Pregabalin for the Treatment of Men With Chronic Prostatitis/Chronic Pelvic Pain Syndrome

A Randomized Controlled Trial

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Background: Evidence suggests that the urogenital pain of chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) may be neuropathic.

Methods: This randomized, double-blind, placebo-controlled trial was conducted across 10 tertiary care centers in North America to determine whether pregabalin, which has been proved effective in other chronic pain syndromes, is effective in reducing CP/CPPS symptoms. In 2006-2007, 324 men with pelvic pain for at least 3 of the previous 6 months were enrolled in this study. Men were randomly assigned to receive pregabalin or placebo in a 2:1 ratio and were treated for 6 weeks. Pregabalin dosage was increased from 150 to 600 mg/d during the first 4 weeks. The primary outcome was a 6-point decrease in the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) total score. Multiple secondary outcomes were assessed.

Results: Of 218 men assigned to receive pregabalin, 103 (47.2%) reported at least a 6-point decrease in the NIH-CPSI total score at 6 weeks compared with 35.8% (38 of 106 men) assigned to receive placebo (P = .07, exact Mantel-Haenszel test, adjusting for clinical sites). Compared with the placebo group, men assigned to receive pregabalin experienced reductions in the NIH-CPSI total score and subscores (P < .05), a higher Global Response Assessment response rate (31.2% and 18.9%; P = .02), and improvement in total McGill Pain Questionnaire score (P = .01). Results for the other outcomes did not differ between groups.

Conclusion: Pregabalin therapy for 6 weeks was not superior to placebo use in the rate of a 6-point decrease (improvement) in the NIH-CPSI total score in men with CP/CPPS.

Trial Registration: clinicaltrials.gov Identifier: NCT00371033

Arch Intern Med. 2010;170(17):1586-1593
autonomic nervous systems, suggesting central nervous system sensitization.

Drugs found to be effective for treating neuropathic pain may prove beneficial in treating the symptoms of CP/CPPS. Pregabalin is an antiepileptic drug that has been approved for use in the chronic pain of postherpetic neuralgia, diabetic neuropathy, and fibromyalgia. We conducted a randomized clinical trial to determine whether pregabalin therapy reduces symptoms in men with CP/CPPS.

### METHODS

#### PARTICIPANTS

We recruited men from 10 tertiary care clinical centers in North America (Cleveland Clinic, Cleveland, Ohio; Harvard Medical School, Massachusetts General Hospital & Brigham and Women’s Hospital, Boston; Northwestern University, Chicago, Illinois; Queen’s University, Kingston, Ontario, Canada; Stanford University Medical Center, Stanford, California; Temple University, Philadelphia, Pennsylvania; University of California, Los Angeles/King Drew University, Los Angeles; University of Maryland, Baltimore; University of Mississippi, Jackson; and University of Washington, Seattle). The protocol was approved by the institutional review board at each participating institution, and written informed consent was obtained from each participant. Participants were enrolled consecutively at each site. Men were eligible for the study if their age was at least 18 years, they reported symptoms of discomfort or pain in the pelvic region during at least 3 of the previous 6 months, and they had a total score of at least 15 of 43 on the National Institutes of Health Chronic Prostateitis Symptom Index (NIH-CPSI) at screening and randomization visits approximately 2 weeks apart. The exclusion criteria included a calculated creatinine clearance less than 60 ml/min/1.73 m² (to convert to milliliters per second per square meter, multiply by 0.0167), a platelet count less than 100,000 x 10³/µL (to convert to x 10⁶ per liter, multiply by 1.0), allergy to any antiseizure medication, known sensitivity to pregabalin, treatment with thiazolidinediones or antidiabetic agents, New York Heart Association class III or IV congestive heart failure, a history of thrombocytopenia or bleeding diathesis, and a history of alcohol abuse. Participants were not excluded if they had previous treatment for CP/CPPS or for taking analgesics for another condition if they were considered for use in the chronic pain of postherpetic neuralgia, diabetic neuropathy, and fibromyalgia. We conducted a randomized clinical trial to determine whether pregabalin therapy reduces symptoms in men with CP/CPPS.

