Supplementary Data

Veliparib plasma pharmacokinetic parameters were extracted from the data by non-compartmental methods with PK Solutions 2.0 (Summit Research Services). Day 1 and end of dosing interval (day 7, 14, or 21) data were used to estimate pharmacokinetic parameters. Apparent clearance (Cl/F) was calculated with $AUC_{0\text{-}inf}$ (area under the curve) on day 1 and the AUC from time zero to the end of dosing interval ($AUC_{0\text{-}24}$) on day 7, 14, or 21. Only the data from patients with full pharmacokinetic profiles on both collection days were used in subsequent statistical analyses comparing the two days. Dose linearity for day 1 $AUC_{0\text{-}inf}$ and maximum plasma concentration (C_{max}) was assessed through the power model on log-transformed data as described (1), under the null-hypothesis of dose linearity.

References

1. Smith BP, Vandenhende FR, DeSante KA, Farid NA, Welch PA, Callaghan JT, et al. Confidence interval criteria for assessment of dose proportionality. Pharm Res 2000;17:1278-83.

Supplementary Table S1. Veliparib plasma pharmacokinetic parameters

Dose (mg)	Sample Day (1, 7, 14, or 21)	No. of subjects	C_{max} (ng/mL)	T_{max} (h)	$t_{1/2}$ (h)	Cl/F (L/h)	Vd/F (L)
20	1	3	125 (86)	2.0 (1.7)	9.5 (0.8)	20.1 (6.5)	269 (70)
	7	3	135 (36)	1.2 (0.3)	9.8 (4.8)	23.0 (6.0)	308 (147)
30	1	6	321 (100)	1.3 (0.4)	6.4 (1.9)	14.8 (3.6)	132 (37)
	7/14	3/3*	354 (63)	0.92 (0.58)	6.2 (1.8)	13.6 (1.9)	118 (27)
40	1	6	414 (302)	1.4 (0.9)	5.1 (1.0)	19.2 (7.7)	138 (54)
	21	6	408 (336)	1.3 (0.4)	5.0 (1.5)	19.7 (9.1)	138 (71)
50	1	4	373 (84)	2.9 (2.1)	5.9 (0.1)	16.7 (7.1)	143 (63)
	21	2	281 (10)	3.3 (2.3)	6.1 (0.1)	17.9 (6.2)	158 (58)
60	1	13	550 (184)	2.2 (1.8)	5.8 (1.4)	15.3 (5.5)	122 (32)
	21	12	622 (240)	1.9 (2.0)	6.4 (1.4)	16.5 (5.9)	147 (45)
80	1	3	620 (100)	1.7 (0.6)	5.8 (1.4)	15.1 (1.1)	124 (22)
	21	1	683	1	6	18	145
		P D1 vs D7/14/21	0.23	0.20	0.74	0.37	0.27
		R_{ac} D7/14/21 (SD)		1.12 (0.40)			

NOTE: Data displayed as mean (SD). *, Patients on DL2 (N=3) had their second pharmacokinetic study on day 7 and patients on DL3 (N=3) had their second pharmacokinetic study on day 14. Because both cohorts received 30 mg ABT-888, their data were pooled for the purposes of pharmacokinetic analyses.

Abbreviations: SD, standard deviation; R_{ac}, accumulation index; C_{max}, maximum plasma concentration; T_{max},time of maximum concentration; $t_{1/2}$, half-life; Cl/F, clearance; Vd/F, volume of distribution.

Supplementary Figures

Figure S1. PAR levels relative to baseline (100%) in PBMCs from seven patients who had samples collected on days 1 and 21 over a period of 24 hours (0, 2, 4, 6, and 24 hours) at dose levels 6 (Pt 17), 7 (Pt 20, 21, 22, 24, and 25), and 8 (Pt 34). The day 1, 0-hour time point was before drug administration and was used as baseline (100%) for PAR levels. Dotted lines indicate patients with *BRCA* mutations.

Figure S2. γH2AX measured as percent nuclear area positive (%NAP) in PBMC samples from 17 patients on day 1 of treatment at dose levels 1 (Pt 1-3), 2 (Pt 4-5), 3 (Pt 7-9), 5 (Pt 13), 6 (Pt 16), 7 (Pt 20-23), and 8 (Pt 33-35). Eleven of 17 patients had < 0.1 %NAP at all time points. Dotted lines indicate patients with *BRCA* mutations.