Letter to the Editors

Lamotrigine does not prolong QTc in a thorough QT/QTc study in healthy subjects, Dixon *et al.* 2008; request for publication of PR interval data

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Dixon *et al.* reported the results of the most thorough study of lamotrigine effects on electrocardiogram (ECG) intervals that has been published to date [1]. In this placebo- and moxifloxacin-controlled trial, lamotrigine monotherapy at doses up to 400 mg day⁻¹ was shown to not prolong the QTc interval in healthy subjects. The report stated that additional ECG conduction intervals were measured, including the PR interval and the QRS duration. While QRS duration results were reported in the paper, the PR interval results from the study were neither reported nor discussed.

Approved labelling for lamotrigine does not include evidence indicating that lamotrigine has any effect on PR interval [2, 3]; however, the literature contains at least two trials where lamotrigine was reported to be associated with a small increase in mean PR (or PQ) interval in patients with epilepsy. Matsuo *et al.* reported a mean 5 ms increase in PR interval in epilepsy patients randomized to treatment with lamotrigine [4]. Recently, Saetre *et al.* reported that lamotrigine was associated with a mean 8.8 ms increase in PQ interval in a group of elderly epilepsy patients treated with a relatively low mean daily lamotrigine dose (~110 mg day⁻¹, serum concentration ~2.6 µg ml⁻¹) [5]. Given these findings, a complete reporting of the ECG data, including PR interval, is important for an accurate assessment of the cardiac profile of lamotrigine.

The extensive ECG data acquisition and relatively high steady-state plasma concentrations of lamotrigine (9.6 µg ml⁻¹ for the 400 mg day⁻¹ dose group) evaluated in the Dixon *et al.* trial [1] would provide the specific data needed to determine whether there is an effect of lamotrigine on PR interval. As such, we respectfully request an addendum to this publication that would allow the inclusion of a graphical presentation of PR interval data, such as that used in the report for QRS duration, as well as a quantitative statement of the mean placebo-subtracted change from baseline for PR interval at steady state (C_{max}) for the three lamotrigine doses that were studied.

Competing interests

GDR and JKS are UCB employees and hold UCB shares.

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