Table S8 Mean changes of ECG parameters from baseline, time averaged and placebo corrected, for each ETC-206 dose level and administration conditions.

Parameters*	**ETC-206 10 mg FASTED** (N=16) [Standard Deviation]	**ETC-206 20 mg FASTED** (N=14) [Standard Deviation]	**ETC-206 10 mg FED** (N=9) [Standard Deviation]
HR (bpm)	-2.0 [3.2]	0.1 [3.5]	2.4 [4.3]
PR (ms)	4.3 [5.1]	-3.6 [4.9]	-1.5 [5.5]
QRS (ms)	3.7 [3.3]	-1.0 [1.6]	-1.2 [3.3]
QT (ms)	9.5 [9.1]	-7.1 [8.1]	-3.5 [10.9]
QTcF (ms)	4.3 [4.0]	-5.5 [5.8]	1.8 [5.6]

Legend - *: All parameters are reported as "placebo corrected mean changes from baseline). Abbreviations - HR: Heart rate; bpm: beats per minute; ms: milliseconds, QTcF: Fridericia correction.

The panel shows that, HR changes ranged from -2.0 to 2.4 bpm respectively for the 10 mg fasted and 10 mg fed dosing conditions of ETC-206. PR changes ranged from -3.6 to 4.3 ms respectively for the 20 mg fasted and 10 mg fasted dosing conditions of ETC-206. QRS changes ranged from -1.2 to 3.7 ms respectively, for the 10 mg fed and 10 mg fasted dosing conditions of ETC-206. None of the changes was clinically relevant. For HR, PR and QRS none of the subjects met criteria for outlier ^ (outlier brief definitions provided below), and the time point analysis also did not show any clinically significant effects of ETC-206 (not shown). QTcF changes ranged from -5.5 to 4.3 ms respectively for the 20 mg fasted and 10 mg fasted dosing conditions of ETC-206 and, as for other parameters, they were not clinically relevant. Moreover, no clinically significant effect of ETC-206 on cardiac repolarization were shown with time point data analysis, neither outliers were found with the analysis of categorical cut points of the ECG (i.e. new U waves, new > 500 ms absolute QTc duration, and > 60 ms changes in QTc from baseline, 30-60 ms changes from baseline of QTcF) (not shown).

Outliers – **HR:** <50 bpm and at least 25% decrease from baseline (i.e. bradycardic event) or >100 bpm and at least a 25% increase from baseline (i.e. tachycardic event). **PR**: >200 ms and it was at least a 25% increase from baseline. **QRS**: >100 ms and it was at least a 25% increase from baseline.

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