

## Denosumab breakthrough for rare bone tumour

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Denosumab, a targeted therapy to prevent bone loss, stops progressive bone destruction and tumour spread in some patients with inoperable giant-cell tumour (GCT) of bone. The article, published in *The Lancet Oncology*, is the first to clearly show a promising systemic treatment option for this rare type of bone tumour, and could change standard treatment practice.

GCT causes pain, impaired function and mobility, and can be limb and life threatening. GCT is usually benign, and surgery is the standard treatment, but GCT can become malignant after radiation therapy or several recurrences. Additionally, some patients are unable to undergo surgery because of multiple lesions, location of the tumour (eg, spine), or because of tumour spread, and have limited treatment options.

Denosumab is a monoclonal antibody that targets and disables RANK ligand (a key mediator of osteoclast activity), blocking the action of osteoclasts, the cells that break down bone. Denosumab has been beneficial in the treatment of conditions linked to bone destruction including multiple myeloma and bone metastases, and might improve outcomes in patients with GCT.

David Thomas from Peter MacCallum Cancer Centre, Melbourne, Australia, and colleagues did a phase 2 trial to investigate the safety and effectiveness of denosumab in patients with recurrent or inoperable GCT.

37 patients with non-malignant GCT were recruited from the USA, Australia, and Europe, and given monthly injections of denosumab, with additional loading doses on days 8 and 15 of month 1. Patients were also instructed to take daily calcium and vitamin D supplements.

Findings showed that 30 of 35 (86%) patients had a tumour response (elimination of at least 90% of giant cells or no radiological progression of the target lesion up to week 25), including some who had lung lesions.

Additionally, among the 31 patients who were assessed for clinical response, 26 (84%) reported clinical benefit, including reduced pain and improvements in function and mobility, and 9 (26%) had bone repair. Denosumab also led to rapid and sustained suppression of bone turnover.

33 of 37 patients experienced an adverse event, the most common being pain in an extremity such as back pain and headaches. Five patients had grade 3–5 adverse events, only one of which was related to treatment.

The authors say: “These findings suggest that continued denosumab may have a therapeutic role in cases of unsalvageable GCT, particularly with pulmonary metastases, but also in the neoadjuvant setting where the drug might improve surgical outcomes.”

In an accompanying Comment, Maurice Balke from the University of Witten-Herdecke, Hospital Cologne-Merheim, Germany, and Jendrik Harges from University Hospital Muenster, Germany welcome the study which they say: “Might change clinical practice in the treatment of complicated GCT of bone.”

They call for more studies on the mechanism of action of denosumab and suggest that neoadjuvant treatment with denosumab might also be given to reduce tumour size before surgery for typical benign lesions.

**Source:** Lancet Oncology

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