No clinically relevant electrocardiogram effects in a randomized TQT study of single

therapeutic/supratherapeutic rimegepant doses in healthy adults

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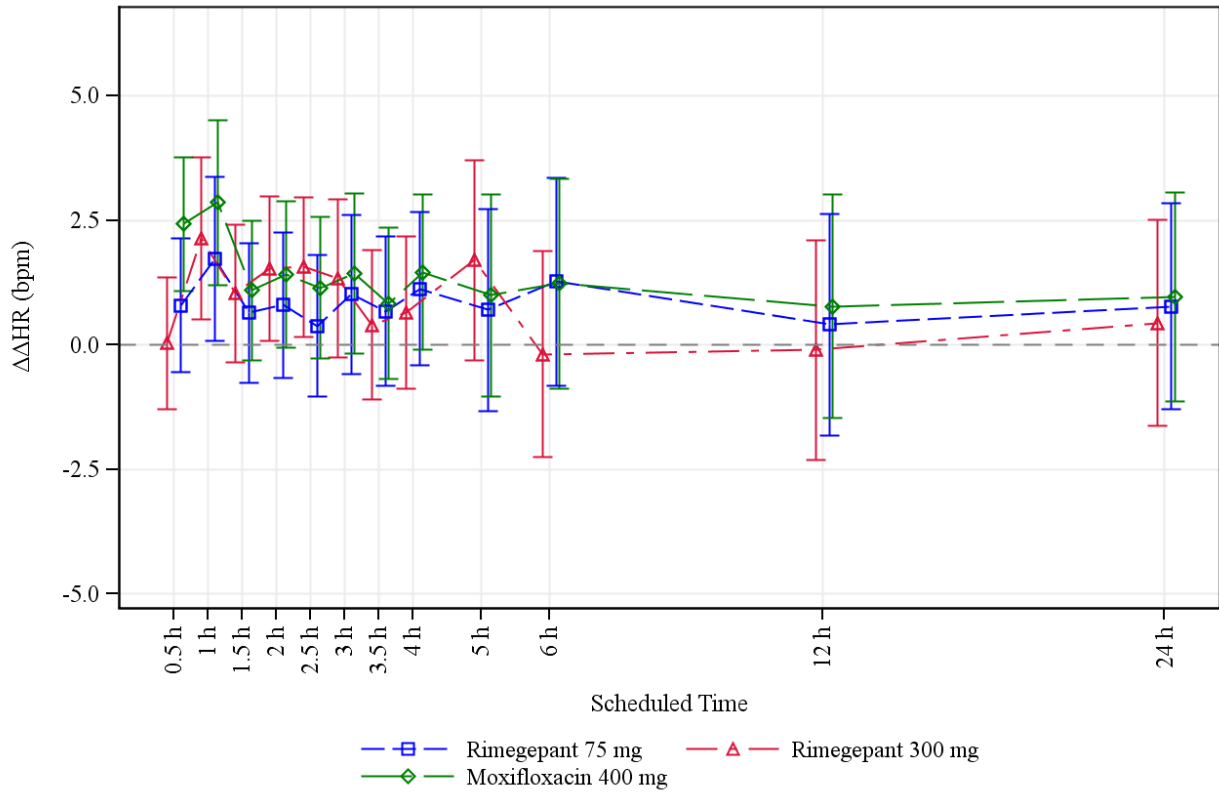[1]Certara USA, Princeton, NJ, USA; [2]Biohaven Pharmaceuticals Inc, New Haven, CT, USA;

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Supplementary Information

Table S1. Concentration-QTc analysis of rimegepant and associated ΔΔQTcF prolongation (PK/QTc population)

Parameter	Estimate (90% Confidence Interval)	P-value	Between-Subject Variation
Intercept (milliseconds)	0.43 (-1.22; 2.08)	0.6624	5.57
Rimegepant slope (milliseconds per ng/mL)	0.00002 (-0.00022; 0.00027)	0.8705	0.06
Slope of the centered baseline QTcF (milliseconds)	-0.24 (-0.31; -0.17)	< 0.0001	-
Residual variability (milliseconds)	5.38	-	-
QTc, Fridericia corrected QT; ΔΔQTcF, placebo-corrected change-from-baseline Fridericia corrected QT; PK, pharmacokinetics QTcF.			

