

Improvements in Pain Associated with Fibromyalgia: Results from 3 Clinical Trials of Milnacipran

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Purpose

Chronic widespread musculoskeletal pain is the hallmark symptom of fibromyalgia (FM) and can contribute to significant impairment in multidimensional function and reduced quality of life. Milnacipran, a dual serotonin-norepinephrine reuptake inhibitor, is approved for the management of FM. In FM clinical trials conducted to date, milnacipran produced statistically significant improvements in the primary composite responder endpoints, as well as pain and multiple additional symptoms (ie, fatigue, global status, and physical functioning). The objective of this study is to further characterize the effect of milnacipran on pain in these trials.

Method

Data from 3 months of treatment were analyzed from 3 FM trials (Study 1, N=888; Study 2, N=1196; Study 3, N=1025). In these studies, patients were randomized to placebo, milnacipran 100 mg/day (all studies), or milnacipran 200 mg/day (Studies 1 and 2 only). Pain data included 5 VAS measures collected via an electronic diary at various recall intervals (daily, weekly, or real-time) or by paper or computerized methods at each study visit (daily and weekly recall). Study 3 also used the Brief Pain Inventory (BPI), administered at each study visit, to assess improvements in various aspects of pain.

Results

Analysis of observed cases at 3 months showed that milnacipran treatment of patients with FM resulted in improvements in all 5 VAS pain measures with both doses in all studies. All improvements were significant compared with placebo ($P < .05$) except for the 100 mg/day arm in Study 1, in which the effect size was similar but the treatment arm was underpowered to detect differences with placebo, due in part to the proscribed randomization for the trial. Significant improvements in BPI pain interference and average pain severity scores were observed with milnacipran 100 mg/day compared with placebo (Study 3; $P < .001$). Milnacipran treatment resulted in a significant reduction in pain scores compared with placebo during the second week of double-blind treatment, which was sustained through the 3-month endpoint. Additionally, a higher percentage of milnacipran-treated patients compared with placebo reported a $\geq 30\%$ reduction from baseline in pain scores in all 3 studies ($P < .01$).

Conclusions

In 3 large FM clinical trials, milnacipran consistently resulted in significant and sustained pain improvements over placebo across a variety of pain measures.