#### STUDY DESIGN

Eligible participants were randomly assigned 2:1 in each clinical site via a centrally controlled Web-based data management system to receive treatment with either pregabalin or matching placebo using a permuted block randomization procedure with randomly assigned block sizes of 3, 6, and 9. Treatment dosage was escalated as follows: 150 mg/d (50 mg orally 3 times daily) for 2 weeks, then 300 mg/d (100 mg orally 3 times daily) for 2 weeks, and then 600 mg/d (200 mg orally 3 times daily) for 2 weeks. Men assigned to receive placebo underwent a similar escalation in the number of capsules prescribed. If a participant could not tolerate a scheduled dose increase, he was allowed to remain at the previously tolerated dosage. Study investigators and participants were unaware of treatment assignment. Percentage adherence to treatment was calculated by taking the mean of the percentage of capsules taken based on capsule counts reported by the participants at the 2-, 4-, and 6-week contacts.

Adverse events (AEs) were evaluated by means of standardized queries at each study contact, including telephone calls at weeks 2 and 4 and a clinic visit at week 6. All adverse signs and symptoms and preexisting conditions that worsened, whether considered related to the study drug, were reported and were graded according to Medical Dictionary for Regulatory Activities version 6.0 criteria.

### OUTCOMES

The primary outcome was response, defined as a decrease (improvement) in the NIH-CPSI score of at least 6 points from baseline to week 6. The NIH-CPSI measures the 3 key domains of CP/CPPS: pain (location, frequency, and severity; possible score, 0-21), urinary symptoms (irritative and obstructive; possible score, 0-10), and impact/quality of life (possible score, 0-12), for a total possible score of 0 to 43. A 6-point decrease in NIH-CPSI score has been shown to be clinically perceptible in previous clinical trials of men with CP/CPPS.

Men who withdrew from the study before primary outcome at 6 weeks were considered nonresponders and were included in the denominator for determining the primary outcome response rate in an intent-to-treat analysis. Several secondary outcomes were assessed, including the Global Response Assessment (GRA). The GRA is a 7-question patient self-reported assessment that measures perception of change in symptoms (improvement, no change, or deterioration). The responses are centered at zero (no change in symptoms). It has been used as a primary end point for trials of intrstitial cystitis (IC) and has been adopted for use in trials of CP/CPPS. Changes in the GRA correspond to changes in all the major symptom indices used for trials in IC and CP/CPPS.

Men who reported that they were moderately or markedly improved on a 7-point GRA at the end of the study were identified as treatment responders for this secondary outcome. Comparison of the GRA between treatment arms includes men who withdrew early (3 in the placebo group and 8 in the pregabalin group), as prespecified in the Data Analysis and Monitoring Plan.

Other measures included the subscores of the NIH-CPSI (pain, urinary symptoms, and quality of life); the McGill Pain Questionnaire (ranges: 0-45 for total, 0-33 for sensory, and 0-12 for affective scores, with higher scores indicating greater pain); the Medical Outcomes Study 12-Item Short Form Health Survey (SF-12) (range, 0-100 for the Physical [PCS] and Mental [MCS] Component Summary scores, with the mean set at 50 and higher scores indicating better quality of life); the Hospital Anxiety and Depression Scale (HADS) (range, 0-42, with higher scores indicating greater anxiety and depression); and the Sexual Health Inventory for Men (SHIM) (range, 1-25, with higher scores indicating better sexual function).

### DATA MANAGEMENT AND STATISTICAL METHODS

Descriptive statistics were computed by treatment arm at baseline randomization for demographics, selected medical history measures, and all the primary and secondary symptom measures. Distributions of baseline characteristics were compared between treatment groups using Fisher exact tests, exact Kruskal-Wallis tests (for ordered categories), or Wilcoxon rank sum tests. These tests were conducted primarily to evaluate the success of randomization, thereby identifying any imbalances that could potentially affect treatment arm comparisons.

