPTD.

Our findings affirm that prolonged treatment with TPTD not only contributes to elevating bone density in the lumbar spine and hip joint but also plays a vital role in mitigating the risk of both vertebral and non-vertebral fractures. A multicenter clinical study by Miyauchi et al.[22]

assessed the safety and efficacy of TPTD in osteoporotic patients at elevated risk of fractures. Their study revealed that TPTD led to a notable increase in lumbar spine BMD, with a 10.04% increment observed after 12 months of treatment.

Additionally, Cohen et al.[23] documented an 8.1% increase in lumbar spine BMD after 12 months of TPTD treatment for osteoporotic patients. Furthermore, Hassan et al.[24] reported that in patients treated with TPTD and zoledronic acid over 24 months, there was a substantial reduction in the incidence of non-vertebral fractures by 34% and clinical fractures by 52% within the TPTD group. These studies provide additional evidence supporting our findings and confirming the excellent outcomes achieved with DEN and TPTD. We believe that advocating for the combined use of DEN and TPTD in clinical practice can provide more reliable and secure support for the rehabilitation of PMO patients, ultimately reducing the global burden of PMO.

Concerning adverse reactions, numerous studies have documented that TPTD can result in adverse events like hyperuricemia, back pain, and joint pain.[25-26] However, during this meta-analysis, we observed no substantial difference in the incidence of adverse reactions between the two groups. This observation suggests that the utilization of DEN in combination with TPTD does not lead to an increased occurrence of adverse events. Further, it highlights the significant clinical value of this treatment regimen.

However, it is important to note that DEN and TPTD are contraindicated for patients with compromised immune function, renal insufficiency, and certain other conditions, potentially due to their metabolic pathways. Furthermore, when employing DEN in combination with TPTD, it is imperative to strictly avoid medications such as prazosin and linagliptin to prevent the occurrence of additional adverse reactions in patients.[20-26] However, to gain a comprehensive understanding of the safety profile of these two drugs, further research and a detailed categorization analysis of various adverse events are warranted.

Lastly, the findings of the funnel plot revealed that the publication bias for the outcome indicators in both study groups in this analysis was generally low. The symmetrical distribution observed in the funnel plot adds confidence to the study's conclusions, indicating a low level of publication bias. This reaffirms the credibility of the results derived from this analysis.

Study Limitations

It is important to acknowledge a few limitations in this study. Firstly, the available references for DEN combined with TPTD were relatively scarce. Therefore, only eight studies were included. This limited reference pool may impact the generalizability of the results. Additionally, some included literature presented data in graphical form, necessitating manual extraction of mean and standard deviation values, potentially introducing errors.

Moreover, the sample sizes in some cases were relatively small, and the follow-up durations in certain literature were relatively short. This limitation might have resulted in the omission of some fractures and complications, potentially reducing the study's statistical power. To address these limitations, we plan to conduct supplementary analyses and encourage further research to expand the reference base for future investigations of DEN combined with TPTD. Future studies should conduct additional clinical trials to confirm and expand upon the findings.

CONCLUSION

In conclusion, the combined use of DEN and TPTD emerges as a highly effective approach for enhancing bone density and mitigating the incidence of fractures in individuals suffering from PMO. This therapeutic combination demonstrates a remarkable safety profile. Therefore, advocating for its incorporation into clinical practice holds great promise, offering a robust support system for the recovery and long-term prognosis of PMO patients. The results from this study underscore the substantial clinical value of this treatment regimen, providing a solid foundation for further research and implementation in the management of PMO.

CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be interpreted as a potential conflict of interest.

AVAILABILITY OF DATA AND MATERIALS

The data supporting the findings of this study are available from the corresponding author upon request, subject to reasonable conditions.

ACKNOWLEDGEMENT

None

FUNDING

No funding was received.

