Supplementary Data

Supplementary Table S1. IC_{50} values of ipatasertib on cell viability in cell lines with or without alterations in PTEN or *PIK3CA*.

Cell Line	Tissue Type	Ipatasertib IC_{50} (μmol/L)[a]	PTEN[b]	*PIK3CA*[c]
22rv1	Prostate	9.09		HETp.Q.546R
AN3 CA	Endometrial	0.63	N	
ASPC-1	Pancreatic	10		
AU565	Breast	3.55		HET.p.L847F;HET.pK863I; HET.p.F872I
BPH1	Prostate	10		
BPH1025	Prostate	8.63		
BT474	Breast	0.52		HET.p.K111N
BT483	Breast	10		HET.p.E542K
BT549	Breast	5.51	N;HOM.p.V275fs*1	
BxPC-3	Pancreatic	10		
C33A	Cervical	0.60	N	
CAL-120	Breast	10		
CAL-51	Breast	0.36	N	HET.p.E542K
CAL-85-1	Breast	10		
CAMA-1	Breast	0.26	P;HOM.p.D92H	
Caov-3	Ovarian	10		
Capan-1	Pancreatic	10		
Capan-2	Pancreatic	10		
CFPAC-1	Pancreatic	10		HET.p.I391M
Colo704	Ovarian	0.93	N	
DLD-1	Colon	10		HETp.E.545K;HET.p.D549N
DU145	Prostate	8.41		
DU4475	Breast	10		
ECC-1	Endometrial	1.05	N	
EFM-19	Breast	0.39		HOM.p.H1047L
EFM-192A	Breast	0.73		HET.pC420R
EFO-21	Ovarian	0.51	N	
ES-2	Ovarian	10		
EVSA-T	Breast	0.07	N	
FU-OV-1	Ovarian	10		
HCC-1143	Breast	10		
HCC-1395	Breast	0.45		
HCC-1419	Breast	10		

Cell Line	Tissue Type	Ipatasertib IC_{50} (μmol/L)[a]	PTEN[b]	*PIK3CA*[c]
HCC-1569	Breast	0.88	HETDEL.267fs*9	HET.p.I391M
HCC-1954	Breast	1.01		HET.p.H1047R
HCC-2218	Breast	4.44		
HCC-38	Breast	10	N	HET.p.W386L
HCC-70	Breast	0.53	N	
HCC1428	Breast	10		
HCT-116	Colon	10		
HCT-15	Colon	10		HET.p.E545K;HET.p.D549N
HDQ-P1	Breast	10		
HEC 1-B	Endometrial	10		
HEC-1A	Endometrial	5.76		
HPAC	Pancreatic	10		
HPAF-II	Pancreatic	10		
Hs 766T	Pancreatic	10		
HS578T	Breast	2.22		
HT-55	Colon	4.25		
HT3	Cervical	10		
Hup T3	Pancreatic	10	N	HET.p.H556Q
KLE	Endometrial	10		
KM12	Colon	2.63	N	
KP4	Pancreatic	10		
KPL-1	Breast	1.95		HET.p.E545K
LNCaP	Prostate	0.11	N;HOM.p.K6fs*4	
LoVo	Colon	3.36		
MCF7	Breast	1.88		HET.p.E545K
MDA-MB-175	Breast	0.43		
MDA-MB-231	Breast	10		
MDA-MB-415	Breast	0.23	N;HOM.p.C136Y;p.T277fs*13	
MDA-MB-436	Breast	10	N	HOM.p.I391M
MDA-MB-453	Breast	1.92	HET.p.E307K	HET.p.H1047R
MDA-MB-468	Breast	10	N;HOM.c.253+1G>T	HET.p.C769G;HET.p.T435I

Cell Line	Tissue Type	Ipatasertib IC_{50} (µmol/L)[a]	PTEN[b]	*PIK3CA*[c]
MFM-223	Breast	0.42		HET.p.1047R;HET.p..E176Q
MiaPaCa2	Pancreatic	10		
MS 751	Cervical	10		
MT-3	Colon	1.66		HET.p.H1047R
OV-90	Ovarian	10		
Panc 02.03	Pancreatic	10		
Panc 03.27	Pancreatic	7.38		
Panc 04.03	Pancreatic	7.22		
Panc 05.04	Pancreatic	10		
Panc 08.13	Pancreatic	10		
Panc 10.05	Pancreatic	10	N	
Panc-1	Pancreatic	10		
PATU 8902	Pancreatic	10	N	
PATU 8988T	Pancreatic	10	N	HET.p.I391M
PC-3	Prostate	1.37	N	HET.p.N996H
PC3M	Prostate	1.45	N	
PC3M-LN4	Prostate	4.483	N	
PC3MM2	Prostate	1.55	N	
PL45	Pancreatic	8.17	N	
PSN-1	Pancreatic	10		
RKO	Colon	10		HET.p.H1047R;HET.p.I391M
RL 95-2	Endometrial	0.54	N	
SiHa	Cervical	10		
SK-CO-1	Colon	10		
SK-OV-3	Ovarian	2.46		HET.p.H1047R
SK-UT-1B	Endometrial	0.22	N	
SKBR3	Breast	0.81		
SU.86.86	Pancreatic	10	N	
SW 1990	Pancreatic	10	N	
T47D	Breast	0.76		HET.p.H1047R
TOV-112D	Ovarian	10		
TOV-21G	Ovarian	0.65	N	HET.p.H1047Y
ZR-75-1	Breast	0.81	N;HOM.pL108R	
ZR-75-30	Breast	10		HET.p.I391M

[a] Measured by the CellTiter-Glo Assay (Promega).

[b] Negative protein (N) or known mutations in the gene are noted.

[c] Known mutations are noted.

Supplementary Table S2. Percent tumor growth inhibition (%TGI) in xenograft models with or without alterations in PTEN or *PIK3CA*.

Tumor Type	Tumor Model	Ipatasertib Max %TGI	PTEN[a]	*PIK3CA* mut/amp[b]
Breast	HCC1954	138		H1047R
Breast	KPL4	135		H1047R
Breast	BT474M1	113		K111N
Breast	MCF7-neo/ Her2	65		E545K
Breast	MDA-MB-231	46		
Breast	Fo5	88		
Colon	HM-7	89		H1047R
Colon	HCT-116	-13		H1047R
Gastric	HGC-27	126	N	
GBM	U87MG	164	N	
Melanoma	A2058.x1	40	N	
Melanoma	537MEL	125	N	
NSCLC	H520.x1	34	N	amp
NSCLC	NCI-H460	7		E545K
NSCLC	NCI-H441	69		
NSCLC	NCI-H2122	41		
NSCLC	EBC-1	-11		
Ovarian	TOV-21G.x1	128	N	H1047Y
Ovarian	IGROV-1	115	N	O1069W
Ovarian	SKOV3	40		H1047R
Prostate	22RV1	68		Q546R
Prostate	LuCap141	141		amp
Prostate	LNCaP	188	N	
Prostate	LuCap35V	97	Low	
Prostate	LuCaP96.1	96	Low	
Prostate	PC-3	93	N	
Prostate	DU-145.x1	60		
Prostate	LuCap145.2	20		

Amp = amplification, Max %TGI = maximum percent tumor growth inhibition, Mut = mutation, N = negative protein

[a] Negative protein (N) or low protein expression for PTEN is noted.

