NYX-2925 impacts functional and chemical neuroimaging biomarkers and patient-reported outcomes of pain in patients with fibromyalgia

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Background

Fibromyalgia (FM) is a chronic, debilitating disease typified by widespread musculoskeletal pain, accompanied by fatigue, sleep disturbance, memory issues, and mood disorders. FM has been described as the prototypical centralized chronic pain syndrome.

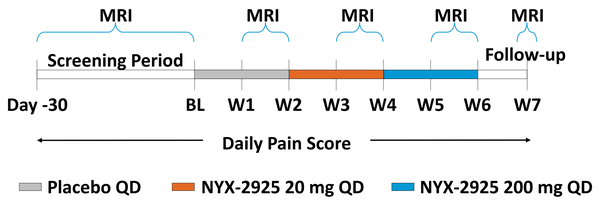
NYX-2925 is a novel, non-opioid small-molecule modulator of the N-methyl-D-aspartate receptor (NMDAR). NYX-2925 is Phase 2 development for FM and painful diabetic peripheral neuropathy.

Methods

An exploratory, placebo-controlled neuroimaging clinical trial was conducted in 22 right-handed female subjects with FM according to ACR 2010 criteria.

Following a screening period, all subjects received 2 weeks of placebo once-daily (QD), followed by 2 weeks of 20 mg NYX-2925 QD, followed by 2 weeks of 200 mg NYX-2925 QD in fixed sequence.

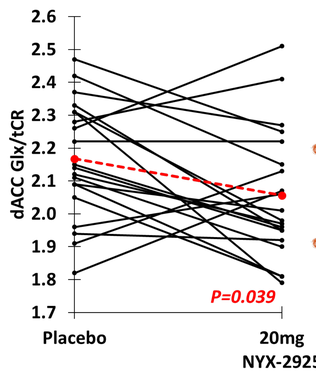
Subjects underwent resting state functional connectivity magnetic resonance imaging (rs-fcMRI) and proton magnetic resonance spectroscopy (^{1}H-MRS) as shown below. Subjects and neuroimaging analysts were blinded to study drug sequence.



Results

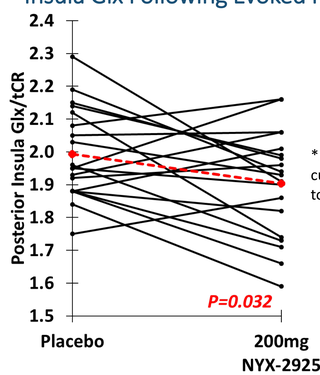
Compared to placebo, NYX-2925 produced statistically significant reductions of glutamate and glutamine (Glx) in key pain-regulating brain regions, although effects varied between doses.

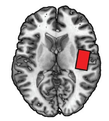
NYX-2925 Reduces Basal Levels of dACC Glx



- dACC: dorsal anterior cingulate cortex, a pronociceptive brain region
- Glx/tCR: glutamate & glutamine ratio/total creatine, a marker of excitatory neural activity

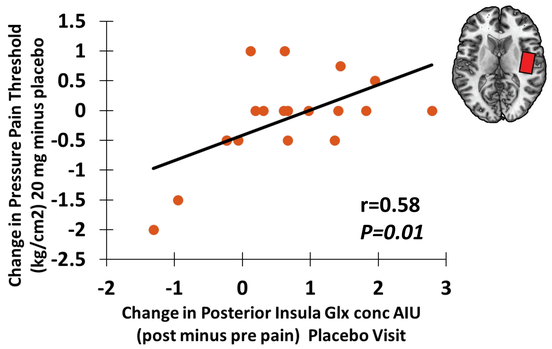
NYX-2925 Reduces Resting Posterior Insula Glx Following Evoked Pain*



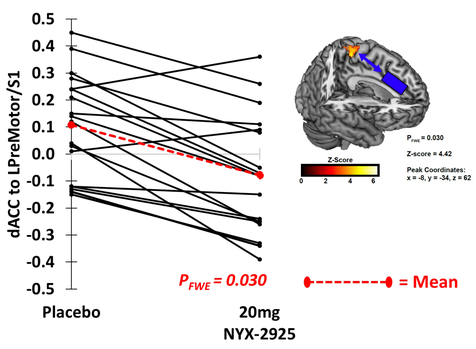


*Pain was evoked by cuff pressure applied to the left calf.

Greater concentrations of pain-evoked Glx in posterior insula at baseline was associated with greater reductions in pain sensitivity following treatment.

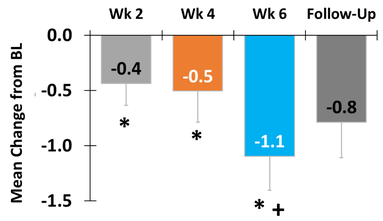


NYX-2925 (20 mg) administration resulted in reduced connectivity between pain-related brain regions, including connectivity between dACC and primary somatosensory cortex.

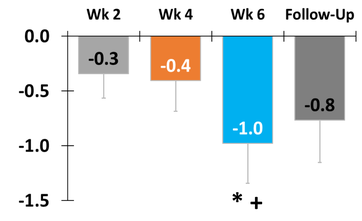


Clinically meaningful and statistically significant improvements were observed following treatment with NYX-2925 compared to baseline (BL) and placebo (Wk 2) for pain and quality of life measures.

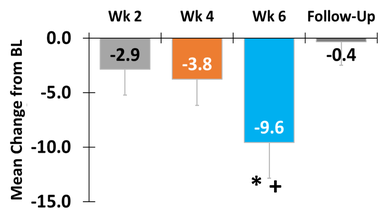
Average Daily Pain



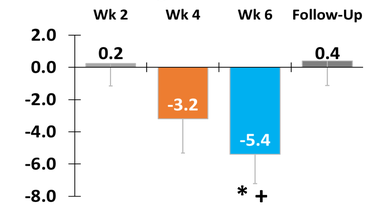
Worst Daily Pain



Total FIQR Score



PROMIS$_{FM}$ Total Fatigue Profile Score



Placebo QD | NYX-2925 20 mg QD | NYX-2925 200 mg QD

* p < 0.05 vs baseline (BL); + p < 0.05 vs placebo

In the study, NYX-2925 was safe and well tolerated with no discontinuations due to treatment-emergent adverse events (TEAE). No serious adverse events were reported. The most commonly reported adverse events were abdominal distension (reported by 3 subjects) and anxiety, diarrhea, eructation, tension headache, and upper respiratory tract infection (each reported by 2 subjects).

Conclusions

- In this exploratory study, NYX-2925 demonstrated antinociceptive activity in neuroimaging evaluations.
- Clinically meaningful and statistically significant improvements were also observed in pain, fatigue, the overall intensity of fibromyalgia symptoms, and their impact on function.
- These data support further evaluation of NYX-2925 for the treatment of fibromyalgia.

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