TNX-102 SL* for Treatment of Fibromyalgia: Approaches to Pain Measurement

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Introduction

- TNX-102 SL is a novel sublingual investigational formulation of low dose (2.8 mg) cyclobenzaprine designed for rapid absorption and routine bedtime use.
- We recently completed a Phase 2b trial (BESTFIT) of TNX-102 SL, which was the first large scale evaluation of this therapeutic approach in fibromyalgia patients.
- In addition to assessments of the efficacy of TNX-102 SL in reducing symptoms of fibromyalgia, we explored various methodological approaches to evaluation of changes in patient reported symptoms.

Methods

BESTFIT Study Characteristics and Endpoint Measures

- BESTFIT = Bedtime Sublingual TNX-102 SL as Fibromyalgia Intervention Therapy
- 12-week, randomized, double-blind, placebo-controlled study in patients diagnosed with fibromyalgia by 2010 ACR criteria
- 201 participants in 17 centers in the United States
- Placebo (n=102)
- TNX-102 SL 2.8 mg (n=103)

Primary efficacy endpoint

- Mean change from baseline in the daily diary pain score during week 12
- 11-point (0-11) Numerical Rating Scale (NRS) to assess prior 24-hour average pain intensity

Key secondary efficacy endpoints

- Patient Global Impression of Change (PGIC)
- Fibromyalgia Impact Questionnaire-Revised (FIQ-R)
- Daily Sleep Diary
- PROMIS Sleep Disturbance Instrument

Safety Evaluation
- Adverse events
- Oral adverse events

Change from Baseline (CFB) in Mean Pain over 12 Weeks Was Numerically Lower for TNX-102 SL Than for Placebo (MMRM)

Responder Analysis versus Mean Pain Analysis Has More Clinical Relevance and Greater Statistical Significance in Certain Cases

Hypothetical Clinical Trial Result

- Quadratic fitting normalizes anomalies that may occur in continuous responder analysis on FIQ-R total score at week 12

- In BESTFIT, TNX-102 SL had a significant effect on 30% responder rate but not mean pain change from baseline (CFB) in mean pain over 12 weeks

- Regulators have recognized that responder analyses have face validity and are a viable alternative to mean change analyses to determine therapeutic efficacy

Conclusions

- To convey the benefits of a pain medication to patients and physicians, responder analysis is more clinically relevant and comprehensible than change from baseline.
- Change from baseline analysis is often preferred because it generally has more power to detect a treatment effect, thus necessitating fewer patients in the study.
- Using predicted pain score values for response categorization of individual patients may improve the statistical significance of the response rates.
- TNX-102 was significantly better than placebo on the pain responder rates determined using the pain numeric rating scale.
- The most common local adverse event was transient tongue or mouth numbness occurring in 42% of treated patients. No systemic adverse events were noted in ≤5% of treated patients.
- Regulators have recognized that responder analyses have face validity and are a viable alternative to mean change analyses to determine therapeutic efficacy.

References


*TNX-102 SL is an Investigational New Drug and has not been approved for any indication.