[b] Known mutations are noted.

Supplementary Table S3. PI3K/Akt pathway status in archival tumors.

Archival tissue tumor samples were collected from the majority of patients and were assessed centrally for PTEN status by immunohistochemistry (IHC) and for *PIK3CA* and/or *AKT* mutations. PTEN expression was quantified by an H-score, ranging from complete loss compared to normal stroma (H-score 0) to normal expression (H-score 400). In addition to *PIK3CA* and *AKT*, mutations from other relevant signaling pathways were also examined, including *BRAF*, *EGFR*, *ERBB2*, *FGFR3*, *FLT3*, *HRAS*, *JAK2*, *KIT*, *KRAS*, *MET*, *MYD88*, *NRAS*, and *RPPH1*.

Supplementary Table S3. PI3K/Akt pathway status in archival tumors.

Tumor Type	Ipatasertib (mg)	PTEN H-score	*PIK3CA*/*AKT* Mutations	Other Mutations
Gastric	25	N/A	N/A	N/A
Ovarian	25	0	MND	MND
Thyroid, Papillary	25	50	MND	MND
Chondrosarcoma	50	N/A	MND	MND
Colon	50	200	*PIK3CA* H1047R	*KRAS* G12A
Head and Neck	50	300	MND	MND
Breast	100	N/A	*PIK3CA* R88Q	MND
Breast	100	300	MND	MND
Colon	100	130	MND	MND
Colon	200	N/A	MND	*KRAS* Q61L
Colon	200	100	*PIK3CA* H1047R	MND
Renal	200	0	MND	MND
Cholangiocarcinoma	400	300	MND	MND
Colon	400	250	MND	MND
Colon	400	300	MND	*KRAS* G12A
Breast	600	N/A	N/A	N/A
Breast	600	N/A	N/A	N/A
Breast	600	0	MND	MND
Breast	600	0	MND	MND
Breast	600	0	MND	*NRAS* Q61R
Breast	600	5	MND	MND
Breast	600	20	*PIK3CA* E542K	MND
Breast	600	100	MND	MND
Breast	600	115	*PIK3CA* H1047R	MND
Breast	600	155	MND	MND
Breast	600	165	*PIK3CA* E545K	*MET* N375S
Breast	600	200	MND	*MET* 1010I
Breast	600	300	*AKT1* E17K	MND
Chondrosarcoma	600	N/A	MND	MND
Cholangiocarcinoma	600	230	MND	MND

MND = mutation not detected, N/A = not available

Supplementary Table S3 (cont.)

Tumor Type	Ipatasertib (mg)	PTEN H-score	*PIK3CA/AKT* Mutations	Other Mutations
Colon	600	60	MND	*KRAS* G12D
Colon	600	140	MND	*KRAS* G12V
Colon	600	150	MND	MND
Colon	600	140	MND	MND
Endometrial	600	N/A	N/A	N/A
Lung	600	N/A	N/A	N/A
Neuroendocrine	600	200	MND	*KRAS* G12V
Ovarian	600	175	MND	MND
Pancreatic	600	N/A	MND	*KRAS* G12D
Prostate	600	N/A	N/A	N/A
Prostate	600	N/A	N/A	N/A
Prostate	600	N/A	N/A	N/A
Prostate	600	N/A	N/A	N/A
Prostate	600	0	MND	MND
Prostate	600	300	MND	MND
Breast	800	N/A	N/A	N/A
Colon	800	100	MND	MND
Colon	800	100	MND	*KRAS* G12V
Colon	800	200	MND	MND
Colon	800	200	MND	MND
NSCLC	800	300	MND	MND
Unknown primary	800	260	MND	MND

MND = mutation not detected, N/A = not available

Supplementary Table S4. Reasons for discontinuation of study

	Number (%) of Patients by Ipatasertib Daily Dose [a]							All Patients (n=52)[c]
	25 mg (n=3)	50 mg (n=3)	100 mg (n=3)	200 mg (n=3)	400 mg (n=3)	600 mg (n=30) [b]	800 mg (n=7)	
Disease progression	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	21 (70)	6 (86)	42 (81)
Patient decision	0	0	0	0	0	6 (20)	0	6 (12)
Adverse event	0	0	0	0	0	1 (3)	1 (14)	2 (4)
Death	0	0	0	0	0	1 (3)	0	1 (2)
Physician decision	0	0	0	0	0	1 (3)	0	1 (2)

n=number of patients.

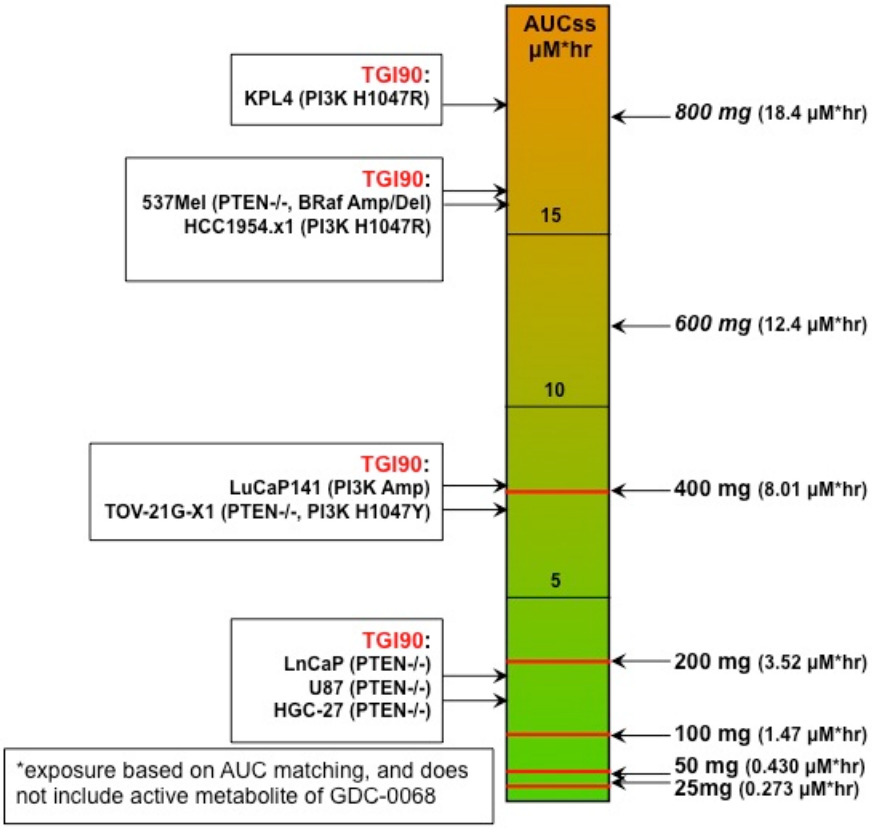
[a] Patients are categorized by initial dose cohort assignment, regardless of subsequent dose modification.

