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Study: Denosumab effective in treating osteoporosis in transfusion dependent thalassemia

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For patients with osteoporosis caused by transfusion-dependent thalassemia (TDT), a twice-yearly injection appears to improve spinal bone mineral density, according to a new study.

The study, published online today in the journal *BloodAdvances*, also suggests that this treatment, denosumab, could reduce pain and improve quality of life for people with TDT and osteoporosis.

Osteoporosis is a bone disease that affects 40 percent of people with TDT—an inherited congenital blood disorder that results in the decreased production of hemoglobin and red blood cells—and is one of the most prevalent comorbidities associated with the disorder. People with osteoporosis have porous, weak bones that are susceptible to fractures and often cause pain. Current standard therapy for people with TDT and osteoporosis is to administer intravenous bisphosphonate agents such as pamidronate or zoledronic acid.

It is believed that people with thalassemia and osteoporosis exhibit elevated levels of the osteoporosis regulator gene known as RANKL. Denosumab, delivered under the skin instead of intravenously, is an FDA-approved anti-RANKL therapy that is not yet approved for use in people with TDT-induced osteoporosis.

Researchers established a single-site, randomized, placebo-controlled,

double blind phase IIb trial to evaluate the efficacy and safety of denosumab in patients with TDT and osteoporosis. 63 patients were randomly assigned to receive either 60mg of denosumab (n=32) or placebo (n=31) on days 0 and 180 over a period of 12 months. Each patient was also provided with daily supplements of calcium and vitamin D throughout the study.

Each patient's bone mineral density was measured in the L1-L4 lumbar spine, the wrist, and the femoral neck. Patients receiving denosumab had a 5.92 percent increase in lumbar bone density compared to a 2.92 percent increase in the placebo arm. Similarly, patients receiving denosumab lost less bone mineral density in their wrist compared to placebo (-0.26% vs -3.92%, respectively), while increasing density in the femoral neck (4.008% and 1.96%, respectively).

Additionally, patients receiving denosumab reported a significant reduction in pain compared to those in the placebo arm.

"Not only is denosumab associated with improved bone health and reduced pain, but its ease of administration may very well make this drug superior to bisphosphonates for the treatment of osteoporosis in patients with TDT and osteoporosis," said senior study author Evangelos Terpos, MD, of the National and Kapodistrian University of Athens, Greece.

Three serious adverse events were reported in the denosumab arm, including pleural effusion, supraventricular tachycardia, and atrial fibrillation, though investigators found no link between the treatment and these adverse events.

This study suggests that future studies should directly compare denosumab to bisphosphonates for the treatment of bone mineral density loss and pain management for people with TDT and osteoporosis.

More information: Ersi Voskaridou et al. Denosumab in transfusion-dependent thalassemia osteoporosis: a randomized, placebo-controlled, double-blind phase 2b clinical trial, *Blood Advances* (2018). DOI: 10.1182/bloodadvances.2018023085