NE-OSTEO BONE GROWTH FACTOR FOR POSTEROLATERAL LUMBAR SPINE FUSION: A PROSPECTIVE HUMAN CLINICAL PILOT STUDY

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Introduction: Preclinical studies have demonstrated that Ne-Osteo, an extract containing bone morphogenetic proteins, was successful at generating spine fusion in rabbits and rhesus monkeys. Translations of lower animal studies to humans for osteoinductive bone growth factors has been extremely challenging. Demonstration of efficacy in a rhesus monkey model has proven to be a critical step in the road to successful human trials; however, confirmation of efficacy in humans in a controlled-risk situation is desirable before full scale clinical trials can begin safely. The purpose of this human pilot trial was to test the dose and carrier scale-up required for radiographic bone induction in humans prior to initiating a pivotal trial of posterolateral spine fusion.

Methods: Institutional Ethics Committee approval was granted for this study which was performed at the Schulthess Clinic. One (DG) or both of the authors was present for all surgeries. Patients were recruited in three successive phases, with modifications in dose or carrier made based on results. Twenty-two patients (18F, 4M) with a mean age of 55 years (range, 30-80) had lumbar spinal stenosis and/or spondylolisthesis requiring spine arthrodesis. Internal fixation (translaminar facet screws or pedicle screws/rods) was used in 8/12 patients in Phase I+II and in all patients in Phase III.

To minimize patient risk of nonunion, patients in all three phases received autogenous iliac crest corticocancellous bone graft on one side of the spine and Ne-Osteo growth factor on the other side. The amount of iliac bone graft harvested was similar to that for a bilateral fusion and the entire amount was implanted on the “autograft” side. Phase I used a dose of 12.5 mg Ne-Osteo per side; Phase II used a dose of 25 or 50 mg Ne-Osteo per side; and, Phase III used a dose of 25 mg Ne-Osteo per side mixed with either local laminctomy bone or with allograft cancellous chips (4-10mm) in addition to the demineralized bone matrix (DBM) paste used in all three phases.

Results: There were no adverse events or complications related to Ne-Osteo. In Phase I, 3/6 patients had radiographic (plain xray, CT scans – blindly evaluated) nonunion with resorption of autograft; the other 3 had continuous fusion masses by 12 months. Four of six patients did not show bone induction on the Ne-Osteo side and 1 of 2 that did was graded as fused by 6 months. In Phase II, the autograft side was graded as fused in 6/6 patients; the Ne-Osteo side was fused in 6/6 and in 2 of those patients by 6 months. There was no improvement in the results using the 50 mg dose compared to the 25 mg dose, so the lower dose was used in Phase III. Although graded as fused, the 6-month scans demonstrated a ring of new bone with the center filling in slower (12-24 months) than was predicted by non-human primate studies. Thus, Phase III carrier was designed to have a more porous/open early fusion mass than with the dense DBM paste by mixing in local bone or cancellous allograft chips. In Phase III, all ten autograft sides were fused by 12 months. Five of five patients with Ne-Osteo + local bone were graded as fused (facet and intertransverse process) by 6 months. Five of five patients with Ne-Osteo + allograft chips were graded as fused in the facet joint and 4/5 at the transverse process site (one was indeterminate due to scan quality).

Discussion: This pilot study is the first with two-year followup to demonstrate successful posterolateral spine fusion using a BMP-based bone graft substitute using CT scan as the determinant. Ne-Osteo, an extracted protein mixture containing BMPs, was able to consistently induce bone in the posterolateral lumbar spine when delivered at a dose of at least 25 mg/side. Healing may have been slightly faster when NeOsteo was delivered with local bone compared to allograft chips, but the results were acceptable in both cases. Since this pilot study was designed to measure bone induction and minimize patient risk of nonunion the use of more than the normal volume of autogenous iliac bone graft on the control side may have falsely increased the success rate of autograft but it should not have changed the likelihood that the BMP dose present in Ne-Osteo would induce new bone. In addition, rapid fusion on the Ne-Osteo side may have improved the likelihood of fusion on the autograft side. Although the use of internal fixation was variable, patients without internal fixation in Phases II+III still had good bone induction.

Conclusion: Ne-Osteo bone growth factor was capable of achieving a continuous spine fusion mass in 16/16 patients at a dose of at least 25 mg/side. This result was at least as good as autograft (100%) in this side-by-side model using twice the normal volume of autograft on one side and may prove better than autograft in a traditional bilateral model which usually has substantially lower autograft success rates. These results warrant confirmation in a pivotal trial with Ne-Osteo on both sides of the spine and avoiding iliac crest bone graft harvest.

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