[b] Thirty patients were enrolled in the 600 mg dosing cohort, but one enrolled patient was not treated with ipatasertib (GDC-0068); thus, 29 patients were treated.

[c] Fifty-two patients were enrolled in the study, but one enrolled patient was not treated with ipatasertib (GDC-0068); thus, 51 patients were treated.

Supplementary figure S1. Exposure plots confirm that exposures achieved in patients in the dose-escalation stage (right side) correlated with exposures in preclinical models at TGI_{90} (left side).

Preclinical *in vivo* efficacy data with ipatasertib was obtained in multiple xenograft models, including LNCaP prostate cancer (PTEN-null), U87MG glioma (PTEN-null), HGC-27 gastric cancer (PTEN-null), LuCaP141 prostate cancer (*PIK3CA* amplified), and TOV-21G-X1 ovarian cancer (PTEN-null, *PIK3CA* H1047R mutation, and *KRAS* G13C mutation). The dose of ipatasertib that produced 90% tumor growth inhibition (TGI_{90}) was determined in each xenograft model. The TGI_{90} values for each cell line are graphed along the left of the panel, and the equivalent exposures obtained in patients are shown on the right.



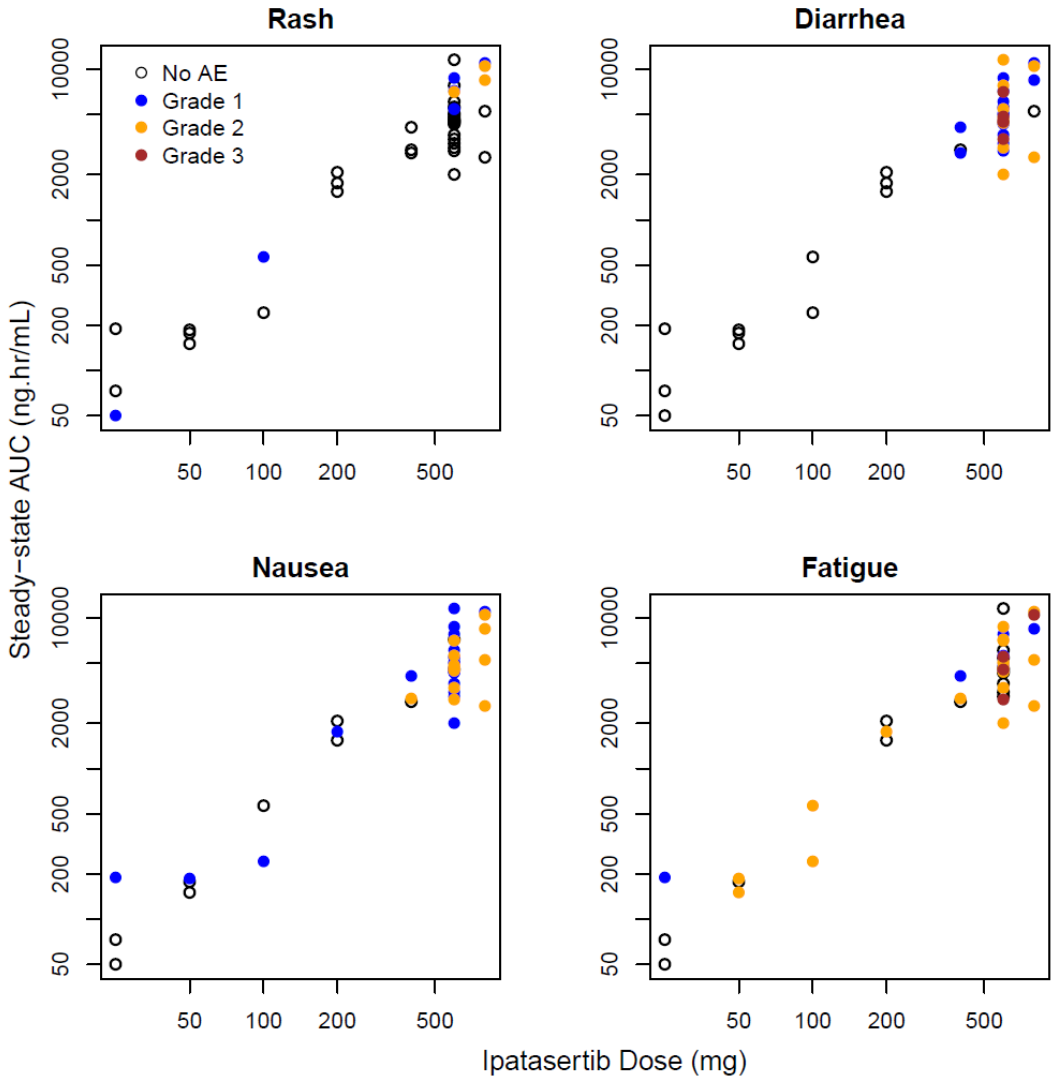
Supplementary Figure S2. Relationship between exposure of ipatasertib to the most common ipatasertib-related AEs of fatigue, diarrhea, nausea, and rash.

A, An analysis was performed to compare the dose (in mg along the horizontal axis) and exposure (at steady-state AUC in ng*hour/mL) of ipatasertib to the grades of the four most common AEs related to ipatasertib (fatigue/asthenia, diarrhea, nausea, and rash) for all treated patients. The grade of each AE is plotted as a color-coded circle: blue for Grade 1, yellow for Grade 2, red for Grade 3 and white for no AE. Overall, the severity of each of the four most common drug-related AEs is increased relative to the dose and exposures for ipatasertib. All of the Grade 3 AEs occur at ipatasertib doses > 600 mg with exposures above 2000 ng*hour/mL, and most of the Grade 2 AEs occur at similar high doses and exposures, except for Grade 2 fatigue which occurs at lower exposures.