REFERENCES

1. Arceo-Mendoza RM, Camacho PM. Postmenopausal Osteoporosis: latest Guidelines. *Endocrinol Metab Clin North Am*. 2021;50(2):167-178. doi:10.1016/j.ecl.2021.03.009
2. Wu D, Cline-Smith A, Shashkova E, Perla A, Katyal A, Aurora R. T-Cell Mediated Inflammation in Postmenopausal Osteoporosis. *Front Immunol*. 2021;12:687551. doi:10.3389/fimmu.2021.687551
3. Brown JP. Long-Term Treatment of Postmenopausal Osteoporosis. *Endocrinol Metab (Seoul)*. 2021;36(3):544-552. doi:10.3803/EnM.2021.301
4. Kanis JA, Cooper C, Rizzoli R, Reginster JY; Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis (ESCEO) and the Committees of Scientific Advisors and National Societies of the International Osteoporosis Foundation (IOF). European guidance for the diagnosis and management of osteoporosis in postmenopausal women. *Osteoporos Int*. 2019;30(1):3-44. doi:10.1007/s00198-018-4704-5
5. Kobayakawa T, Miyazaki A, Saito M, Suzuki T, Takahashi J, Nakamura Y. Denosumab versus romosozumab for postmenopausal osteoporosis treatment. *Sci Rep*. 2021;11(1):11801. doi:10.1038/s41598-021-91248-6
6. Wu J, Zhang Q, Yan G, Jin X. Denosumab compared to bisphosphonates to treat postmenopausal osteoporosis: a meta-analysis. *J Orthop Surg Res*. 2018;13(1):194. doi:10.1186/s13018-018-0865-3
7. Miller PD, Pannacciulli N, Brown JP, et al. Denosumab or Zoledronic Acid in Postmenopausal Women With Osteoporosis Previously Treated With Oral Bisphosphonates. *J Clin Endocrinol Metab*. 2016;101(8):3163-3170. doi:10.1210/jc.2016-1801
8. Yuan F, Peng W, Yang C, Zheng J. Teriparatide versus bisphosphonates for treatment of postmenopausal osteoporosis: A meta-analysis. *Int J Surg*. 2019;66:1-11. doi:10.1016/j.ijsu.2019.03.004
9. Agarwal S, Shane E, Lang T, et al. Spine Volumetric BMD and Strength in Premenopausal Idiopathic Osteoporosis: Effect of Teriparatide Followed by Denosumab. *J Clin Endocrinol Metab*. 2022;107(7):e2690-e2701. doi:10.1210/clinem/dgac232
10. Cosman F, McMahon D, Dempster D, Nieves JW. Standard Versus Cyclic Teriparatide and Denosumab Treatment for Osteoporosis: A Randomized Trial. *J Bone Miner Res*. 2020;35(2):219-225. doi:10.1002/jbmr.3850
11. Hirooka Y, Nozaki Y, Okuda S, et al. Four-Year Teriparatide Followed by Denosumab *vs*. Continuous Denosumab in Glucocorticoid-Induced Osteoporosis Patients With Prior Bisphosphonate Treatment. *Front Endocrinol (Lausanne)*. 2021;12:753185. doi:10.3389/fendo.2021.753185
12. Kocjan T, Rajic AS, Janez A, et al. Switching to Denosumab or Bisphosphonates After Completion of Teriparatide Treatment in Women With Severe Postmenopausal Osteoporosis. *Endocr Pract*. 2021;27(9):941-947. doi:10.1016/j.eprac.2021.05.012
13. Leder BZ, Tsai JN, Uihlein AV, et al. Two years of Denosumab and teriparatide administration in postmenopausal women with osteoporosis (The DATA Extension Study): a randomized controlled trial. *J Clin Endocrinol Metab*. 2014;99(5):1694-1700. doi:10.1210/jc.2013-4440

14. Leder BZ, Tsai JN, Uihlein AV, et al. Denosumab and teriparatide transitions in postmenopausal osteoporosis (the DATA-Switch study): extension of a randomised controlled trial. *Lancet*. 2015;386(9999):1147-1155. doi:10.1016/S0140-6736(15)61120-5
15. Suzuki T, Nakamura Y, Kato H. Efficacy of 4-year denosumab treatment alone or in combination with teriparatide in Japanese postmenopausal osteoporotic women. *Mod Rheumatol*. 2019;29(4):676-681. doi:10.1080/14397595.2018.1524997
16. Tsai JN, Uihlein AV, Burnett-Bowie SA, et al. Comparative effects of teriparatide, denosumab, and combination therapy on peripheral compartmental bone density, microarchitecture, and estimated strength: the DATA-HRpQCT Study. *J Bone Miner Res*. 2015;30(1):39-45. doi:10.1002/jbmr.2315
17. Management of osteoporosis in postmenopausal women: the 2021 position statement of The North American Menopause Society. *Menopause*. 2021;28(9):973-997. doi:10.1097/GME.0000000000001831
18. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis-2020 Update. *Endocr Pract*. 2020;26(suppl 1):1-46. doi:10.4158/GL-2020-0524SUPPL
19. Fischer V, Haffner-Luntzer M. Interaction between bone and immune cells: implications for postmenopausal osteoporosis. *Semin Cell Dev Biol*. 2022;123:14-21. doi:10.1016/j.semcdb.2021.05.014
20. Tian A, Jia H, Zhu S, et al. Romosozumab versus Teriparatide for the Treatment of Postmenopausal Osteoporosis: A Systematic Review and Meta-analysis through a Grade Analysis of Evidence. *Orthop Surg*. 2021;13(7):1941-1950. doi:10.1111/os.13136
21. Chiba K, Okazaki N, Kurogi A, et al. Randomized controlled trial of daily teriparatide, weekly high-dose teriparatide, or bisphosphonate in patients with postmenopausal osteoporosis: the TERABIT study. *Bone*. 2022;160:116416. doi:10.1016/j.bone.2022.116416
22. Miyauchi A, Matsumoto T, Sugimoto T, Tsujimoto M, Warner MR, Nakamura T. Effects of teriparatide on bone mineral density and bone turnover markers in Japanese subjects with osteoporosis at high risk of fracture in a 24-month clinical study: 12-month, randomized, placebo-controlled, double-blind and 12-month open-label phases. *Bone*. 2010;47(3):493-502. doi:10.1016/j.bone.2010.05.022
23. Cohen A, Shiau S, Nair N, et al. Effect of Teriparatide on Bone Remodeling and Density in Premenopausal Idiopathic Osteoporosis: A Phase II Trial. *J Clin Endocrinol Metab*. 2020;105(10):e3540-e3556. doi:10.1210/clinem/dgaa489
24. Hassan N, Gregson CL, Tobias JH. Anabolic treatments for osteoporosis in postmenopausal women. *Fac Rev*. 2021;10:44. doi:10.12703/r/10-44
25. Kendler DL, Marin F, Zerbini CAF, et al. Effects of teriparatide and risedronate on new fractures in post-menopausal women with severe osteoporosis (VERO): a multicentre, double-blind, double-dummy, randomised controlled trial. *Lancet*. 2018;391(10117):230-240. doi:10.1016/S0140-6736(17)32137-2
26. Wang YK, Qin SQ, Ma T, et al. Effects of teriparatide versus alendronate for treatment of postmenopausal osteoporosis: A meta-analysis of randomized controlled trials. *Medicine (Baltimore)*. 2017;96(21):e6970. doi:10.1097/MD.0000000000006970