

Denosumab delays development of prostate cancer bone metastasis

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An international clinical trial has found that treatment with a drug that suppresses the normal breakdown of bone can delay the development of bone metastases in men with prostate cancer. The study, receiving Online First publication in *The Lancet*, is the first to successfully reduce bone metastasis in such patients and supports the importance of targeting the bone microenvironment to prevent prostate tumor spread.

"Prostate cancer patients who develop bone [metastases](#) usually have poor outcomes, so preventing the development of metastasis has been a major unmet clinical need," says Matthew Smith, MD, PhD, of the MGH Cancer Center, lead and corresponding author of the *Lancet* paper. "This first demonstration of a treatment that can meet that goal is a significant accomplishment that should lead to better [treatment strategies](#)."

Bone is the most common site - in some patients the only site - for the development of prostate cancer metastases, which can lead to pain, fractures and the need for surgery or radiation therapy. Almost all men who die from prostate cancer have [bone metastasis](#). Previous research has suggested that metastatic development involves interactions between tumor-secreted growth factors and the normal process by which bone tissue is broken down and rebuilt. Animal studies have indicated that inhibiting osteoclasts - cells that cause the resorption of bone - can prevent metastasis and that expression on cancer cells of a signalling protein called RANKL, which activates osteoclasts, may prepare the bone microenvironment for tumor spread.

Denosumab is a monoclonal antibody against RANKL and is FDA approved for two uses - treatment of osteoporosis and prevention of fractures in patients with [bone metastases](#) from solid tumors. Denosumab is marketed by Amgen - which supported the current study - under the brand names Prolia for osteoporosis treatment and

Xgeva for cancer treatment. The current study enrolled 1,432 participants at 319 centers in 30 countries - all prostate cancer patients whose tumors had stopped responding to androgen-deprivation therapy and were metastasis-free, although rising PSA levels indicated they were at risk for metastasis.

Participants were randomly assigned to receive injections of either denosumab or a placebo every four weeks. During the two-year study period, patients were examined - including a bone scan - every four months, and X-ray skeletal surveys performed annually. If a bone scan indicated the presence of metastasis, it was confirmed with either X-ray, CT scan or MRI. After that confirmation, study treatment was discontinued, since other therapies are approved to treat metastatic [prostate cancer](#).

Study results indicated that denosumab treatment increased bone-metastasis-free survival - defined as the time to either the first metastasis or death from any cause - by an average of more than four months, extended the time to first metastasis and delayed symptoms of metastasis. Biochemical markers indicated that denosumab treatment did reduce bone turnover. While there was no survival difference between the two study groups, the authors note that that fact that denosumab was discontinued when the first [metastasis](#) was diagnosed makes judging the drug's effects on survival difficult.

Provided by Massachusetts General Hospital

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