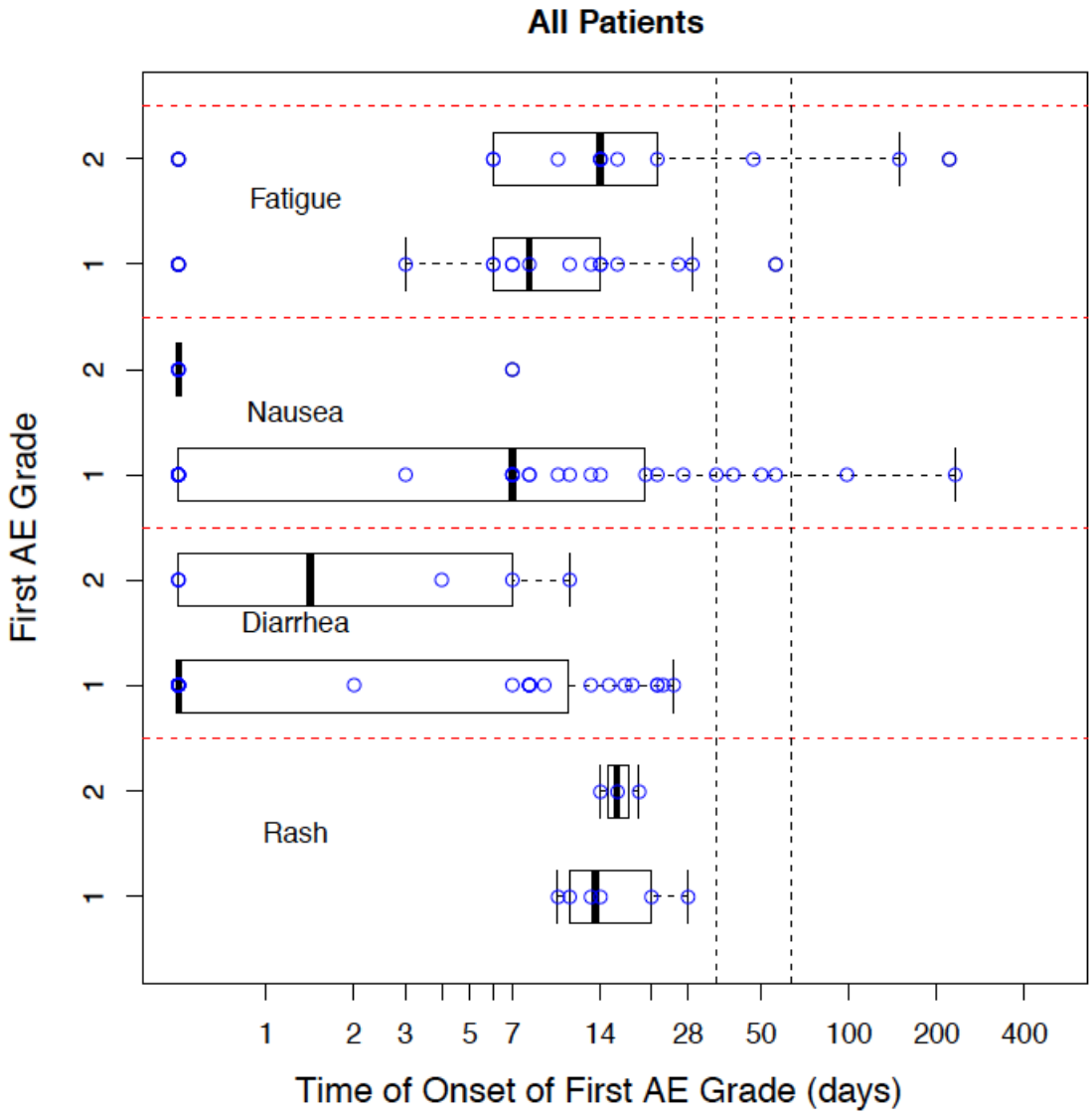
B, Time to onset in days (graphed on the horizontal axis) for the most common AEs related to ipatasertib (fatigue, nausea, diarrhea, and rash), ranked by severity from Grade 1 to Grade 2 along the vertical axis, was analyzed. All four AEs occurred early, during Cycle 1, although nausea and diarrhea tended to occur earlier, within the first week of dosing, whereas fatigue and rash tended to occur later at 7 to 14 days of dosing. Continued chronic dosing of ipatasertib beyond Cycle 1 did not lead to the further development of these most common AEs, as no diarrhea or rash occurred in patients after the first month of dosing, and only two patients developed fatigue or nausea after the first two months of dosing.

C, Time to onset in days (graphed on the horizontal axis) for the worst grade for the most common AEs related to ipatasertib (ranked by severity of Grade 1, 2, or 3 for fatigue, diarrhea, nausea, and rash) was analyzed. Onset of the first Grade 1 to Grade 2 nausea or Grade 1 diarrhea both occurred on average within 7 days of dosing, whereas the higher grades of nausea and of diarrhea occurred within 14 days of dosing. The worst grade of fatigue (Grade 3) and of rash (Grade 2) also occurred later in the study, following 7 to 14 days. Chronic dosing of ipatasertib did not lead to the significant development of the higher grade AEs, as no Grade 3 nausea or Grade 2 rash is seen after the first cycle, and only 3 patients developed Grade 2 to Grade 3 fatigue or diarrhea after the first two cycles.

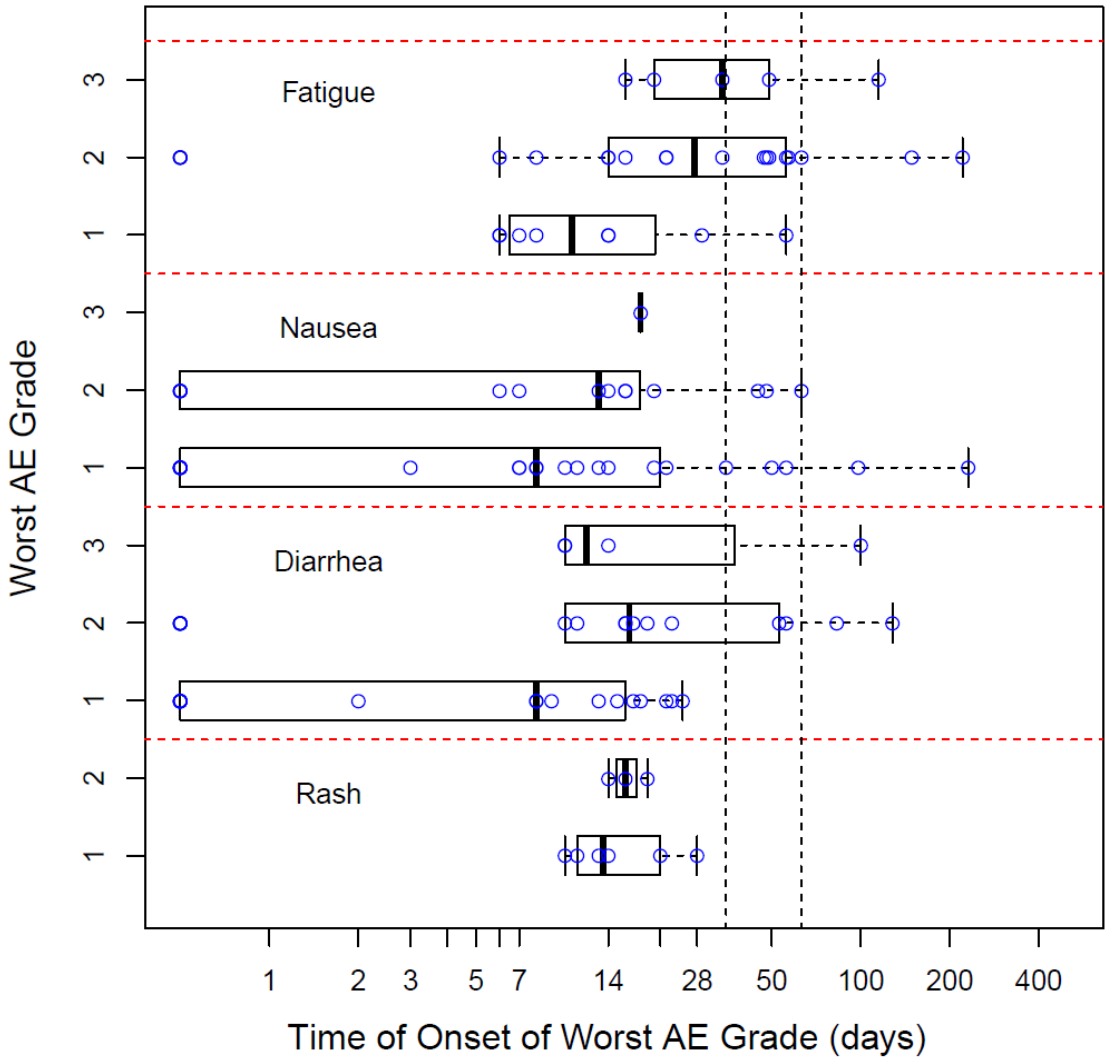
Supplementary figure 2A.



