The Effect of Teriparatide on Femoral Neck Fracture Healing in Men and Postmenopausal Women

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Introduction: Osteoporotic hip fractures cause substantial morbidity and mortality in the elderly. Surgical repair by internal fixation is associated with less initial surgical trauma and blood loss, and shorter operation time than arthroplasty; however, 10% to 49% of patients who undergo internal fixation require reoperation. Teriparatide (TPTD) is an osteoanabolic agent indicated for postmenopausal women and men with osteoporosis at high risk for fracture. While no systemic therapy is approved to promote fracture healing, TPTD has been shown to accelerate healing in several preclinical studies, case reports, and preliminary clinical trials at various skeletal sites, including the hip, pelvis, and radius. We originally designed two large phase 3 clinical trials to enroll 1220 patients each with 24-month study duration to detect a difference in overall fracture healing success rates between TPTD and placebo (PBO). Due to very slow patient recruitment, the enrollment of both studies was stopped early, and 161 patients who had been randomized in both studies were followed up to complete the studies at 12 months. The data from these two studies were pooled for statistical analyses to explore the potential effect of TPTD on fracture healing.

Methods: Men and postmenopausal women aged ≥50 years with a new-onset low trauma femoral neck fracture who underwent internal fixation were enrolled in 2 small prospective, randomized, double-blind, placebo-controlled studies. Objectives were to assess the effects of 6-months’ treatment with TPTD 20 µg daily SQ injection vs PBO on revision surgery rates and radiographic healing 12 months post initial surgery. Patients were randomized within 14 days post-surgery, received a daily injection of blinded study drug for 6 months, and continued for an additional 6-month blinded observation period. Radiographs of fracture sites were collected before and after initial surgery, at week 10, month 6 and month 12 after randomization, and/or before and after revision surgery. During the study, orthopedic surgeons would identify patients who required a revision surgery based on clinical and radiological assessments. A central adjudication committee (CAC), including 4 orthopedic surgeons and 1 radiologist, reviewed revision surgery cases and all radiographs for fracture healing and complications. Functional
measures and patient reported outcomes were collected post-randomization. Between-group differences were compared using Log-rank test based on Kaplan Meier analysis and Fisher exact test.

Results: Patient characteristics: A total of 161 patients were randomized, and 159 patients received at least one dose of study drug. Per CAC adjudication 155 patients were confirmed having femoral neck fractures, 79 in the PBO group and 76 in the TPTD group. Four patients who had an intertrochanteric fracture were excluded from efficacy analyses in this abstract, but included in safety analyses. Of the 159 patients, 118 completed study and 41 (25.8%) discontinued early from the study. There were no significant differences between groups in patient disposition. Treatment groups were balanced with respect to patient demographics and baseline characteristics; mean age was 70 years and 74% were women. The randomization was stratified by fixation type (sliding hip screws or multiple cancellous screws) and fracture type (displaced or nondisplaced). By CAC adjudication, 97% had femoral neck fractures, and correct implant type, surgical reduction, and implant placement, and 73% of patients had nondisplaced fractures. The randomization resulted in well balanced treatment groups.

Revision surgery rate: Eleven patients in PBO and 13 in TPTD had revision surgery performed or recommended as reported by investigators. By the CAC, 2 patients in PBO were excluded from the primary efficacy analysis. There was no significant difference between treatment groups in the proportion of patients having no revision surgery, as either adjudicated by CAC or reported by investigators. The common complaints in patients with revision surgery were hip pain or pain during ambulation, and/or poor function or non-ambulation. The main reasons for recommending revision surgery by investigators were non-union, poor function or mobility, painful hardware, implant failure or breakage, or avascular necrosis. There were numerical differences between treatment groups in some of the subcategories, but the numbers of the cases were small.

Radiographic evidence of fracture healing: Overall in both groups, approximately 40%, 70%, and 75% of patients had radiographic evidence of fracture healing at 10 weeks, 6 months, and 12 months, respectively. There were no significant differences between treatment groups.

Pain: No significant differences were observed between groups in any secondary endpoints associated with pain - either no severe or worsening pain, or mean pain scores at each visit. Approximately 90% of patients in both groups who remained in the study had pain scores <7 (numerical rate scale 0 -10) with no worsening at 12 months.

Gait Speed: Statistically significantly higher proportions of patients in TPTD were able to ambulate (gait speed ≥ 0.05 m/s) without worsening (change from baseline ≥ 0.1 m/s) at Month 12 (LOCF) or regained their pre-fracture ambulatory status at Month 12 (observed). But there were no significant differences between groups in the proportion of patients achieving a gait speed ≥ 0.05 m/s.

Safety: The total number of adverse events, serious adverse events, deaths, and discontinuations due to adverse events were similar between groups. Three death cases (1 PBO, 2 TPTD) were reported and adjudicated by CAC that the causes of death were not related to hip fractures.


Discussion: Due to a lower than expected patient recruitment, the enrollment of two large randomized trials was stopped early. The combined data from the 155 patients enrolled who had femoral neck fractures did not show a significant difference on revision surgery rate or radiographic fracture healing between teriparatide and placebo groups; however, the study had very limited power to detect a difference and the results were exploratory in nature. The adverse event data observed were consistent with the teriparatide safety profile with no new safety signals identified. Functional and health outcome data from the studies may help improve our understanding of patients recovering from femoral neck fractures.

Significance: Although the studies were stopped early and the results did not meet the primary objective, these two combined studies are the largest prospective clinical trial to date with pharmacological intervention conducted in patients with femoral neck fractures in multiple countries and study sites. The data collected from the studies will add to our understanding of patient recovery after a femoral neck fracture.

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