All AEs were included in a safety analysis regardless of whether these events were considered by the investigator to be...
related to treatment. Conditions that were present at baseline but did not change were excluded from the AE analysis. Comparisons of overall AE rates were performed using the Kruskal-Wallis test after classifying each patient according to worst grade reported across all body systems. The AE rates were compared between treatment arms for any body system with more than 5% AEs in either arm by classifying each patient according to the worst grade reported in that specific body system.

The primary outcome analysis compared response rates between treatment arms using the exact conditional test version of the Mantel-Haenszel test to control for clustering by clinical center. For secondary efficacy outcomes, cross-sectional descriptive statistics and changes from baseline were calculated across time. Changes across time were presented only for those with complete data at all follow-up visits to aid in assessment of changes. Pooled rate differences (and their 95% confidence intervals) in response rates across clinical centers were calculated using the “metan” routine in STATA version 10 (StataCorp LP, College Station, Texas) to implement a Mantel-Haenszel estimator for the pooled rate difference across clinical centers. Sample size requirements for this trial were based on 90% power to detect a difference in response rates of 40% to 60% (effect size of 20%) in the primary outcome, defined as a decline of 6 points or more in the NIH-CPSI total score. The estimated response rate of 40% for the placebo group was based on additional analyses (Richard Landis, PhD, unpublished data, 2005) of the data from a previous CP/CPPS study. Using a 2-sided \( \alpha = .05 \) level of significance, a total of 318 participants (212 taking pregabalin and 106 taking placebo) were required. This proposed sample size included 15% inflation to compensate for clinical site variability and interim monitoring. An independent Data and Safety Monitoring Board established by the National Institute of Diabetes and Digestive and Kidney Diseases reviewed safety and efficacy data when 171 patients had reported the primary outcome; the board recommended continuation of the trial at that time.