Supplementary figure 2B.



Supplementary figure 2C.



Supplementary Table S5. Common adverse events for ipatasertib in ≥ 10% of patients in any presented group

MedDRA System Organ Class/ Preferred Term	All Patients		600 mg Cohort	
	All AEs (n=51) [b]	Ipatasertib-Related AEs [a] (n=51) [b]	All AEs (n=29) [c]	Ipatasertib-Related AEs [a] (n=29) [c]
Any Adverse Event, n (%)	51 (100)	47 (92.2)	29 (100)	29 (100)
Diarrhea	37 (72.5)	35 (68.6)	29 (100)	29 (10%)
Nausea	40 (78.4)	36 (70.6)	27 (93.1)	25 (86.2)
Vomiting	30 (58.8)	26 (51)	23 (79.3)	20 (69)
Asthenia	32 (62.7)	19 (37.3)	17 (58.6)	8 (27.6)
Decreased appetite	22 (43.1)	12 (23.5)	10 (34.5)	4 (13.8)
Hyperglycemia	18 (35.3)	17 (33.3)	9 (31)	8 (27.6)
Dyspepsia	13 (25.5)	10 (19.6)	7 (24.1)	7 (24.1)
Abdominal pain upper	8 (15.7)	6 (11.8)	6 (20.7)	5 (17.2)
Back pain	11 (21.6)	0	6 (20.7)	0
Musculoskeletal pain	7 (13.7)	2 (3.9)	6 (20.7)	2 (6.9)
Constipation	8 (15.7)	0	5 (17.2)	0
Headache	9 (17.6)	3 (5.9)	5 (17.2)	1 (3.4)
Anemia	6 (11.8)	2 (3.9)	4 (13.8)	0
Cough	7 (13.7)	0	4 (13.8)	0
Dyspnea	5 (9.8)	1 (2)	4 (13.8)	1 (3.4)
Pyrexia	9 (17.6)	0	4 (13.8)	0
Abdominal distension	4 (7.8)	2 (3.9)	3 (10.3)	2 (6.9)
Abdominal pain	5 (9.8)	2 (3.9)	3 (10.3)	1 (3.4)
Arthralgia	4 (7.8)	1 (2)	3 (10.3)	1 (3.4)
Aspartate aminotransferase increased	3 (5.9)	1 (2)	3 (10.3)	1 (3.4)
Dry skin	3 (5.9)	3 (5.9)	3 (10.3)	3 (10.3)
Dysgeusia	7 (13.7)	6 (11.8)	3 (10.3)	2 (6.9)

Supplementary Table S5 (cont.)

MedDRA System Organ Class/ Preferred Term	All Patients		600 mg Cohort	
	All AEs (n=51) [b]	Ipatasertib-Related AEs [a] (n=51) [b]	All AEs (n=29) [c]	Ipatasertib-Related AEs [a] (n=29) [c]
Hypomagnesemia	4 (7.8)	3 (5.9)	3 (10.3)	3 (10.3)
Influenza like illness	3 (5.9)	0	3 (10.3)	0
Insomnia	4 (7.8)	0	3 (10.3)	0
Pain in extremity	5 (9.8)	0	3 (10.3)	0
Rash	7 (13.7)	6 (11.8)	3 (10.3)	3 (10.3)

AE = adverse event; MedDRA = Medical Dictionary for Regulatory Activities; n = number of patients.

Note: Patients are categorized by initial dose cohort assignment, regardless of subsequent dose modification.

[a] Assessed by the investigator as at least in part attributable to ipatasertib.

[b] Fifty-two patients were enrolled in the study, but 1 enrolled patient was not treated with ipatasertib; thus, 51 patients were treated.

[c] Thirty patients were enrolled in the 600-mg dosing cohort, but 1 enrolled patient was not treated with ipatasertib; thus, 29 patients were treated.

Supplementary Table S6. All Grade ≥ 3 adverse events related to ipatasertib.

Ipatasertib Dose (mg) [a]	Adverse Event	NCI CTCAE Grade	SAE	Onset Day	Duration (Days)	Action Taken with Ipatasertib
100	Hypercholesterolemia	3	No	14	21	None
600	Diarrhea	3	No	101	1	None
600	Diarrhea [b]	3	Yes	11	3	Dose reduced
600	Diarrhea [b]	3	No	34	8	Held
600	Diarrhea	3	No	11	3	Dose reduced
600	Diarrhea	3	No	15	5	Dose reduced
600	Asthenia	3	No	116	15	Dose reduced
600	Toxic skin eruption	3	Yes	11	4	Held
600	Hyperglycemia	3	Yes	28	2	Held
600	Hypophosphatemia	3	No	35	3	None
800	Nausea [c]	3	No	19	10	None
800	Asthenia [c]	3	No	21	8	Discontinued
800	Asthenia [c]	3	Yes	17	4	Dose reduced

