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Linking Changes in Pain Severity to Other Outcomes in Patients With Posttraumatic Peripheral Neuropathic Pain Treated With Pregabalin

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To evaluate the relationship between changes in pain severity and changes in patient-reported outcomes (PROs) in patients with posttraumatic peripheral neuropathic pain (PT-PNP) treated with pregabalin in a 8-week, double-blind, randomized, placebo-controlled study.

METHODS

Objectives

• To evaluate the relationship between changes in pain severity and changes in patient-reported sleep disturbance, pain interference with daily function, and anxiety and depression in patients with posttraumatic peripheral neuropathic pain

Background

• Chronic pain impacts many aspects of patients’ lives, including daily functioning, sleep, and mood
• Numerous patient-reported outcome (PRO) measures have been developed to assess pain severity and other outcomes in clinical trials of chronic pain

Assessment of daily function and mood is recommended in clinical trials of chronic pain, while assessment of sleep is not specifically recommended, but is justified by strong evidence for an adverse effect of pain on sleep.

• Understanding the relationship between changes in pain severity and impact on daily function, mood, and sleep disturbance may help inform treatment decisions and set patient expectations for impact of analgesic therapy

Design

• This is a secondary analysis of data derived from a randomized, double-blind, placebo-controlled, 8-week, clinical trial of flexible-dose pregabalin in patients with posttraumatic peripheral neuropathic pain

Patients

• All patients with data from the clinical trial were included in this analysis regardless of treatment allocation or effects

Assessments

• Average weekly score on the numeric rating scale (NRS; 0 = no pain to 10 = worst possible pain) was determined daily by patients

• Pain Severity Index (PSI; 0–100) (0 = no pain to 100 = worst possible pain) and Pain Interference Index (PII; 0–100) (0 = no interference to 100 = completely interferes) were determined from the modified Brief Pain Inventory (BPI), which was used to assess severity and interference with daily function

• Hospital Anxiety and Depression Scale (HADS) anxiety (HADS-A) and depression (HADS-D) subscales were determined based on 1-week recall

• Medical Outcomes Study Sleep-Scale (MOS-SS-SIS-II) 8-item Sleep Problems Index and 6-item sleep disturbance subscale were determined based on 24-hour recall

Analyses

• Changes from baseline to end of treatment at week 8 in PRO scores were evaluated as a function of the change in pain NRS score over the same period

• Linear regression models were used to evaluate the relationship between change in pain and PROs

• Mean changes in PROs were estimated for a 2-point improvement in pain severity score (a clinically meaningful improvement)

• Four sensitivity analyses were performed

• Patients with <25% pain response

• Patients with <50% pain response

• Patients treated with pregabalin

• Patients treated with placebo

• Analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, North Carolina, USA)

• PD-03 was considered statistically significant

RESULTS

• Main results have been reported elsewhere

• Patients (n=55) had a mean age of 51.7 years and 50.8% were female (Table 1)

• Table 1. Patient Demographic and Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Placebo (n=127)</th>
<th>Pregabalin (n=127)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y) Mean (SD)</td>
<td>51 (13)</td>
<td>52 (14)</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>52 (40.9)</td>
<td>77 (60.6)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>120 (94.5)</td>
<td>124 (97.6)</td>
</tr>
<tr>
<td>Mean age (y)</td>
<td>51.71 (13.43)</td>
<td>52.53 (14.26)</td>
</tr>
<tr>
<td>Nerve injury, n (%)</td>
<td>12 (9.4)</td>
<td>8 (6.3)</td>
</tr>
<tr>
<td>Surgical, n (%)</td>
<td>41 (32.3)</td>
<td>44 (34.6)</td>
</tr>
<tr>
<td>NSAIDs/COX-2, n (%)</td>
<td>46 (36.2)</td>
<td>57 (44.9)</td>
</tr>
<tr>
<td>TCAs, n (%)</td>
<td>39 (30.7)</td>
<td>41 (32.3)</td>
</tr>
<tr>
<td>Opioids, n (%)</td>
<td>15 (11.8)</td>
<td>20 (15.8)</td>
</tr>
<tr>
<td>Tramadol, n (%)</td>
<td>41 (32.3)</td>
<td>42 (33.1)</td>
</tr>
</tbody>
</table>

• Linear relationships were observed between change in patient-reported sleep disruption (Figure 1), pain interference in daily function (Figure 2), and anxiety and depression symptoms (Figure 3) as a function of changes in pain severity on the NRS

• The derived plots can be interpreted as showing, at the individual patient level, the mean change in PRO scores (y-axis) that can be expected with the various incremental changes in pain severity (x-axis)

• For example, a 2-point decrease in pain corresponded to an estimated 7.6-point decrease in the MOS-SS-SIS-II Sleep Problems Index (1.1-point decrease in MOS-SS-SIS-II Sleep Disturbance, and 1.6-point decrease in sleep interference (Figure 2))

• A 2-point decrease in pain was associated with an estimated 1.5-point decrease in pain interference on daily function (Figure 2)

• Significant associations between change in pain severity and change in each PRO were observed (Figures 4–6; P<0.05)

• The mean improvements in sleep, pain interference on daily function, and mood outcome scores that correspond to a 2-point improvement in pain severity scores (a clinically important improvement) are shown in Table 2

• In general, the results of this analysis may be helpful in setting patient expectations for the benefit of analgesic treatment

CONCLUSIONS

• A clear relationship was observed between improvements in pain and improvements in patient-reported sleep, pain, anxiety, and depression in patients with chronic posttraumatic peripheral neuropathic pain

• The current analysis is the first study that demonstrates this set of relationships in patients with posttraumatic peripheral neuropathic pain

• Limited clinical studies provide a direct quantitative relationship between an incremental change in pain severity and the expected magnitude of change of a given PRO for an individual patient with posttraumatic peripheral neuropathic pain

• The results of this analysis may help in setting patient expectations for the benefit of analgesic treatment

References