Author's response to reviews

Title: Duloxetine for the long-term treatment of Major Depressive Disorder in patients aged 65 and older: an open-label study

Authors:

Madelaine M Wohlreich (mwmd@lilly.com)
Craig H Mallinckrodt (cmaillnc@lilly.com)
John G Watkin (watkinjg@lilly.com)
Donald P Hay (hay_donald_p@lilly.com)

Version: 2 Date: 30 November 2004

Author's response to reviews: see over
Thank you for forwarding the reviewers comments for the manuscript titled “Duloxetine for the Long-Term Treatment of Major Depressive Disorder in Patients Aged 65 and Older: An Open-Label Study” (MS: 2003105344347764). We describe below our responses to the reviewers’ comments, and summarize the changes which have been made to the manuscript in response to those comments.

**Reviewer 1 (EA)**

“Even if the measures, which include scales for depression and improvement, are suitable, they could be integrated with a scale regarding cognitive changes.”

We agree with the reviewer that cognitive changes are of great interest when studying an elderly population. However, since the primary goal of this study was to assess the safety and tolerability of duloxetine in a general population aged ≥18 years, no measures of cognition were included. All of the efficacy measures that were collected during the study are discussed within this manuscript.

**Reviewer 2 (JIS)**

“It is not clear how the decision of increasing the dose from 40 mg b.i.d. to 60 mg b.i.d. was made. Was it purely on the basis of clinical need or was it a-priori scheduled?”

We have added an extra paragraph to the Methods section, which describes further details of the dosing regimen utilized in the study. The paragraph reads as follows:

“The primary objective of the study was to evaluate the safety of duloxetine (80 or 120 mg/d given as two equal doses per day, i.e. 40 to 60 mg BID) for up to 52 weeks. During the first week of therapy, all patients received duloxetine 40 mg BID. Patients unable to tolerate 40 mg BID could have their dose decreased to 20 mg BID, but were required to increase the dose to 40 mg BID at Week 2. Patients unable to tolerate 40 mg BID were discontinued from the study. During the remainder of the study, the patient’s dose could be adjusted up to 60 mg BID or down to 40 mg BID, based upon the physician’s clinical evaluation of tolerability and efficacy.”
“It will be helpful to see whether there was a difference in response or remission rates, and adverse effects between the two doses.”

Given the dosing schedule described above, it can be seen that patients received flexible dosing that could be adjusted up or down to provide optimal tolerability and efficacy. As a result, it is not possible to separate patients into “40 mg BID” and “60 mg BID” dose groups, and we are unable to perform any comparisons of efficacy or tolerability based upon dose.

**Comments from the editorial board:**

“The only point, unclear for me is the range of age, in spite of the SD given on Table 1; in that respect we cannot know whether, for instance, the good tolerance is maintained at the extreme of the tested population. The question of the daily dosage which is not the one recommended in this population should be clearly announced in the summary.”

We have added an extra line in Table 1, which states that the age range of study participants was 65 to 87 years. We have also added a sentence to the Results section stating that the median age was 70 years. This should provide the reader with a clearer picture of the age distribution of study participants.

With regard to the question of daily dosage, we have added a sentence to the Background section which reads as follows:

“While patients in this study received doses of 80 mg/d or 120 mg/d, it should be noted that the approved dose range for duloxetine for the treatment of MDD is 40-60 mg/d.”

In addition, we have addressed all of the editorial comments in your e-mail message (removed unnecessary capitalization, inserted a Conclusions section, reformatted tabbed Tables to cell/field Tables, removed figure title from image files, and cropped figures to size).

We hope that these modifications will result in a manuscript that is suitable for publication. If you have any further questions, please let me know.

I look forward to hearing from you.

Sincerely,

John G. Watkin