

Supplemental Material

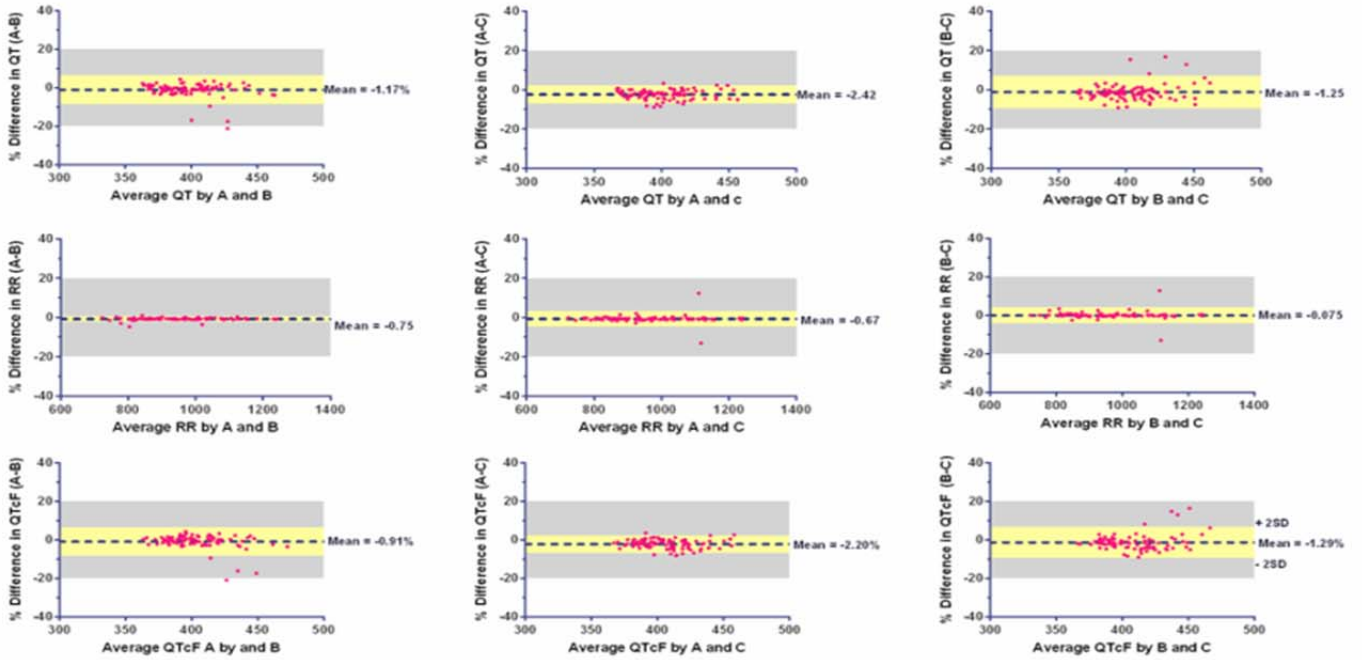
Antimicrobial Agents and Chemotherapy

Piperaquine population pharmacokinetics and cardiac safety in Cambodia

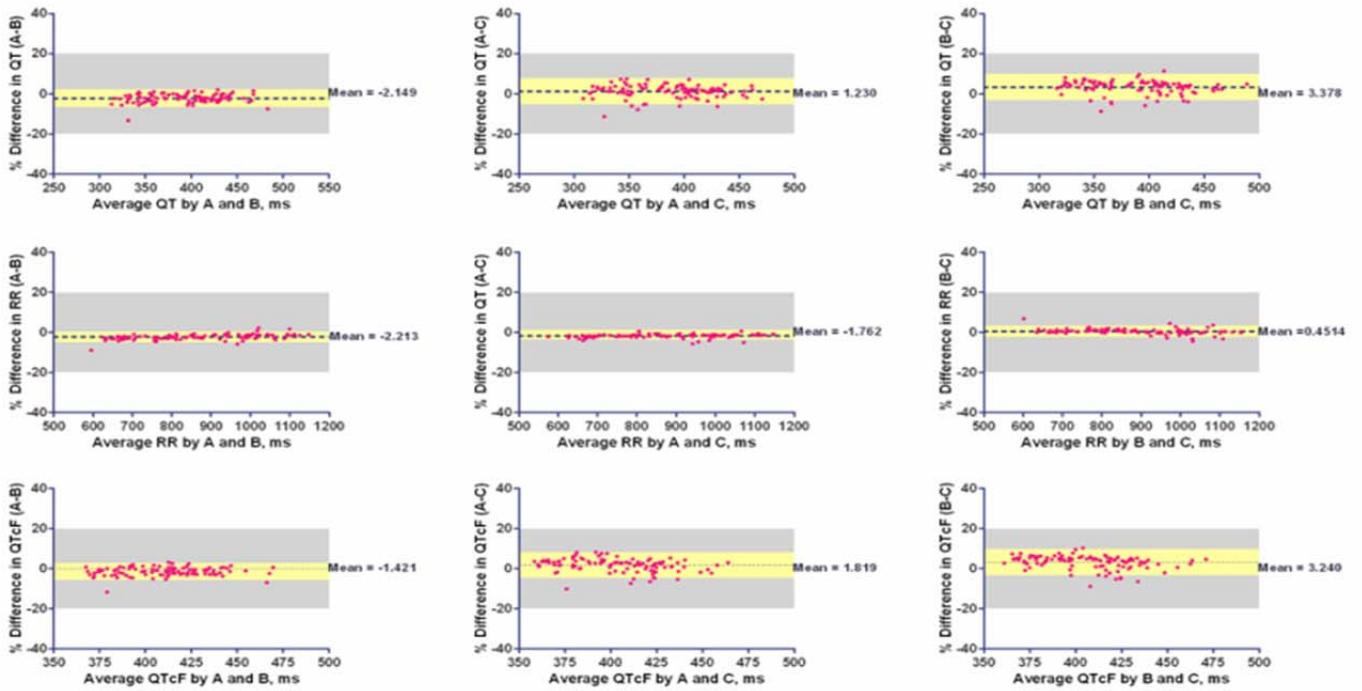
Vanachayangkul et al.

Supplemental Figure 1. Interrater variability for manual EKG readings from **A)** the 2012 study (WR1849) of a monthly 2 day course of DHA-piperaquine for malaria prophylaxis vs. matched placebo and **B)** the 2013 study (WR1877) of a 3 day course of DHA piperaquine for the treatment of acute *P. falciparum* malaria. For each study, the 3 investigators designated as EKG readers read 100 de-identified 12 lead EKGs in blinded fashion. The upper 3 panels in each figure are pairwise comparisons of manual QT interval readings for readers A, B and C, the middle panels are RR intervals, and the lower panels are the calculated QTcFm results. Mean % difference between readers was less than 3% for the 2012 study and 4% for the 2013 study. Bland-Altman plots were used for each pairwise comparison.

A) WR1849



B) WR1877



95% limit of agreement

Supplemental Figure 2. A-C) Scatter plots of plasma piperazine versus change in QTcBm in ms (Δ QTcBm) over baseline. Pink, green and yellow circles represent normal 2DP, normal 3DP and halted volunteers, respectively.

