'DESIRABLE' or not?

We read with great interest the recently published study 'Effects of the anti-RANKL antibody denosumab on joint structural damage in patients with rheumatoid arthritis treated with conventional synthetic disease modifying antirheumatic drugs (DESIRABLE study): a randomised, double-blind, placebo-controlled phase 3 trial' by Takeuchi *et al.*¹ This trial has shown a beneficial effect of denosumab in reducing radiographic progression (modified total Sharp score) and erosions in patients of rheumatoid arthritis (RA), in two dosing regimens, that is, 60 mg subcutaneous 6 monthly and 3 monthly.

However, there are some concerns. While there has been a significant reduction in erosion score over 12 months, the above study failed to demonstrate any beneficial effect of denosumab on joint space narrowing.¹ Radiographic scores are surrogates for reflecting disability and functional limitation, and thus any reduction in these is the gold-standard for 'disease-modification' in RA. But, it is the joint space narrowing which is a better predictor of function than erosions.² In that regard, it is notable that there was no improvement in function per se measured by health assessment questionnaire - disability index (HAQ-DI) in this study. Also, at the end of 12 months of therapy, no difference was seen in ACR20/50/70 response. Thus, the benefit in erosions may not translate into clinically meaningful improvement.

Denosumab is proven to have a beneficial effect on RA-associated osteoporosis.³ This effect was also evident on lumbar spine bone mineral density in 'DESIRABLE' trial.¹ However, denosumab has been associated with rebound osteoporosis and increased risk of multiple fractures after withdrawal when used in osteoporosis.⁴ Whether a similar effect would also occur on erosions remains to be seen.

Finally, patients with RA are at a 10% increased risk for development of malignancies than the general population.⁵ A previous study found that malignancies in patients treated with denosumab were higher, though were not statistically significant.⁶ In the 'DESIRABLE' study, three patients in the denosumab groups developed malignancies and two developed interstitial lung disease.¹ Though there was no statistically significant difference between the treatment and placebo groups, the study was not adequately powered to study adverse effects. A longer follow-up is needed to ensure the safety of denosumab.

To conclude, in the absence of clinical improvement and lack of long-term safety data, it would be still early to consider denosumab for a non-osteoporotic indication, such as reducing RA erosion scores.

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REFERENCES

- 1 Takeuchi T, Tanaka Y, Soen S, *et al.* Effects of the anti-RANKL antibody denosumab on joint structural damage in patients with rheumatoid arthritis treated with conventional synthetic disease-modifying antirheumatic drugs (desirable study): a randomised, double-blind, placebo-controlled phase 3 trial. *Ann Rheum Dis* 2019;78:899–907.
- 2 Navarro-Compán V, Landewé R, Provan SA, *et al.* Relationship between types of radiographic damage and disability in patients with rheumatoid arthritis in the EURIDISS cohort: a longitudinal study. *Rheumatology* 2015;54:83–90.
- 3 Nakamura Y, Suzuki T, Kato H. Denosumab significantly improves bone mineral density with or without bisphosphonate pre-treatment in osteoporosis with rheumatoid arthritis: Denosumab improves bone mineral density in osteoporosis with rheumatoid arthritis. *Arch Osteoporos* 2017;12:80.
- 4 Tsoardi E, Langdahl B, Cohen-Solal M, *et al.* Discontinuation of Denosumab therapy for osteoporosis: a systematic review and position statement by ECTS. *Bone* 2017;105:11–17.
- 5 Simon TA, Thompson A, Gandhi KK, *et al.* Incidence of malignancy in adult patients with rheumatoid arthritis: a meta-analysis. *Arthritis Res Ther* 2015;17.
- 6 Saag KG, Wagman RB, Geusens P, *et al.* Denosumab versus risedronate in glucocorticoid-induced osteoporosis: a multicentre, randomised, double-blind, active-controlled, double-dummy, non-inferiority study. *Lancet Diabetes Endocrinol* 2018;6:445–54.