



Comparison of the Effects of Levofloxacin on QT/QTc interval Assessed in both Healthy Japanese and Caucasian Subjects

A Sugiyama¹, Y Nakamura¹, S Nishimura¹, S Adachi-Akahane¹, Y Kumagai², J Gayed³, A Naseem^{3*}, G Ferber³, J Taubel³, J Camm³

Issue



British Journal of Clinical Pharmacology

Accepted Article (Accepted, unedited articles published online for future issues)

DOI: 10.1111/j.1365-2125.2011.04110.x

© 2011 The Authors. British Journal of Clinical Pharmacology © 2011 The British Pharmacological Society

Additional Information (Show All)

[Author Information](#) | [Publication History](#)

This is an Accepted Article that has been peer-reviewed and approved for publication in the *British Journal of Clinical Pharmacology*, but has yet to undergo copy-editing and proof correction.

Please cite this article as an "Accepted Article"; doi: 10.1111/1365-2125.2011.04110.x

Abstract

[Cited By](#)

[Get PDF \(169K\)](#)

Keywords: Cardiac safety; ECG; 12-lead ECG; QTc; TQT; Caucasian; Japanese; pharmacology; clinical trial methodology; ethnic bridging studies; ethnic comparisons; levofloxacin; moxifloxacin

What is already known about this subject

- Although the ICH guidelines state that it is not expected that the results of a "thorough QT/QTc" study would be affected by ethnic factors and consequently be independent of the race of the study population, there is little documented evidence to support or refute this.
- Since 2010 the ICH E14 guidelines have been fully adopted in Japan and the question has arisen as to whether specific ethnic studies will become necessary to assess cardiac safety in Japanese individuals.

What this study adds

- The findings of this study suggest that there is no difference in QTc prolonging effect between Japanese and Caucasian subjects following levofloxacin dosing. However, a trend – not statistically significant – suggests that Caucasian subjects are more sensitive. Age and gender did not have an impact on the comparison of QTcF effects in this study.

Abstract

Aims There is no consensus as to what extent the results of thorough QT (TQT) studies need to be bridged.

Methods The results of two studies using levofloxacin in Japanese and Caucasian subjects were compared in a post hoc analysis to investigate the similarity of dose effect responses.

Results Concentration-response analysis based on the change of QTcF from time matched placebo was planned and performed in the combined data sets. At the geometric mean C_{max} for the two doses in the Caucasian study, a predicted effect on QTcF comparable to the actual effects observed was found. For the Japanese study, the predicted effect was lower but the difference was not statistically significant.

Conclusions No statistically significant differences in QTc prolonging effect between Japanese and Caucasian subjects were observed following levofloxacin dosing. However, a trend suggests that Caucasian subjects may be more sensitive. Age and gender did not have an impact.

[Get PDF \(169K\)](#)

More content like this

Find more content: [like this article](#)

Find more content written by: [A Sugiyama](#) | [Y Nakamura](#) | [S Nishimura](#) | [S Adachi-Akahane](#) | [Y Kumagai](#) | [J Gayed](#) | [A Naseem](#) | [G Ferber](#) | [J Taubel](#) | [J Camm](#)
[All Authors](#)