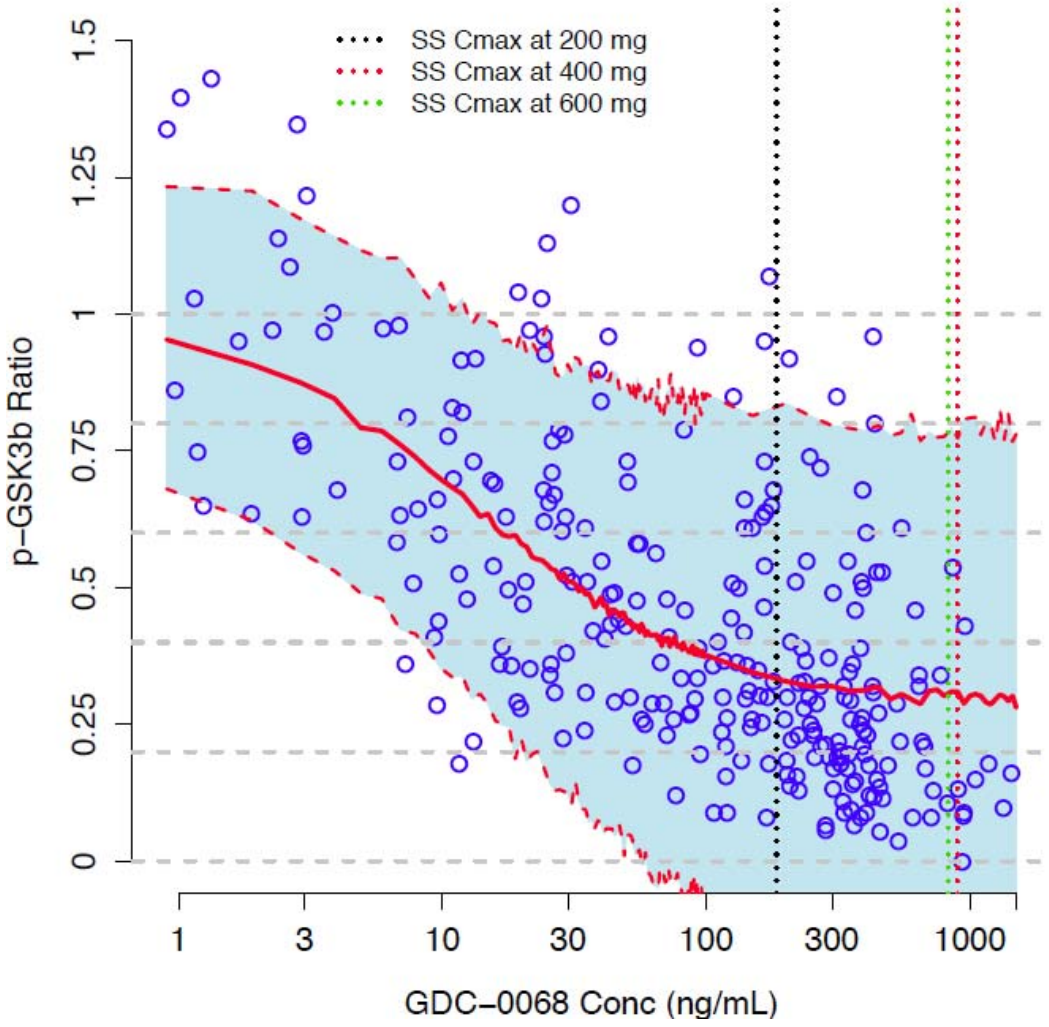
CTCAE = Common Terminology Criteria for Adverse Events v. 3.0; ID = identification; NCI = National Cancer Institute; QD = once daily; SAE = serious adverse event.

[a] Patients are categorized by initial dose cohort assignment, regardless of subsequent dose modification.

[b] Patient 25102 experienced the same adverse event of diarrhea twice.

[c] Both the Grade 3 asthenia at 800 mg in one patient, and Grade 3 nausea in another patient qualified as dose-limiting toxicities (DLTs).

Supplementary Figure S3. Suppression of pGSK3β in platelet-rich plasma versus ipatasertib concentrations.



Supplementary figure S4. Pharmacodynamic (PD) dose-dependent elevations in glucose and insulin following treatment with ipatasertib.

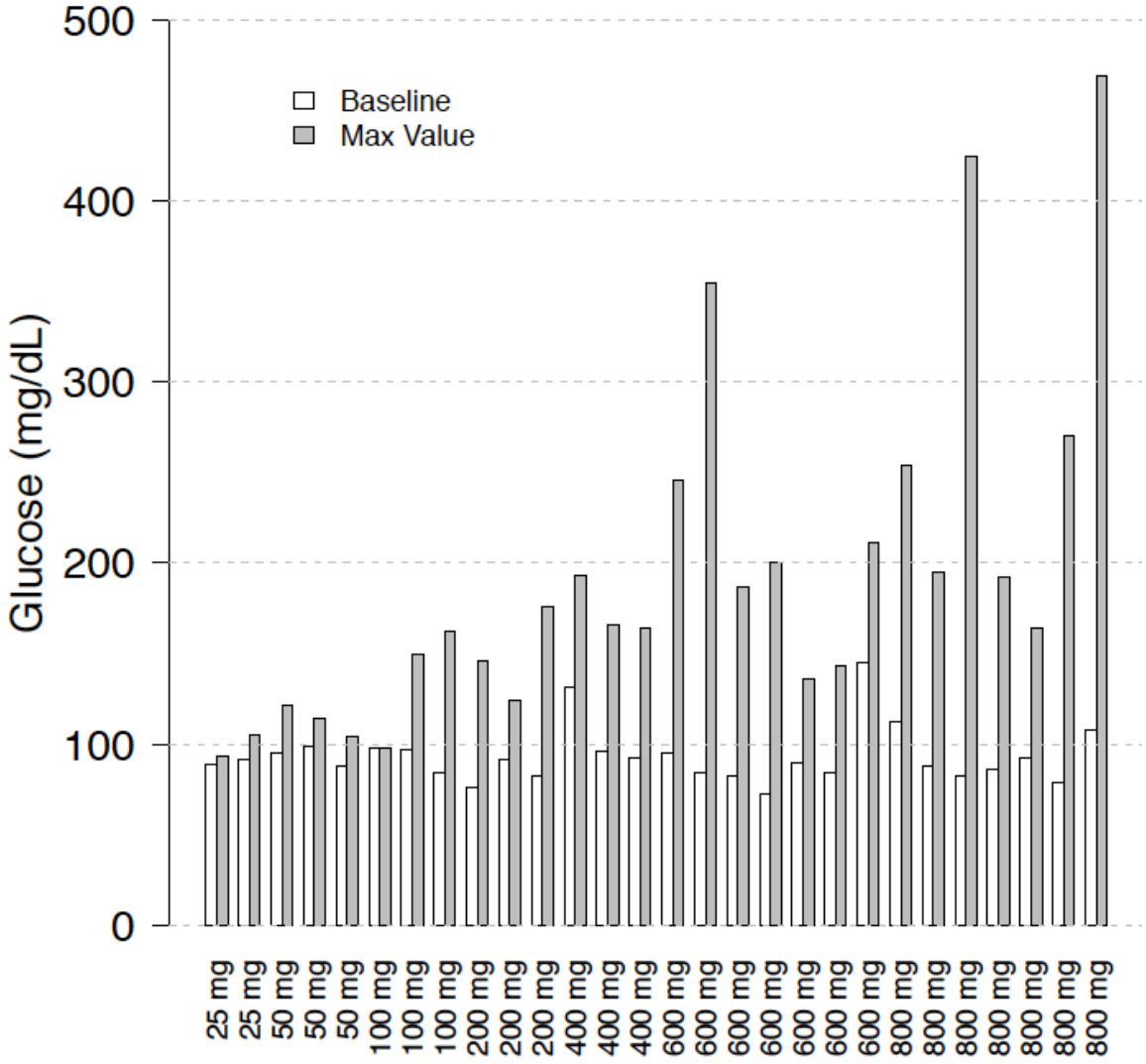
A, After 15 days of dosing, baseline glucose (white bars, in mg/dL) and maximum post-dose glucose (gray bars) are shown for patients in Stage 1, ranked by increasing doses of ipatasertib (25 mg to 800 mg). Glucose values are generally below 200 mg/dL at ipatasertib doses < 600 mg. Beginning at 600 mg, however, higher glucoses can be observed and were more frequent at 800 mg. Elevations in glucose were transient and generally returned to baseline within 6 hours.

