

**Supplemental Digital Content 4. Table 1:** Categorical Summary of Maximum Postbaseline and Maximum Increase From Baseline of ECG Parameters for Safety-Analysis Population

Parameter	Criterion	Palbociclib +		Placebo +	
		N	n (%)	N	n (%)
Maximum QTcS, ms	<450	441	355 (80.5)	220	189 (85.9)
	450–<480	441	79 (17.9)	220	26 (11.8)
	480–<500	441	5 (1.1)	220	5 (2.3)
	≥500	441	2 (0.5)	220	0
Maximum QTcF, ms	<450	441	379 (85.9)	220	197 (89.5)
	450–<480	441	54 (12.2)	220	21 (9.5)
	480–<500	441	7 (1.6)	220	2 (0.9)
	≥500	441	1 (0.2)	220	0
Maximum QTcB, ms	<450	441	286 (64.9)	220	152 (69.1)
	450–<480	441	142 (32.2)	220	60 (27.3)
	480–<500	441	10 (2.3)	220	7 (3.2)
	≥500	441	3 (0.7)	220	1 (0.5)
Maximum QTcS increase from baseline, ms	Change <30	441	409 (92.7)	220	208 (94.5)
	30 ≤ change <60	441	29 (6.6)	220	12 (5.5)
	Change ≥60	441	3 (0.7)	220	0
Maximum QTcF increase from baseline, ms	Change <30	441	404 (91.6)	220	206 (93.6)
	30 ≤ change <60	441	35 (7.9)	220	14 (6.4)
	Change ≥60	441	2 (0.5)	220	0

Maximum QTcB increase from baseline, ms	Change <30	441	392 (88.9)	220	201 (91.4)
	30 ≤ change <60	441	45 (10.2)	220	18 (8.2)
	Change ≥60	441	4 (0.9)	220	1 (0.5)
Maximum PR interval increase from baseline, ms	Change ≥25% and baseline ≥200 ms	441	0	219	0
	Change ≥50% and baseline <200 ms	441	0	219	0
Maximum QRS complex increase from baseline, ms	Change ≥25% and baseline ≥100 ms	443	2 (0.5)	220	0
	Change ≥50% and baseline <100 ms	443	4 (0.9)	220	1 (0.5)

N, number of patients who had at least 1 pair of time-matched baseline and postbaseline ECG data; n, number of subjects in each category.

**Supplemental Digital Content 4. Table 2.** Parameter Estimates for the Final Concentration-  
QTc Models

Parameter	Estimate (95% CI)		
	QTcS	QTcF	QTcB
Intercept at nominal time 0, $\theta_1$ , ms	414 (410, 418)	412 (408, 416)	426 (422, 431)
Intercept at nominal time 2, $\theta_2$ , ms	417 (413, 421)	415 (411, 419)	430 (425, 434)
Intercept at nominal time 4, $\theta_3$ , ms	416 (412, 420)	414 (410, 418)	430 (426, 435)
Intercept at nominal time 6, $\theta_4$ , ms	415 (411, 419)	414 (410, 417)	430 (426, 434)
Intercept at nominal time 8, $\theta_5$ , ms	414 (410, 418)	412 (408, 416)	429 (424, 433)
Slope, $\theta_6$ , ms/ng/mL	0.0347 (0.00776, 0.0616)	0.0355 (0.00826, 0.0628)	0.0272 (−0.000536, 0.0549)
IIV-intercept, $\omega_1$ , ms [shrinkage, %]	15.4 [1.29] (13.0, 18.4)	15.6 [1.29] (13.1, 18.5)	17.6 [1.27] (14.8, 21.0)
IIV-slope, $\omega_2$ , ms/ng/mL [shrinkage, %]	0.0988 [13.0] (0.0795, 0.123)	0.100 [12.9] (0.0807, 0.125)	0.0982 [16.0] (0.0771, 0.125)
Correlation between slope and intercept, $\omega_1$ - $\omega_2$	−0.263 (−0.496, 0.00559)	−0.270 (−0.503, −0.000402)	−0.285 (−0.525, −0.00192)

<b>Parameter</b>	<b>Estimate (95% CI)</b>		
	<b>QTcS</b>	<b>QTcF</b>	<b>QTcB</b>
Residual error, $\sigma$ , ms	7.14 [9.38] (6.72,	7.21 [9.39] (6.79,	8.25 [9.07] (7.77,
[shrinkage, %]	7.58)	7.66)	8.76)

IIV, interindividual variability.