

An Open-Label, Randomized Comparison of Duloxetine, Pregabalin, and the Combination of Duloxetine and Gabapentin among Patients with Inadequate Pain Response

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Purpose

The primary goal of this open-label noninferiority study was to determine whether treatment with duloxetine was as least as good as (noninferior to) pregabalin in reducing pain associated with diabetic neuropathy in patients who were inadequately responding to treatment with gabapentin. A secondary goal was to determine whether treatment with duloxetine was as least as good as (noninferior to) the combination of duloxetine and gabapentin in reducing DPNP in this study population.

Method

This was a 12-week, phase IV, open-label, randomized, multi-center parallel study in patients with DPNP, who had been treated with a stable dose of gabapentin (at least 900 mg/d) and had an inadequate response (defined by having a daily pain score ≥ 4 on an 11-point likert scale). Patients were randomly assigned to duloxetine (D) monotherapy (N=138), pregabalin (P) monotherapy (N=134), or a combination of duloxetine and gabapentin (D+G) (N=135). The primary efficacy variable was improvement in weekly mean 24-hour average pain at 12 weeks (based on a 0-to-10 likert scale). The primary objective was a non-inferiority comparison on the intent-to-treat population between P and D on this primary efficacy measure. Non-inferiority to P would be declared if the mean improvement for D was no worse than mean improvement for P within the statistical variability of 0.8 units.

Results

Estimated mean improvement (decrease in pain score) at 12 weeks was 2.12 for P and 2.62 for D, representing an observed +0.49 advantage for D. The 97.5% lower confidence bound was -0.05, establishing non-inferiority. The estimated mean improvement for D+G was 2.39, the 97.5% lower confidence bound was -0.32, also establishing non-inferiority. Completion rates did not differ significantly between the groups (D, 63%; P, 71.6%; D+G, 73.3%). Discontinuation due to adverse events (AEs) was significantly greater in D vs. P patients (19.6% vs. 10.4%; $p=.042$); D+G (13.3%) vs. P or D was not significant ($p=.573$; $p=.193$, respectively). AEs that occurred significantly more frequently between groups were: D>P: nausea, insomnia, hyperhydrosis, decreased appetite; D>D+G: insomnia; P>D: peripheral edema; D+G>P: nausea, hyperhydrosis, decreased appetite, and vomiting.

Conclusions

Findings from the current study indicate that treatment with duloxetine 60 mg/d was found to be at least as good as (noninferior to) pregabalin 300 mg/d in the treatment of pain in patients with DPNP, who had a suboptimal response to gabapentin.