



Denosumab, an effective osteoporosis treatment option for men

Sung Hye Kong

Department of Internal Medicine,
Seoul National University Bundang
Hospital, Seoul National University
College of Medicine, Seongnam,
Korea

See Article on Page 1011-1020

As osteoporosis is commonly considered a disease of women, osteoporosis in men is undertreated because of the low screening frequency. However, men at high fracture risk are not treated appropriately [1,2]. Consequently, although women have a significantly higher prevalence of osteoporosis, 40% of osteoporotic fractures happen in men [2,3]. In addition, the prognosis of osteoporotic fracture is worse in men than in women and their mortality after osteoporotic fractures is about twice the rate in women [2]. Therefore, appropriate, effective treatment in men at high fracture risk is clinically and economically important. Denosumab is one of the most potent antiresorptive agents for treating osteoporosis [4]. However, relatively few studies have examined its effects in men compared to women and no studies have examined men who used bisphosphonates before starting denosumab, which we frequently encounter in our practice.

In this issue of the *Korean Journal of Internal Medicine*, Jeong et al. [5] report that 12 months of denosumab treatment effectively increased the bone mineral density (BMD) in a retrospective cohort of osteoporotic men, both in those who were drug naïve and those who had initially used bisphosphonate. They showed that BMD was significantly increased from baseline by 5.2% in the lumbar spine,

2.3% in the femur neck, and 1.9% in the hip, in drug-naïve patients. The trabecular bone score (TBS) was increased by 0.5% in drug-naïve patients. Patients previously treated with bisphosphonates were analyzed separately in their study and their BMD increased by 4.8% in the lumbar spine, 1.4% in the femur neck, and 0.8% in the hip, but the increase was significant only in the lumbar spine. Thus, the study implied that 12 months of denosumab treatment effectively increased the lumbar spine BMD in Korean osteoporotic men regardless of prior bisphosphonate exposure, and increased femur neck and hip BMD in drug-naïve men with osteoporosis.

The study is clinically attractive for several reasons. First, Jeong et al. [5] analyzed the effect of denosumab in men only, one of the first such studies in an Asian population. Most major clinical studies have studied only postmenopausal women [4,6]; even the studies that included both sexes included only a few men [7-9]. Jeong et al. [5] reported a significant increase in BMD to a degree similar to that of previous reports [10]. In European and American men, denosumab treatment for 12 months resulted in significantly increased BMD, by 5.7% in the lumbar spine and 2.1% in the femur neck [10], which was similar to the results of Jeong et al. [5]. It was also comparable to the results in women, i.e., the lumbar spine and total hip BMD increased by 6.7% and

Received : August 3, 2022
Accepted : August 12, 2022

Correspondence to
Sung Hye Kong, M.D.

Department of Internal Medicine,
Seoul National University Bundang
Hospital, Seoul National University
College of Medicine, 82 Gumi-
ro 173beon-gil, Bundang-gu,
Seongnam 13620, Korea
Tel: +82-31-787-8126
Fax: +82-31-787-7029
E-mail: shkong@snu.ac.kr
<https://orcid.org/0000-0002-8791-0909>

3.1%, respectively [4]. The study has clinical significance as it shows that denosumab is an effective option for osteoporosis in Asians, regardless of sex.

It is also interesting that, although statistically insignificant, the increase in BMD was more prominent in drug-naïve patients than in those who had previously used bisphosphonates. Jeong et al. [5] demonstrated that the additional BMD gain using denosumab was evident only in the lumbar spine, not in the hip area, in patients who had initially used bisphosphonates. This is consistent with the previous finding in women that the effect of denosumab in those with prior bisphosphonate use was blunted compared with that of drug-naïve women [11,12]. However, there could be differences in the effect of denosumab according to the duration of the prior bisphosphonate treatment and cessation time of bisphosphonate before the start of denosumab. Jeong et al. [5] did not present additional data on these concerns, which warrants caution when interpreting their results. They also demonstrated that the bone microarchitecture, reflected in the TBS, was increased after 12 months of denosumab in drug-naïve patients [5], implying that denosumab improved both the bone density and microarchitecture.

In conclusion, the article provides clinically meaningful information that the effect of denosumab in men is seen on both BMD and TBS. Of note, they provided quantitative data on how much BMD increased after denosumab use in men who had used bisphosphonate previously, a question that is frequently asked in clinical practice. Therefore, in men at high fracture risk who need active treatment, denosumab is an effective, potent treatment option for reducing the risk of fracture.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Harvey NC, McCloskey EV, Mitchell PJ, et al. Mind the (treatment) gap: a global perspective on current and future strategies for prevention of fragility fractures. *Osteoporos Int* 2017;28:1507-1529.
2. The Korean Society for Bone and Mineral Research. Osteoporosis Fact Sheet 2019 [Internet]. Seoul (KR): The Korean Society for Bone and Mineral Research, 2019 [cited 2022 Aug 12]. Available from: <https://www.ksbmr.org/bbs/index.html?code=fact&category=&gubun=&page=1&number=702&mode=view&keyfield=&key=>.
3. Gennari L, Bilezikian JP. New and developing pharmacotherapy for osteoporosis in men. *Expert Opin Pharmacother* 2018;19:253-264.
4. Cummings SR, San Martin J, McClung MR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. *N Engl J Med* 2009;361:756-765.
5. Jeong C, Ha J, Kim J, et al. The efficacy of denosumab in Korean male patients with osteoporosis. *Korean J Intern Med* 2022;37:1011-1020.
6. Farlay D, Rizzo S, Dempster DW, et al. Bone mineral and organic properties in postmenopausal women treated with denosumab for up to 10 years. *J Bone Miner Res* 2022;37:856-864.
7. Rhee Y, Chang DG, Ha J, et al. Real-world safety and effectiveness of denosumab in patients with osteoporosis: a prospective, observational study in South Korea. *Endocrinol Metab (Seoul)* 2022;37:497-505.
8. Tanaka S, Mizutani H, Tsuruya E, Fukuda R, Kuge K, Okubo N. Long-term safety and effectiveness of denosumab in Japanese patients with osteoporosis: 3-year post-marketing surveillance study. *J Bone Miner Metab* 2021;39:463-473.
9. Okubo N, Matsui S, Matsumoto T, et al. Relationship between bone mineral density and risk of vertebral fractures with denosumab treatment in Japanese postmenopausal women and men with osteoporosis. *Calcif Tissue Int* 2020;107:559-566.
10. Orwoll E, Tegljaerg CS, Langdahl BL, et al. A randomized, placebo-controlled study of the effects of denosumab for the treatment of men with low bone mineral density. *J Clin Endocrinol Metab* 2012;97:3161-3169.
11. Kendler DL, Roux C, Benhamou CL, et al. Effects of denosumab on bone mineral density and bone turnover in postmenopausal women transitioning from alendronate therapy. *J Bone Miner Res* 2010;25:72-81.
12. 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;101:3163-3170.