The Efficacy of a Locally Injectable Prostaglandin EP-2 Receptor Agonist on Fracture Healing

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Background: Identification of novel therapeutics to accelerate acute fracture healing remains critical. A prostaglandin EP-2 receptor agonist (CP-533,536) has demonstrated acceleration of fracture healing in preclinical models.

Methods: In a phase II randomized, blinded, placebo-controlled trial the efficacy of a single local injection of 3 doses of CP-533,536 (0.5mg, 1.5mg and 15mg) was compared to both placebo and a standard of care arm in patients with closed tibial shaft fractures treated with reamed inter-locked intramedullary nails. Patients were followed at 2 week intervals to 6 months with a final evaluation at 1 year. Fracture healing was independently adjudicated by a radiologist panel and an orthopedic surgeon panel.

Results: 99 patients were enrolled ranging in age from 17-76 years. Baseline characteristics were comparable across treatment groups. No statistically significant differences in median healing time between any of the CP-533,536 treatment groups and placebo were observed based on radiology panel assessment, however significant differences were demonstrated by an orthopedic panel. At weeks 8, 10, 12, 14 and 16 a higher percentage of subjects in the CP-533,536 1.5 and 0.5 mg groups were considered healed compared to the placebo and the 15 mg groups by the orthopedic panel assessment. Moreover, the CP-533,536- 0.5 mg group showed a statistically higher (p<0.05) mean radiographic healing score than placebo treated group at weeks 8, 14, 16, 18, and 24.

Conclusions: CP-533,536 demonstrated accelerated healing in patients with acute tibia fractures by an orthopedic panel. Confirmatory trials are required to assure validity of the observed treatment effects.