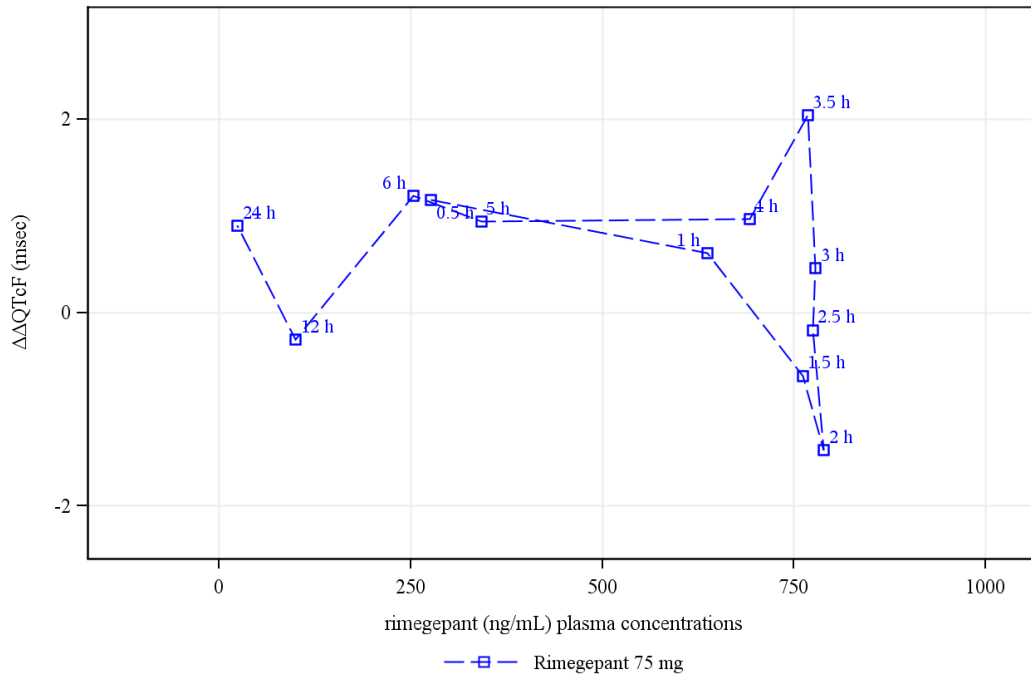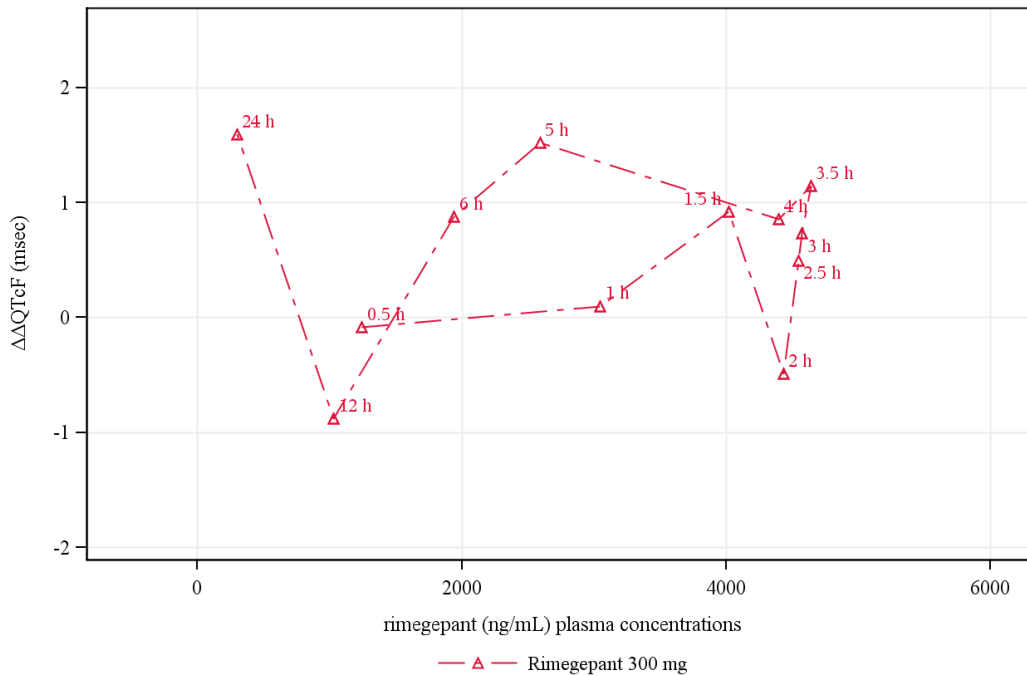**Figure S1.** ΔΔHR across time points (QT/QTc population)

Error bars for ΔΔHR are 90% CI from statistical modeling. ΔΔHR, placebo-corrected change-from-baseline heart rate.