### Table 1. Baseline Characteristics of the Participants by Treatment Arm

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pregabalin Arm</th>
<th>Placebo Arm</th>
<th>Total</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Randomized participants, No.</strong></td>
<td>218</td>
<td>106</td>
<td>324</td>
<td></td>
</tr>
<tr>
<td><strong>Evaluable participants, No.</strong></td>
<td>216</td>
<td>103</td>
<td>319</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>48.0 (13.0)</td>
<td>45.2 (12.2)</td>
<td>47.0 (13.1)</td>
<td>.09</td>
</tr>
<tr>
<td>Median (range)</td>
<td>47.0 (21-78)</td>
<td>46.0 (19-76)</td>
<td>47.0 (19-76)</td>
<td>.</td>
</tr>
<tr>
<td>Race, No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>North American Indian/North Native</td>
<td>1 (0.5)</td>
<td>3 (2.9)</td>
<td>4 (1.3)</td>
<td></td>
</tr>
<tr>
<td>Asian/Asian American</td>
<td>0</td>
<td>4 (3.9)</td>
<td>4 (1.3)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>24 (11.1)</td>
<td>14 (13.6)</td>
<td>38 (11.9)</td>
<td></td>
</tr>
<tr>
<td>Native Hawaiian/other Pacific Islander</td>
<td>0</td>
<td>1 (1.0)</td>
<td>1 (0.3)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>178 (82.4)</td>
<td>75 (72.8)</td>
<td>253 (79.3)</td>
<td>.17</td>
</tr>
<tr>
<td>Other</td>
<td>11 (5.1)</td>
<td>1 (1.0)</td>
<td>12 (3.8)</td>
<td></td>
</tr>
<tr>
<td>Multirace</td>
<td>2 (1.0)</td>
<td>4 (3.9)</td>
<td>6 (1.9)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>0</td>
<td>1 (1.0)</td>
<td>1 (0.3)</td>
<td></td>
</tr>
<tr>
<td>Educational level, No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than high school</td>
<td>5 (2.3)</td>
<td>2 (1.9)</td>
<td>7 (2.2)</td>
<td></td>
</tr>
<tr>
<td>High school/GED</td>
<td>30 (13.9)</td>
<td>17 (16.5)</td>
<td>47 (14.7)</td>
<td>.97</td>
</tr>
<tr>
<td>Some college</td>
<td>58 (26.9)</td>
<td>26 (25.2)</td>
<td>84 (26.3)</td>
<td></td>
</tr>
<tr>
<td>Graduated from college</td>
<td>78 (36.1)</td>
<td>35 (34.0)</td>
<td>113 (35.4)</td>
<td></td>
</tr>
<tr>
<td>Graduate school</td>
<td>45 (20.8)</td>
<td>23 (22.3)</td>
<td>68 (21.3)</td>
<td></td>
</tr>
<tr>
<td>Employment, No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>166 (76.9)</td>
<td>74 (71.8)</td>
<td>240 (75.2)</td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>12 (5.6)</td>
<td>13 (12.6)</td>
<td>25 (7.8)</td>
<td></td>
</tr>
<tr>
<td>Retired</td>
<td>27 (12.5)</td>
<td>11 (10.7)</td>
<td>38 (11.9)</td>
<td>.25</td>
</tr>
<tr>
<td>Full-time homemaker</td>
<td>1 (0.5)</td>
<td>0</td>
<td>1 (0.3)</td>
<td></td>
</tr>
<tr>
<td>Disabled</td>
<td>10 (4.6)</td>
<td>5 (4.9)</td>
<td>15 (4.7)</td>
<td></td>
</tr>
<tr>
<td>Annual family income, No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;$10 000</td>
<td>12 (7.1)</td>
<td>7 (8.4)</td>
<td>19 (7.5)</td>
<td></td>
</tr>
<tr>
<td>$10 001-$25 000</td>
<td>16 (9.4)</td>
<td>7 (8.4)</td>
<td>23 (9.1)</td>
<td></td>
</tr>
<tr>
<td>$25 001-$50 000</td>
<td>29 (17.1)</td>
<td>19 (22.9)</td>
<td>48 (19.0)</td>
<td>.70</td>
</tr>
<tr>
<td>$50 001-$100 000</td>
<td>64 (37.6)</td>
<td>25 (30.1)</td>
<td>89 (35.2)</td>
<td></td>
</tr>
<tr>
<td>&gt;$100 000</td>
<td>49 (28.8)</td>
<td>25 (30.1)</td>
<td>74 (29.2)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>46</td>
<td>20</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td>Ever diagnosis of IC, CP, or CPPS, No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>139 (64.4)</td>
<td>67 (64.4)</td>
<td>206 (64.4)</td>
<td>.99</td>
</tr>
<tr>
<td>No</td>
<td>77 (35.6)</td>
<td>37 (35.6)</td>
<td>114 (35.6)</td>
<td></td>
</tr>
<tr>
<td>Years since first diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>8.7 (9.5)</td>
<td>9.2 (9.2)</td>
<td>8.8 (9.4)</td>
<td>.62</td>
</tr>
<tr>
<td>Median (range)</td>
<td>5.2 (0.2-47.7)</td>
<td>6.0 (0-36.2)</td>
<td>5.3 (0-47.7)</td>
<td></td>
</tr>
<tr>
<td>Missing, No.</td>
<td>78</td>
<td>37</td>
<td>115</td>
<td></td>
</tr>
<tr>
<td>Years since first symptom began</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>10.3 (10.6)</td>
<td>9.9 (9.8)</td>
<td>10.2 (10.3)</td>
<td>.87</td>
</tr>
<tr>
<td>Median (range)</td>
<td>6.5 (0.5-48.7)</td>
<td>6.3 (0-40.8)</td>
<td>6.5 (0-48.7)</td>
<td></td>
</tr>
<tr>
<td>Missing, No.</td>
<td>49</td>
<td>22</td>
<td>71</td>
<td></td>
</tr>
</tbody>
</table>
RESULTS

BASELINE DATA

Recruitment began April 1, 2006, and ended on November 30, 2007. The treatment groups were well balanced with respect to baseline characteristics (Table 1). The mean (SD) age of the pregabalin group was 48.0 (13.0) years (age range, 21-78 years) compared with 45.2 (12.2) years (age range, 19-76 years) for the placebo group. There was no difference in racial composition between groups. Overall, 79.3% of participants were white, 11.9% were black, and the remaining 8.6% were multiethnic/multiracial or other. Educational level, employment status, and annual family income were also comparable between the 2 treatment arms. Of these men 56.7% were college graduates, 75.2% were employed, and 64.4% reported an annual family income exceeding $50 000.

