Effects of Milnacipran Added to Pregabalin on Cognition and Mental Clarity in Fibromyalgia Patients

Introduction
Cognitive dysfunction, also sometimes referred to as fibrofog, is a common symptom in patients with fibromyalgia (FM). The cognitive functions most often affected in FM are working memory, episodic memory, and semantic memory; other effects include impairment of attentional control, short-term memory loss in the face of distraction, and slower access to words in the mental lexicon. The Mental Clutter Scale, a new 16-item measure of fibrofog, is currently being developed to differentiate the memory loss in FM patients from two main dimensions of cognition and mental clarity. The Mental Clutter Scale has been previously shown to be an acceptable measure of fibrofog.

Objective
To measure the effect of milnacipran on self-reported cognitive abilities in patients with FM receiving pregabalin in an open-label study.

Methods
Study Overview
- Male or female outpatients, ages 18 to 70
- FM diagnosis per 1990 ACR criteria
- Multicenter, randomized, open-label, controlled study

Study Design
To measure the effect of milnacipran on self-reported cognitive abilities in patients with FM receiving pregabalin in an open-label study.

Randomized Treatment Period
- Incomplete responders to PGN were randomized on an open-label basis at a 1:1 ratio to either have milnacipran (MLN) 100 mg/day added to their PGN treatment or continue monotherapy with PGN 300 or 450 mg/day (Figure 1).

Key Inclusion Criteria
- FM diagnosis per 1990 ACR criteria
- Male or female outpatients, ages 18 to 70

Study Patients
- All patients continued to receive PGN 300 or 450 mg/day
- All patients underwent a 1-week dose escalation (LOCF) approach

Study Patients
- Baseline demographics were similar between the randomized groups (Table 1).

Table 1. Patient Demographics at Randomization

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No Treatment Added</th>
<th>MLN Added</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean years</td>
<td>58.6</td>
<td>58.7</td>
</tr>
<tr>
<td>Height, mean in</td>
<td>64.9</td>
<td>64.7</td>
</tr>
<tr>
<td>Weight, mean lb</td>
<td>187.8</td>
<td>184.5</td>
</tr>
</tbody>
</table>

Statistical Analyses
- All items are scored on a 1 to 10 scale, with 1 as the best rating, and 10 as the worst.
- All analyses were performed using the intention-to-treat (ITT) population at the beginning of the randomized treatment period.

Conclusions
- Milnacipran resulted in significant improvements in the cognitive impairment measured by the fibrofog scale in patients receiving pregabalin, as measured by a new self-report assessment instrument to measure cognition and mental clarity.
- The Mental Clutter Scale was effective in distinguishing between-group differences in cognitive improvements, suggesting its utility in the assessment of perceived cognitive impairment in fibromyalgia patients.

References
2. Forest Research Institute, Jersey City, New Jersey
3. R.Michael Gendreau3 Ian D’Souza2
4. All of the Mental Clarity Subscale domain scores were significantly reduced in patients treated with MLN added to PGN when compared with those treated with PGN alone (Figure 5).

Figure 1. Study Overview

Figure 2. Change From Baseline in Mental Clutter Full Scale Score

Figure 3. Change From Baseline in Cognitive and Mental Clarity Subscales at Expanded

Figure 4. Change From Baseline in Cognitive and Mental Clarity Subscales at Expanded

Figure 5. Mean Change From Baseline in Mental Clarity Subscale Domain Scores

Figure 6. Forest Laboratories, Inc. and Cypress Bioscience, Inc. were involved in the study design, collection, analysis, interpretation of data, and preparation, review, and approval of the manuscript.

Figure 7. Presented at the American Academy of Neurology Annual Meeting.

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