Figure S2. Rimegepant plasma concentration and ΔΔQTcF connected in temporal order (rimegepant 75 and 300 mg) (QT/QTc population, PK/QTc population)

A.

B.

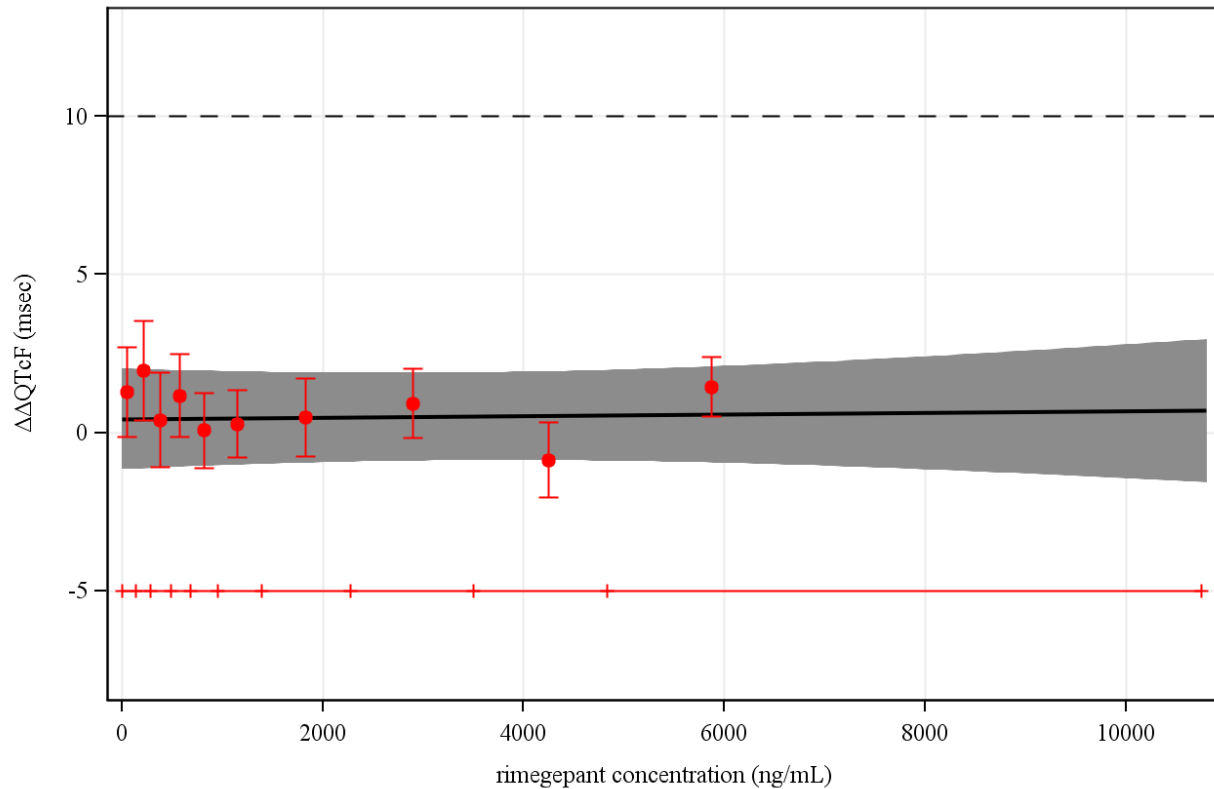The hysteresis loops of mean rimegepant plasma concentrations and ΔΔQTcF across post-dosing time points are shown for treatment with 75 mg rimegepant (A) and for treatment with 300 mg rimegepant (B). PK, pharmacokinetic; ΔΔQTcF, placebo-corrected change-from-baseline Fridericia corrected QT.

Figure S3. Model-predicted ΔΔQTcF (mean and 90% CI) and observed ΔΔQTcF (mean and 90% CI) across deciles of rimegepant plasma concentrations (PK/QTc population)

The red-filled circles with vertical bars denote the mean ΔΔQTcF with 90% CI displayed at the median plasma concentration within each decile for rimegepant. The solid black line with gray-shaded area denotes the model-predicted mean ΔΔQTcF with 90% CI. The horizontal red line with notches shows the range of concentrations divided into deciles for rimegepant. The area between each decile represents the point at which 10% of the data are present; the first notch to second notch denotes the first 10% of the data, the second notch to third notch denotes the 10% to 20% of the data and so on. CI, confidence interval; PK, pharmacokinetics; ΔΔQTcF, placebo-corrected change-from-baseline Fridericia corrected QT.