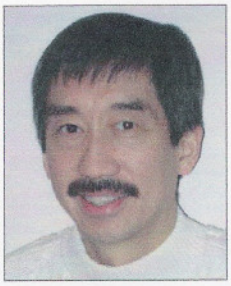
EXPERT COMMENTARY



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The study by Crofford et al outlined here was the first pivotal RCT demonstrating clinical efficacy for pregabalin, the first medication indicated in Canada for the management of pain associated with FM in adults. This study of 529 patients was conducted over eight weeks. Patients were pre-screened carefully using well-known outcome measures (including the VAS scale for pain and a physical examination documenting the ACR's criteria for diagnosing FM).

Efficacy was demonstrated with pregabalin 450 mg/d for the primary endpoints of a drop in the VAS for pain. The results were rapid, with improvements noted over the first week.

A dose-related increase in adverse events and withdrawals due to adverse events was observed.

First Study of Pregabalin in Fibromyalgia

Crofford LJ, et al. Pregabalin for the treatment of fibromyalgia syndrome. Results of a randomized, double-blind, placebo-controlled trial. Arthritis Rheum 2005; 52(4):1264-73.

OBJECTIVES AND METHODS

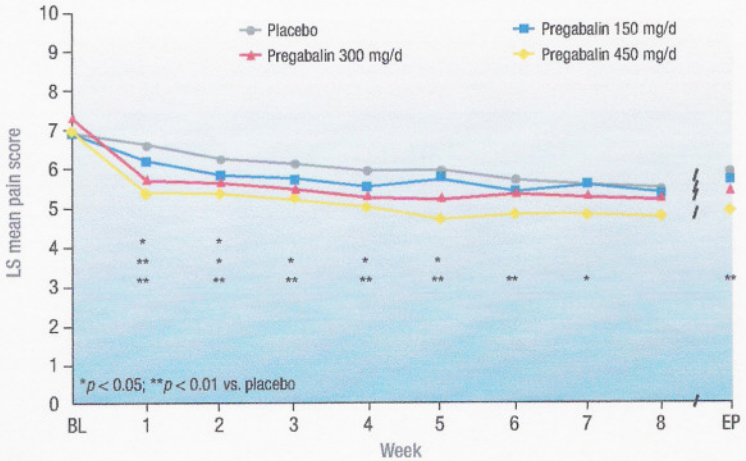
- To compare the effects of placebo with those of pregabalin (150, 300 or 450 mg/d) on pain and pain-related sleep difficulties in patients with fibromyalgia (FM)
- 529 patients (with FM by ACR criteria and a score of ≥ 40 on the pain Visual Analogue Scale) randomized to receive pregabalin (150 mg/d, 300 mg/d or 450 mg/d) or placebo, administered three times daily for 8 weeks*
  - acetaminophen up to 4 g/d was permitted as needed for pain relief
- Primary outcome: comparison of endpoint mean pain scores, derived from daily diary ratings of pain intensity, between each treatment group and the placebo group
- Secondary measures: daily patient diaries to record pain intensity and pain-related sleep quality; Medical Outcomes Study (MOS)-Sleep measure at baseline and endpoint; Patient Global Impression of Change (PGIC) at endpoint

*The recommended dosage in FM patients is 300 to 450 mg/d in two divided doses.

KEY RESULTS

- Endpoint mean pain score was significantly lower in the pregabalin 450 mg/d group vs. placebo ($p = 0.0009$)
  - score decreased from overall mean baseline of 7.0 to 4.94 with pregabalin 450 mg/d and to 5.88 with placebo

Weekly and endpoint mean pain scores

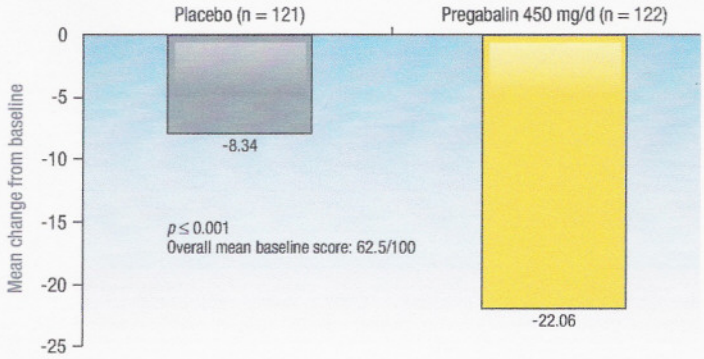


- Weekly mean pain scores: significant improvement with pregabalin 450 mg/d vs. placebo at week 1, maintained through week 7 ($p < 0.05$)
  - scores relative to placebo at each week starting with week 1: -1.2, -0.9, -0.9, -0.9, -1.2, -0.8 and -0.8
- Significantly more patients in the pregabalin 450 mg/d group vs. placebo had ≥ 50% improvement in pain from baseline at endpoint (29% vs. 13%; $p = 0.003$)

DISCUSSION AND CONCLUSION

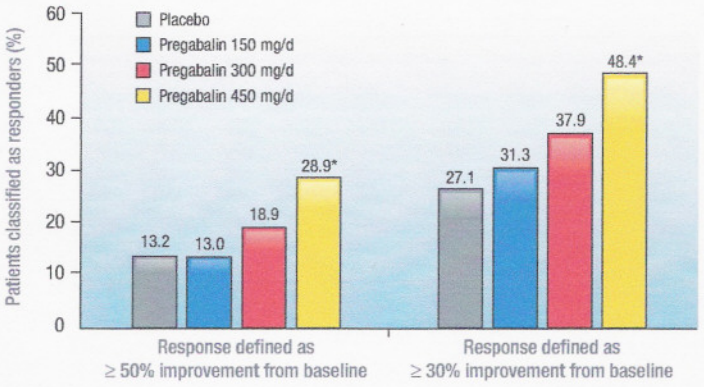
- Pregabalin 450 mg/d was efficacious for the treatment of FM, reducing symptoms of pain and pain-related sleep disturbances vs. placebo
- These data support further study of this agent for treatment of patients with FM

Mean changes from baseline in MOS-Overall Sleep Problems Index**



** The MOS-Overall Sleep Problems Index groups items from the domains of the MOS-Sleep Scale, a 12-item assessment of sleep disturbance, sleep adequacy, somnolence, quantity of sleep, snoring, and awakening short of breath/with a headache

Proportion of responders per treatment group



*$p < 0.003$ vs. placebo