B, After 15 days of dosing, baseline insulin (white bars, in mU/L) and maximum post-dose insulin (gray) are shown for patients in Stage 1, ranked by increasing doses. Similar to the glucose elevations, insulin levels also increase beginning at 600 mg and increase further at 800 mg of ipatasertib. Elevations in insulin were transient and generally returned to baseline within 6 hours.

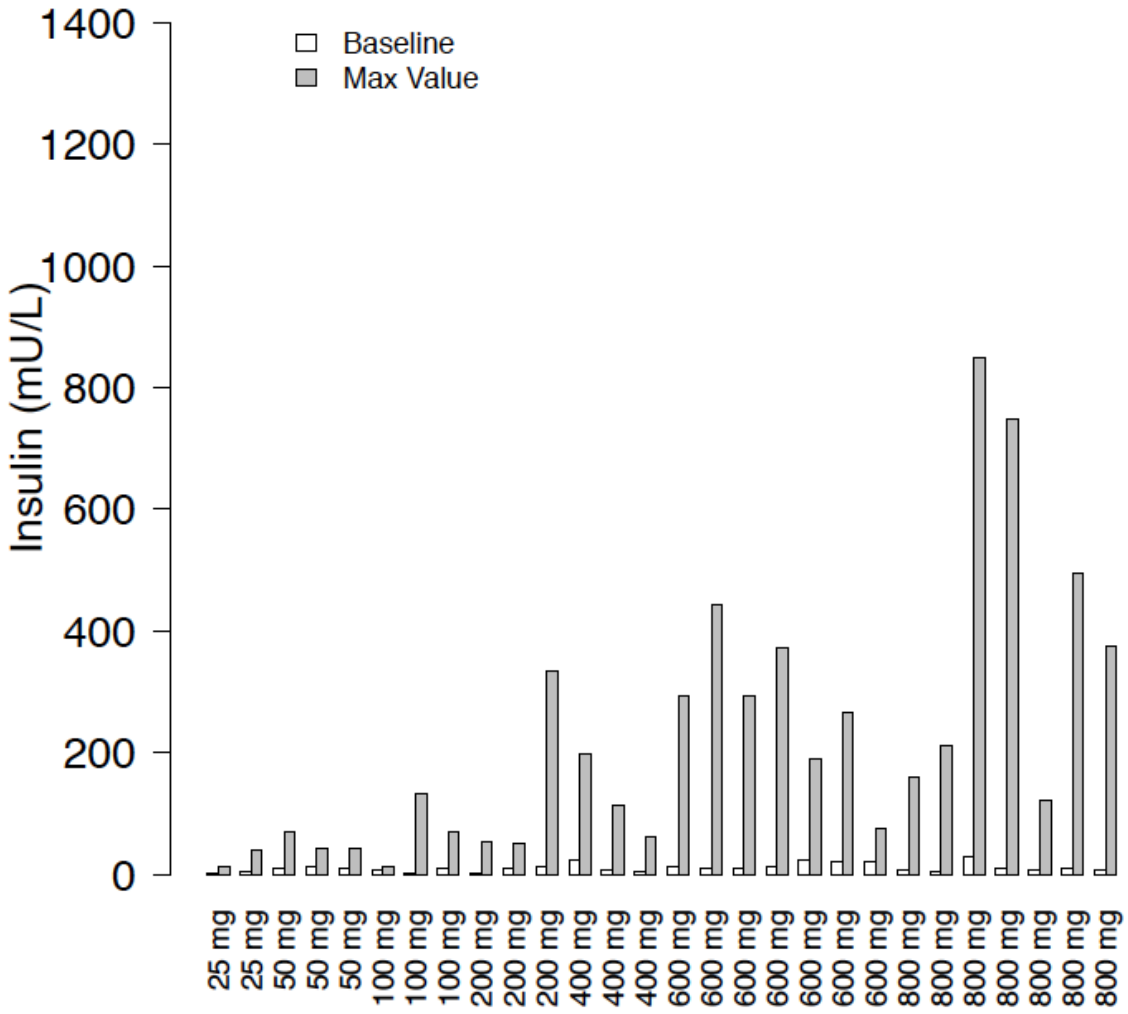
C, As an representative example, glucose (red line, in mg/dL left side) and insulin (blue, in mU/L, right side) are shown with the exposures of ipatasertib (green) for a patient from Stage 1 treated with 600 mg of ipatasertib. Blood samples were checked on Day 1 and on Day 15 in Cycle 1. Glucose and insulin increased following ipatasertib, reaching a peak at 4 hours post-dose, but both values normalized within 6 hours.

D, Changes in fasting pre-dose blood glucoses for all patients (at all dose levels) through Cycles 1 and 2 in Stage 1 are graphed as a percentage of the baseline values. The majority of patients show relatively stable glucose values, without significant elevations.

