Suzetrigine, a Non-Opioid Selective Pain Signal Inhibitor, is Effective in Treating Acute Pain Following a Broad Range of Orthopedic Surgery-related Procedures

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INTRODUCTION: Moderate to severe acute pain after orthopedic surgery is frequently treated with opioids because of the lack of non-opioid treatment options with favorable benefit-risk profiles. The voltage-gated sodium channel 1.8 ($Na_V1.8$) has potential as a therapeutic target for moderate to severe pain due to its selective expression on peripheral nociceptors and its role in transmission of pain signals. Suzetrigine (SUZ), an orally administered small molecule, is a potent and highly selective inhibitor of $Na_V1.8$ with no abuse potential due to its mechanism of action. In two randomized, double-blind, placebo-controlled, phase 3 studies in participants with moderate to severe acute pain after abdominoplasty (n=1,118 dosed) or bunionectomy (n=1,073 dosed), SUZ treatment demonstrated a statistically significant greater reduction in pain compared to placebo. In a single-arm, open-label, phase 3 study, the safety and effectiveness of SUZ was evaluated in a broad population including postoperative surgical and non-surgical patients who had moderate to severe acute pain. Here, we further describe the findings in a sub-population of participants from this open-label, phase 3 study who had acute pain following one or more orthopedic surgeries.

METHODS:

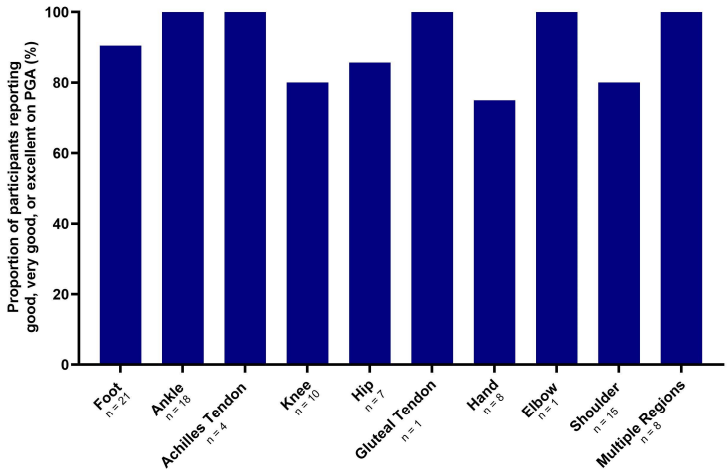
This single-arm, open label, phase 3, study evaluated the treatment of SUZ (100 mg first dose, then 50 mg every 12 hours) in 256 participants (18 to 80 years) for 14 days or until a participant's pain resolved. At baseline, participants had moderate or severe acute pain on a verbal categorical rating scale and ≥4 on the numeric pain rating scale (range, 0 to 10) after a scheduled surgical procedure or after presenting to a medical facility with acute pain of new origin (occurring within the prior 48 hours and not related to a prior known condition). Here, we evaluated the safety (primary endpoint) and effectiveness of SUZ (secondary endpoint) in a subgroup of 93 participants who had moderate to severe acute pain following a broad spectrum of orthopedic surgeries. Effectiveness of SUZ for treating pain at the end of treatment was assessed using a patient global assessment (PGA).

RESULTS:

A total of 93 participants who had orthopedic surgeries received SUZ and the mean (SD) duration of SUZ treatment was 11.7 (4.2) days. SUZ was generally safe and well tolerated. The majority of participants had adverse events that were mild or moderate in severity and there were no serious adverse events related to SUZ. Headache (7.5%) was the most common adverse event. Most participants (89.2%) who had orthopedic surgeries rated the effectiveness of SUZ for treating pain on a PGA as good, very good, or excellent at the end of treatment, which was similar to that reported by participants in the overall study with a broad range of surgical and non-surgical acute pain conditions (83.2%; n= 256). Effectiveness was generally consistent across a broad range of orthopedic surgeries (Figure 1).

DISCUSSION AND CONCLUSION:

These results demonstrate that SUZ, a pain signal inhibitor that selectively inhibits $Na_V1.8$, has the potential to be a safe and effective non-opioid treatment option for various moderate to severe acute pain conditions, including acute pain after orthopedic surgeries, and has the potential to be the first drug in a new class of pain medicines.



PGA: patient global assessment