Abaloparatide and Pelvic Fracture Healing: A Phase 2 Randomized Controlled Trial

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INTRODUCTION:

Pelvic fractures are among the costliest osteoporosis related fractures due to prolonged pain and loss of function, long hospitalizations and rehabilitation, and the lack of interventions to help manage these fractures. Fractures that remain unhealed can cause continued pain and immobility. Given the aging of the population and expected concomitant increase in the incidence of pelvic fractures, there is a pressing need to find effective treatments that will accelerate healing. Furthermore, pelvic fractures can serve as a model of fracture healing for other osteoporosis related fractures.

Abaloparatide (Tymlos) is currently FDA approved for the treatment of osteoporosis in the US. Prior clinical studies of teriparatide did not provide clear evidence of benefit on fracture healing, however, no clinical studies of abaloparatide have been performed. We hypothesized that abaloparatide might augment fracture healing in addition to treating the underlying osteoporosis that resulted in the fracture. We tested this under FDA IND 147692 using a randomized, double blind, placebo-controlled phase 2 clinical trial design in patients >50 years of age with acute pelvic fracture. We evaluated whether treatment with daily subcutaneous abaloparatide (ABL) 80 mcg/day compared with placebo (PBO) improves radiologic healing, pain, and functional outcome at 3 months in patients with acute pelvic fracture.

METHODS:

Women and men >50 years old, enrolled within 4 weeks of pelvic fracture (n=48), were randomized to blinded ABL vs PBO (clinicaltrials.gov NCT 04249232). Randomization was stratified on whether there was a single fracture or multiple rami fractures and whether the fractures were displaced (by 2 mm or more). The primary endpoint, fracture healing, was assessed by 2 blinded radiologists using a 5-point scale for cortical bridging from CT images (0-2=not healed; 3-4=healed). ABL vs. PBO bridging categories were statistically compared with Jonckheere-Terpstra Test. The odds of healing with ABL vs. PBO was analyzed with Mantel-Haenszel relative risks (RR). Pain was assessed monthly using the numeric rating scale (NRS) administered by a research assistant who was blinded to treatment. The Short Physical Performance Battery (SPPB) that includes 4m walk speed, timed repeated chair stands, and balance evaluated functional mobility on a monthly basis. The score for this test is from 0 to 12 with higher scores indicating better performance.

RESULTS: At baseline, groups were balanced with mean age 82 and 83% female. 94% of patients had multiple rami fractures, 60% also had a sacral fracture and 40% had at least one displaced fracture. CT images were available for 40 individuals (20 per group) at 3 months. Overall, bridging score distribution tended to be higher (indicating greater healing) with ABL vs. PBO (p=0.09). In patients with displaced fractures (n= 16), the distribution of bridging scores was higher with ABL vs. PBO (p=0.002). However, in patients with nondisplaced fractures (n=24) there was no significant difference between distribution of bridging scores with ABL vs PBO. When evaluating individual fractures (n=81), bridging scores were overall numerically higher with ABL vs PBO (p=0.002). However, in patients with nondisplaced fractures (n=25), bridging scores were significantly higher with ABL vs. PBO (p=0.002) but again there was no group difference with nondisplaced fractures (n=56). When patients with fractures were categorized as healed/not healed, 61% were healed with ABL and 39% healed with PBO (RR 1.7; 95% CI 0.84, 3.6). In those patients with displaced fractures, 67% were healed with ABL vs 0% with PBO (RR 3.3; 95% CI (1.29, 8.6)). In patients with non-displaced fractures, there was no difference in healing between ABL and PBO (RR=1.1; 95% CI 0.41, 2.96). There was no group difference in NRS pain score at baseline. Pain reduced minimally at week 4 with PBO but decreased 44% with ABL (group difference p=0.04). SPPB scores improved over time in both groups with no group differences.

DISCUSSION AND CONCLUSION:

In this small randomized, blinded study, there was a trend toward improvement in radiographic healing (CT at 3 months) in ABL vs. PBO whether looking at healing of individual fractures or healing by person. However, there was significant benefit of ABL vs. PBO in the subgroup with displaced fractures (40% of population) where there was a 3-fold likelihood of healing if the patient took ABL vs. PBO. Pain appeared to reduce more rapidly with ABL with a clear benefit at 4 weeks, with little reduction in pain in the PBO group. There was no apparent group difference in physical performance, which improved in both groups. We conclude that ABL may provide some benefit in healing pelvic fractures, particularly in fractures that are displaced.