In response to a urologic diagnosis question included in multiple National Institute of Diabetes and Digestive and Kidney Diseases–sponsored clinical trials, only 64.4% of participants in this study reported having ever been diagnosed as having IC, CP, or CPPS. Of those previously diagnosed, the mean (SD) symptom duration since diagnosis was 8.8 (9.4) years (range, 0-47.7 years). Of those reporting that they knew when their IC, CP, or CPPS symp-
toms began, the mean (SD) duration of symptoms was 10.2 (10.3) years (range, 0-48.7 years). None of these diagnosis or duration characteristics differed between treatment arms.

The NIH-CPSI total and domain scores are summarized by treatment arm in Table 1. For each of these measures, the 2 baseline scores were averaged to provide an overall baseline score to which follow-up scores were compared. The mean (SD) NIH-CPSI total score was 26.1 (5.7) (range, 15.0-43.0). Furthermore, at baseline, the SF-12 mean (SD) PCS score was 44.9 (10.1) (range, 17.9-64.3), and the mean (SD) MCS score was 41.8 (10.6) (range, 12.2-62.0), indicating lower-than-average quality of life. None of these baseline symptom scores differed between treatment arms.

PARTICIPANT FOLLOW-UP AND ADHERENCE

Of the 324 randomized participants, 313 (96.6%) completed 6 weeks of follow-up through the primary end-point visit (Figure 1). Of the 11 withdrawals, 8 were treated with pregabalin (3.7% of that group) and 3 were treated with placebo (2.8% of that group) ($P = .62$, log rank test). All the participants were included in the intent-to-treat analysis. Of the 313 individuals who completed the
Table 2. Adverse Events Reported by at Least 5% of Participants in Either Arm

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Pregabalin Arm, %</th>
<th>Placebo Arm, %</th>
<th>P Valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constitutional symptoms</td>
<td>24.3</td>
<td>20.8</td>
<td>.57</td>
</tr>
<tr>
<td>Neurologic symptoms</td>
<td>38.5</td>
<td>22.6</td>
<td>.01</td>
</tr>
<tr>
<td>Gastrointestinal disturbance</td>
<td>19.3</td>
<td>18.9</td>
<td>.99</td>
</tr>
<tr>
<td>Ocular/visual symptoms</td>
<td>6.9</td>
<td>2.8</td>
<td>.20</td>
</tr>
<tr>
<td>Renal/genitourinary symptoms</td>
<td>5.5</td>
<td>1.9</td>
<td>.16</td>
</tr>
<tr>
<td>Pain</td>
<td>17.4</td>
<td>33.3</td>
<td>.003</td>
</tr>
</tbody>
</table>

aFisher exact test.

SAFETY

Overall, 59.0% of the participants (191 of 324) reported at least 1 AE, classified primarily as mild (83 of 324 [25.6%]) or moderate (79 of 324 [24.4%]) in severity. There were no serious AEs. There was no difference in the overall distribution of AEs between treatment arms (P = .40). Categories for which at least 5% of participants reported AEs in either arm are summarized in Table 3. The pregabalin arm had more neurologic AEs than did the placebo arm (P = .01), whereas the placebo arm had more pain AEs than did the pregabalin arm (P = .003). Headache was the most common pain, with 10 patients taking pregabalin (4.6%) and 18 taking placebo (17.0%) reporting this AE.

