RESUME-1: A Phase III study of tolperisone in treatment of painful, acute muscle spasms of the back

Authors
Sanam Ara Vaughan, Kayla Torres & Randall Kaye

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Pain Management
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Objectives

Primary Objective

- Assess the efficacy and safety of 50 mg, 100 mg and 200 mg TID tolperisone for relief of pain due to acute back muscle spasm

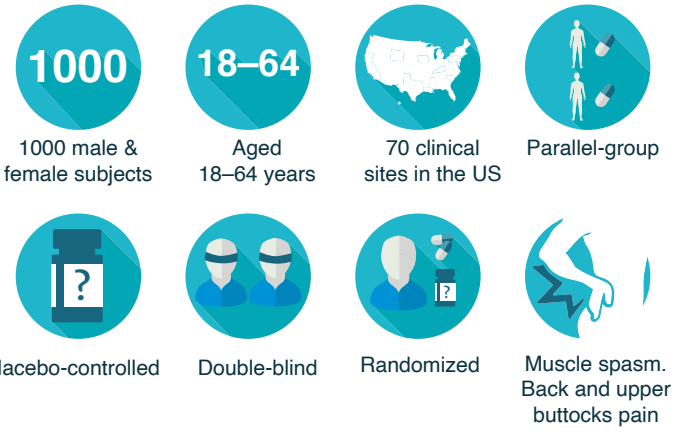
Secondary Objectives

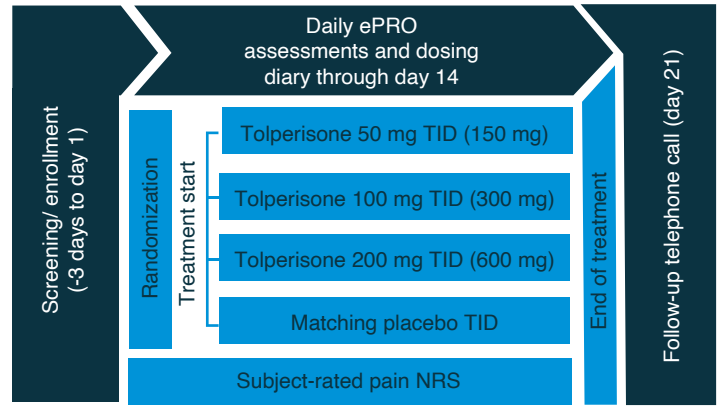
- Assess the tolerability of tolperisone in subjects with pain due to acute back muscle spasm
- Determine onset of action of tolperisone in the treatment of pain due to acute back muscle spasm
- Determine the need for rescue medication when treated with tolperisone for pain due to acute back muscle spasm

Inclusion criteria

- Ambulatory male or female, 18 – 64 years of age, inclusive, for the entire duration of the study (from Screening through Day 21)
- Current acute back pain due to acute muscle spasm starting within 7 days prior to study entry (Day 1) and at least 8 weeks following resolution of the last episode of acute back pain
- Minimum baseline pain using the NRS subject rating of pain "right now" (0-10 scale, "no pain" to "worst possible pain")
- Willingness to discontinue all previous or ongoing treatment of pain or muscle spasm on study entry at Day 1 through the end of treatment including medication, acupuncture, chiropractic adjustment, massage, transcutaneous electrical nerve stimulation [TENS], or physiotherapy
- Pain must be localized from the neck (C-3 or lower) to the inferior gluteal folds and spasm assessed during the Screening physical examination

Study design and treatment





Exclusion criteria

- Presence of acute or chronic back pain for the previous 8 days or longer, where back pain is present on more days than not
- Presence of neurogenic pain in the back, neck, upper or lower extremities, including pain from (or suspected from) nerve root compression or injury (radicular pain or "pinched nerve") or neuropathic pain. Evidence of these types of exclusionary pain includes radiation of pain that radiates beyond the back, chronic pain, and pain associated with abnormal sensation or loss of sensation in the back or extremities
- Presence of pain anywhere other than the target back pain that is bothersome, interferes with activity, or for which pain relief is taken
- History of any neck, back, or pelvic surgery
- History within the previous 3 years of: spinal fracture or spinal infection; inflammatory arthritis; degenerative spine disease; or any other back or spine condition that may reasonably contribute to current back pain
- Subjects who are currently taking medications that are moderate to potent inhibitors of cytochrome P450 (CYP) isozymes CYP2D6 and are unable or unwilling to stop taking the medication for the duration of the clinical study, which are likely to cause drug interactions with tolperisone HCl (e.g., medications such as paroxetine and fluvoxamine)
- Subjects who are unable or unwilling to stop using any medication or dietary supplement to promote sleep, including over-the-counter sleep medications, during their participation in the study

Outcome measures/end points

Primary endpoint

- Subject-rated pain "right now" due to acute back spasm using a NRS (0-10 scale, from no pain to worst possible pain) on Day 14

Key secondary endpoint

- Subject-rated pain "right now" due to acute back spasm using an NRS on Day 4

Other Secondary Endpoints

- Subject-rated average pain "last hour" due to acute back spasm using an average daily (am/pm) NRS over Days 1 to 4
- Subject-rated average pain "last hour" due to acute back spasm using an average daily (am/pm) NRS over Days 1 to 7
- Time to relief of pain due to acute back spasm, defined as first occurrence of a subject-rated NRS (0-10 scale) equal to 2 or lower from subject-rated average pain "last hour" assessed on Days 1 to 14
- Patient's Global Impression of Change (PGI-C) from baseline (1-7 scale, from very much worse to very much improved) on Day 4 and Day 14
- Clinician's Global Impression of Change (CGI-C) from baseline (1-7 scale from very much worse to very much improved) on Day 4 and Day 14
- Oswestry Disability Index questionnaire (10 questions with one answer each for pain intensity, personal care, lifting, walking, sitting, standing, sleeping, sex life [if applicable], social life, and traveling) on Days 4 and 14

Glossary
ePRO: Electronic patient reported outcomes; NRS: Numerical Rating Scale; TID: Three time daily

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