Chemical Neuro Stimulation by FLX-787, a co-activator of TRPA1/ TRPV1, for the Potential Treatment of Cramps, Spasms and Spasticity

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Summary

Objective: Based on our findings that FLX-787, a TRPA1/TRPV1 ion channel co-activator, significantly inhibits electrically induced muscle cramps (ICR) and resultant leg cramps (NC) in healthy adults, we have advanced FLX-787, to study its efficacy, safety and tolerability in multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS) and Charcot-Marie-Tooth Disease (CMT).

Background: Chemical Neuro Stimulation is the topical activation of TRPA1/TRPV1 ion channels in the oropharynx and esophagus which is believed to stimulate descending inhibitory spinal pathways and in-turn decrease hyperexcitability of spinal circuits. Given that muscle cramps, spasms and spasticity are a consequence of motor neuron hyperexcitability, Chemical Neuro Stimulation may be a useful strategy when treating these symptoms in conditions where present.

Methods: We have initiated an US multi-center, randomized, blinded crossover studies to investigate the effects of FLX-787 in patients with MS, and ALS, as well as several US studies to study the effects of FLX-787 in NC. In the most recent NC study, we investigated two doses of FLX-787 (17 mg and 25 mg) formulated as an orally disintegrating tablet (ODT) in a randomized, blinded, placebo-controlled two-part cross-over study in otherwise healthy subjects who claimed to experience at least 4 NCs per week (n=72). At the conclusion of the study, a questionnaire was administered post-hoc to assess the likelihood (not likely, probably, possible) that participants actually suffered from NC relative to other conditions as well as discomfort self-satisfaction (NSS).

Results: Analyses restricted to the first cross-over period of each study part, together with subject selection based on NC likelihood, demonstrated efficacy. By “possible” and “probable” NC criteria (n=26), active treatment demonstrated a 23% decrease in the mean weekly cramp frequency (p=0.02) and a 31% decrease in weekly mean cramp pain (p=0.05). No adverse events were observed.

Conclusions: These results suggest that FLX-787 may be beneficial in the treatment of muscle cramp in NC and MS patients.

Topical Chemical Neuro Stimulation

Objective: To study the effects of FLX-787 on cramp frequency, pain intensity and quality of life in subjects with leg cramps.

Methods: A randomized, placebo-controlled, double-blind, parallel design study was conducted in healthy adults (n=72) with leg cramps causing moderate to severe pain (p<0.01). As expected for subjects with likely RLS, no difference in cramp frequency or pain was observed.

Results: FLX-787 reduced muscle cramp intensity in an EC-model of the foot. FLX-787 was well tolerated, and no treatment-related AEs have been reported in clinical studies to date.

Conclusions: FLX-787 reduces muscle cramp intensity in an EC-model of the foot. FLX-787 is well tolerated, and no treatment-related AEs have been reported in clinical studies to date.

EIC Efficacy of FLX-787

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NLC Efficacy of FLX-787 in Subjects with Confirmed NLC Diagnosis

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NLC Questionnaire & Adjudication

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References