Efficacy/Primary Outcome

Of men assigned to the pregabalin group, 47.2% (103 of 218) were responders (a ≥6-point drop in the NIH-CPSI total score) compared with 35.8% (38 of 106) of men assigned to the placebo group (P = .07, exact Mantel-Haenszel test, controlling for clinical sites) (Table 4).

Secondary Outcomes

Of the men who were assessed at 6 weeks, the NIH-CPSI total score decreased by a mean of 6.0 points in the pregabalin arm and 4.2 points in the placebo arm (median, 5.1-point decrease for pregabalin and 2.5-point decrease for placebo, P = .01). Similar results were observed for each of the 3 NIH-CPSI subscores, with improvements of 3.3 (pregabalin) and 2.2 (placebo) of 21 points for the pain subscore (P = .04), 1.2 (pregabalin) and 0.6 (placebo) of 10 points for the urinary symptoms subscore (P = .01), and 2.1 (pregabalin) and 1.4 (placebo) of 12 points for the quality-of-life subscore (P = .02) (Figure 2).

The GRA response rate was significantly higher in men treated with pregabalin (31.2%) compared with placebo (18.9%) (P = .02). For this comparison, missing or withdrawn participants were considered nonresponders. Men treated with pregabalin showed more improvement than did those receiving placebo in the McGill Pain Questionnaire total score (P = .01), indicating more improvement in the pregabalin group for the sensory (P = .03) and affective (P = .02) subdomains. There were no differences between the pregabalin and placebo groups in SF-12 (P = .34 for PCS and P = .22 for MCS), HADS (P = .36), or SHIM (P = .40) scores.
COMMENT

Among men with long-standing CP/CPPS who had been treated previously for this condition, a 6-week course of pregabalin compared with placebo did not result in a statistically significant reduction in the NIH-CPSI total score by at least 6 points, the primary outcome, an amount of change previously shown to be clinically perceptible to participants. The results of most of the secondary outcomes should be interpreted with caution because only men who completed the 6-week treatment schedule were analyzed. However, for the GRA analysis, men who did not complete the study were considered nonresponders, thereby maintaining an intent-to-treat analysis and minimizing bias introduced by analyzing only men who completed the study.

The reason for the discrepancy between the results for the primary outcome and the GRA is unclear. The underlying NIH-CPSI continuous scales demonstrated “shifts” in efficacy across the entire distribution of the changes (from baseline to 6 weeks) in the total score and each subscore (pain, urinary symptoms, and quality of life) that was not detected at the same level of statistical significance when dichotomizing the change. This slight loss in power attenuates the P value from .01 to .04 for continuous end points to .07 for the dichotomous primary outcome. Although the GRA response (also a dichotomous measure) attained statistical significance, the GRA placebo rate was only 19% compared with 36% for the 6-point decrease in the NIH-CPSI total score criterion for response. The GRA may provide a more comprehensive evaluation of a patient’s overall condition than the condition-specific symptoms measured using the NIH-CPSI. A variety of secondary outcomes, including SF-12, SHIM, and HADS scores, did not differ between treatment arms, suggesting that not all relevant aspects of CP/CPPS may be treated with pregabalin.

Sensitivity analyses from previous clinical trials showed that although a 4-point decrease in the NIH-CPSI total score is clinically perceptible, a 6-point decrease provides a more robust indication of perceived improvement. Although a 4-point decrease was used in another clinical trial for CP/CPPS,27 we chose a 6-point decline in the NIH-CPSI total score as the primary outcome to correspond to a potentially greater clinical ben-
efit that would likely outweigh the possible risk that pregabalin therapy might pose from AEs. The dose range was chosen based on previous trials showing the beneficial dose of pregabalin to be 300 mg/d for postherpetic neuralgia and diabetic neuropathy and 450 mg/d for fibromyalgia. Pregabalin therapy proved safe in the present population. Although 59.0% of participants reported AEs, all were mild or moderate in severity, and the overall incidence was similar in the 2 treatment arms. Neurologic AEs were more common in the pregabalin group, but the rate was not dose related.

