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Denosumab Decreases The Subsidence Of Cementless Tibial Implants By Suppression Of Bone Resorption.
A Randomized, Double-Blinded RSA Study In 54 Patients With 5 Years Follow-Up

Orthopaedics / Knee & Lower Leg / Joint Replacement - Primary

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Keywords: Radiostereometry Analysis, Total Knee Arthroplasty, Bone Mineral Density, Implant Fixation,

Background
Cementless tibial implants migrate initially until osseointegration. Denosumab, an antiresorptive, binds to RANKL and reduces the function and survival of osteoclasts resulting in a suppression of bone resorption. It is shown in animal studies that denosumab enhances fixation more potently than bisphosphonates, and a reduced migration at 1-year follow-up of a cemented knee implant treated postoperatively with denosumab has been reported. However, the effect of denosumab on cementless knee implants is unknown.

Objectives
To study the effect of postoperative injections of denosumab on the bone remodelling process and the fixation of a cementless tibial implant. We hypothesized that denosumab decreases early migration of cementless tibial implants.

Study Design & Methods
A prospective, double-blinded, randomised study including 54 patients operated with a total knee arthroplasty (TKA) using a cementless tibial implant (Regenerex). Patients were randomised to two injections subcutaneously (second postoperative day and 6 months postoperative) of denosumab (60mg) (Dmab group) or 1 ml NaCl (9mg/ml) (placebo group). We compared migration (subsidence/Y-translation) using Radiostereometry Analysis (RSA), biochemical bone turnover markers (CTX, P1NP), and periprosthetic Bone Mineral Density (BMD) by dual-energy X-ray absorptiometry (DXA). RSA, DXA, and blood samples were obtained postoperative and at follow-up at 2 and 6 weeks, 3 and 6 months, and at 1, 2, and 5 years.

Results
The Dmab group had significantly less subsidence than the placebo group. At 5-year follow-up, mean tibial implant subsidence was -0.21 mm (95%CI: -0.41; -0.01) in the Dmab group and -0.51 mm (95%CI: -0.71; 0.32) in the placebo group ($p=0.03$). In the first year after surgery, bone resorption (CTX) was lower in the Dmab group than in the placebo group ($p<0.001$). Bone formation (P1NP) was lower at 6 weeks, 6 months and 1 year ($p<0.02$) but similar at 2 and 5 years ($p>0.61$). In general, periprosthetic BMD was higher in the Dmab group until 12 months follow-up, but similar thereafter ($p>0.151$).

Conclusions

Compared to placebo, two denosumab injections given with a 6-month interval after TKA surgery resulted in lower subsidence of cementless tibial implants throughout follow-up. Bone resorption measured systemically was suppressed and there was a pattern of a higher early postoperative p-BMD in the Dmab group than in the placebo group. However, periprosthetic BMD and CTX were similar after 12 months indicating the treatment did not have a lasting effect on the bone.