

Comparison of the effects of levofloxacin on QT/QTc interval assessed in both healthy Japanese and Caucasian subjects

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WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- Although the ICH guidelines state that it is not expected that the results of a 'thorough QT interval/corrected QT interval (QT/QTc)' study would be affected by ethnic factors and would 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 of 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 sex did not have an impact on the comparison of QT interval corrected using Fridericia's formula (QTcF) effects in this study.

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AIMS

There is no consensus as to what extent the results of thorough QT interval/corrected QT interval (QT/QTc) 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 QT interval corrected using Fridericia's formula (QTcF) from time-matched placebo was planned and performed in the combined data sets. At the geometric maximum mean concentration for the two doses in the Caucasian study, a predicted effect on QTcF comparable to the 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 sex did not have an impact.