This trial has several limitations. Participants had longstanding symptoms; it is possible that patients with a shorter duration of symptoms may respond differently. Therapy was for 6 weeks only. It may take a longer period of treatment before a beneficial effect is seen. However, previous trials of pregabalin in other disorders have demonstrated an improvement in pain after only several days of treatment. There were several positive features of this study. This group of participants with longstanding symptoms represents the most difficult group of men with CP/CPPS to treat. We used the NIH-CPSI, which is a validated outcome measure designed specifically for use in trials of CP/CPPS. We also used a wide range of secondary outcomes that have been shown to be important in CP/CPPS and also gave valuable information on differences in response between treatment arms.

In summary, 6 weeks of treatment with an increasing dosage of pregabalin up to 600 mg/d did not produce a clinically significant (6-point) decrease in a condition-specific symptom index for CP/CPPS compared with placebo therapy. Based on \( P = .07 \), recent recommendations on interpretation of results of clinical trials suggest that pregabalin might be superior to placebo. Given these results, the hypothesis is that men with a neurologic basis for their symptoms respond better to pregabalin therapy. Development and validation of practical approaches to the identification of clinically relevant subpopulations of patients with CP/CPPS to predict response to treatment and direct tailored therapy is the focus of active investigation in ongoing clinical studies.

Accepted for Publication: February 16, 2010.

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Financial Disclosure: Dr Pontari received consulting fees from Sanofi-Aventis, Pfizer, and GlaxoSmithKline and reported clinical trial participation with Pfizer; Dr Krieger received consulting and advising fees from Pfizer; Dr Litwin received consulting fees from Sanofi-Aventis; Dr Anderson received consulting fees from Bioness Inc, investigator fees from Boston Scientific and Allergan, and speaker fees from GlaxoSmithKline and Astella; Dr Nick received consulting fees from Merck, GlaxoSmithKline, Pfizer, Ortho Women’s Health, Farr Labs, Watson, Medtronic, NeurAxon, and Genyous Biomed and research support from Merck, GlaxoSmithKline, Allergan, Watson, Pfizer, and American Medical Systems; Dr Shoskes received consulting fees from Roche, is on the advisory board of Farr Labs, and has a financial interest in Triurol; Dr Alexander received lecture fees from Boehringer Ingelheim; Dr O’Leary received consulting fees from Sanofi-Aventis; Dr Landis received consulting fees from Sanofi-Aventis; Dr Kusek holds stock in Decode Genetics; and Dr Schaeffer was a consultant for Alita Pharmaceuticals, American Medical Systems, NovaBay Pharmaceuticals, Regeneron Pharm Inc, IMS Health, Exomedis Inc, CombinatoRx Inc, Monitor Company Group LP, and Advanstar Communications and received meeting honorarium from the Scientific Consulting Group.

Funding/Support: No author received compensation for the performance of this study except as salary support.
from a grant from the National Institutes of Health. This study was supported by cooperative agreements U01 DK65209, U01 DK65268, U01 DK65297, U01 DK65187, U01 DK65277, U01 DK65189, U01 DK65174, U01 DK65266, U01 DK65257, U01 DK65186, and U01 DK65287 from the National Institute of Diabetes and Digestive and Kidney Diseases and the National Center for Minority Health and Health Disparities. Pregabalin and matching placebo capsules were provided by Pfizer Inc.

Previous Presentation: This study was presented at the meeting of the American Urological Association; April 26, 2009; Chicago, Illinois.

Additional Information: The 10 participating institutions were as follows: Cleveland Clinic, Cleveland, Ohio; Harvard Medical School, Massachusetts General Hospital & Brigham and Women’s Hospital, Boston; Northwestern University, Chicago, Illinois; Queen’s University, Kingston, Ontario, Canada; Stanford University Medical Center, Stanford, California; Temple University, Philadelphia, Pennsylvania; University of California, Los Angeles/King Drew University, Los Angeles; University of Maryland, Baltimore; University of Mississippi, Jackson; and University of Washington, Seattle.

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