Fremanezumab Reduces Pain Behavior in Murine Femoral Fractures

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Purpose: Fracture pain management is challenging and is typically managed with nonsteroidal anti-inflammatory drugs and opioids. Opioids pose a risk for addiction, highlighting the need for novel analgesics with minimal side effects. Calcitonin gene-related peptide (CGRP) is a neuropeptide that plays a causative role in pain and modulates fracture repair. Fremanezumab, a monoclonal antibody against CGRP, is FDA-approved for migraine prophylaxis, and we hypothesized it could reduce fracture-induced pain behavior but may negatively impact fracture healing.

Methods: C57BL/6 male mice underwent femoral fracture surgery and received buprenorphine, ketorolac, or fremanezumab. Biweekly radiographs were assessed through modified Radiological Union Scale for Tibia (mRUST) scoring. Spontaneous pain behavior (grimace scoring) was assessed at baseline and 4 and 7 days post-fracture (dpf).

Results: No differences in mRUST scoring were observed. Fremanezumab treatment compared to standard-of-care controls resulted in significantly lower mouse grimace scores at 4 and 7 dpf.

Conclusion: Fremanezumab resulted in a marked reduction in grimace scores without detriment to mRUST scores, demonstrating its potential to reduce pain without compromising healing. Ex vivo micro CT, histology, and biomechanical analyses are ongoing to further assess fracture healing outcomes. Future studies will evaluate the effects of fremanezumab on additional pain behavior assays, including extended timepoints to determine its utility as a non-opioid therapeutic option for fracture pain management.

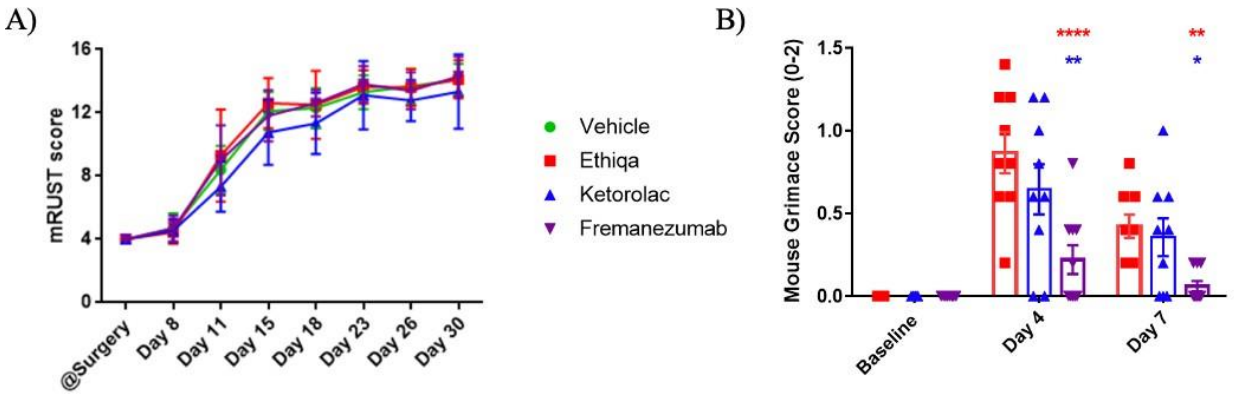

Figure: A) Mean mRUST score over 30 days, and B) mean mouse grimace score over 7 days. *P<0.05, **P<0.01, and ****P<0.0001 as determined by two-way ANOVA and Tukey's post-hoc test for multiple comparisons, n=8-10 for each treatment condition.