

Evaluating the Effectiveness of Fremanezumab on Open Femoral Osteotomy-Induced Pain and Inflammation

Jackson Moss¹, Natalie Nguyen¹, Tyler Nguyen^{1,3}, Alexander Obukhov², Fletcher White^{1,3}

¹Department of Anesthesia, Indiana University School of Medicine

²Department and Anatomy, Cell Biology & Physiology, Indiana University School of Medicine

³Richard Roudebush VA Medical Center, Indianapolis, IN

Background: People who suffer from fractures frequently have injury-associated pain. The current pain management options are opioids and nonsteroidal anti-inflammatory drugs (NSAIDs), however, these drugs present a challenging recovery process impairing skeletal repair. Recent research efforts found that the neuropeptide calcitonin gene-related peptide- α (CGRP) plays a critical role in both bone repair and pain states post-trauma. CGRP is known to be important to vasodilation, neurogenic inflammation peripherally, mechanical and thermal hyperalgesia centrally, and inflammation-dependent bone repair. This neuropeptide has become a potential therapeutic target for bone fracture pain. Fremanezumab (Ajovy), a monoclonal antibody against CGRP, has been shown to reduce clinical pain states and recently received FDA approval for migraine prophylaxis. This study aims to evaluate the effect of Ajovy as an analgesic therapy following femur fracture.

Methods: C57BL/6 female mice were subjected to open femoral osteotomy and then treated with either saline or Ajovy (30mg/kg, intraperitoneally) every day for 7 days following fracture. In vivo bioluminescence imaging (IVIS) was performed to assess caspase-1 mediated inflammation. Grimace Scoring was used to evaluate pain response at various time points before and after treatment.

Results: Through IVIS, we found that mice subjected to femur fracture exhibit profound inflammatory response up to 3 weeks post-trauma and this response was attenuated with Ajovy treatment. Furthermore, preliminary behavioral data found a trend of decreased pain behaviors in the Ajovy-treated fractured mice compared to the saline control. Specifically, at 2 weeks post-fracture there was a significant reduction in the pain score.

Conclusion: The effect of modulating CGRP signaling in bone healing is yet to be determined. However, this preliminary study reveals promising results in reducing inflammation and painful behavior with Ajovy administered near the time of injury. Additional works aiming to increase the cohort number and assess bone healing are currently ongoing.