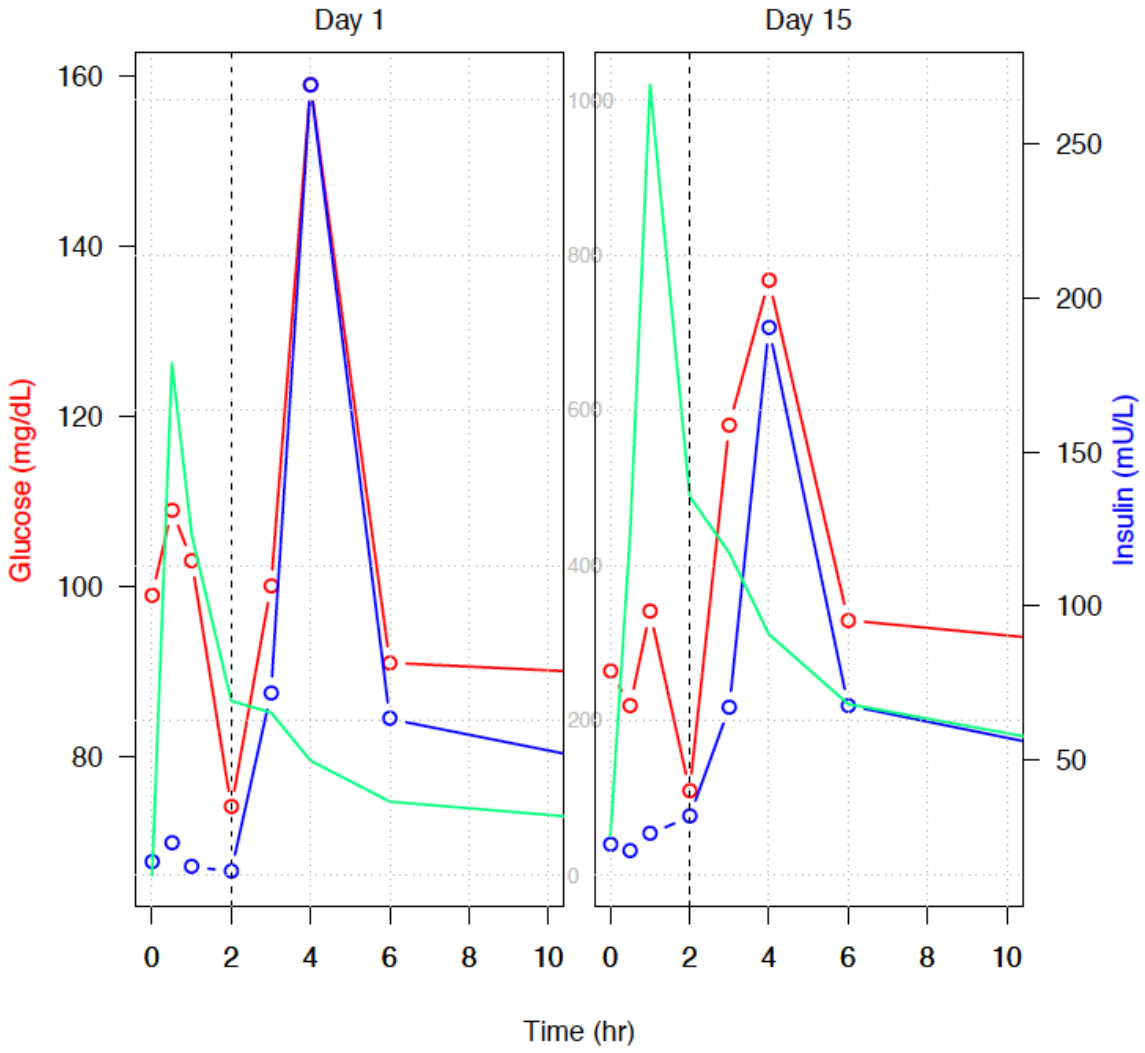
Supplementary figure S4A.



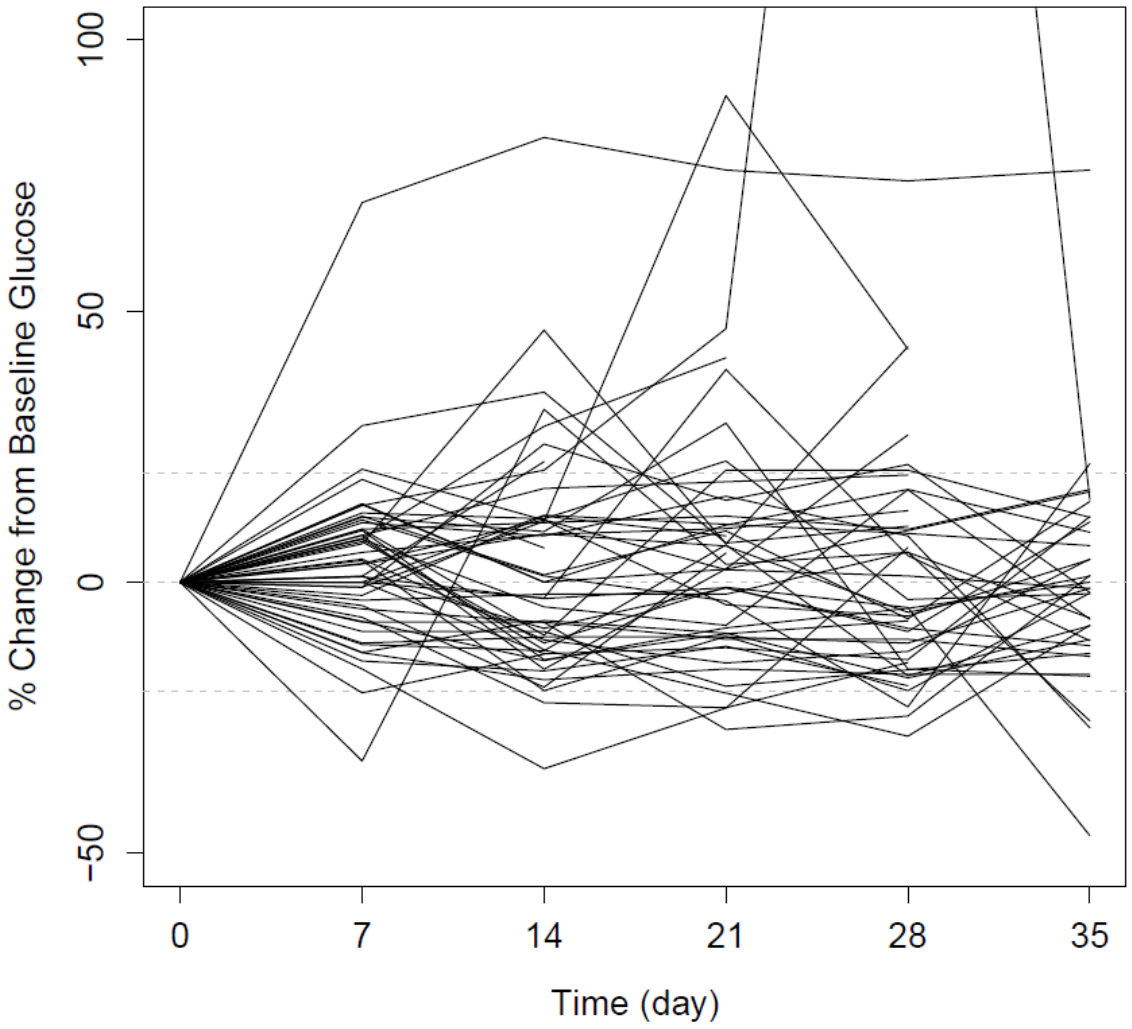
Supplementary figure S4B.



Supplementary figure S4C.



Supplementary figure S4D.



Supplementary Table S7. Hemoglobin A1C (HgbA1C) values for patients who had both pre-treatment and post-treatment values in Stages 1 and 2.

Ipatasertib Dose (mg)	Patient ID	Day	HbgA1C
25	10102	1	5.7
		65	5.2
	10103	1	4.8
		57	5.1
50	10202	1	5
		43	5
100	10301	1	5.4
		43	5.3
	10303	1	5.4
		48	5.4
200	10401	1	5.2
		62	5.4
	10402	1	5.6
		89	5
	10403	1	5.2
		232	5.6
400	10501	1	5.5
		58	5.5
	10502	1	5.7
		38	5.8
	10503	1	5.9
		37	5.7
600	10701	1	6.2
		29	6.3
	10702	1	5.1
		23	6.1
	10705	1	5.7
		36	6.0
	10706	1	5.7
		77	5.8
	10708	1	6.9
		12	6.5

Ipatasertib Dose (mg)	Patient ID	Day	HgbA1C
600	25102	1	5.5
		55	5.5
	25103	1	5.6
		14	5.8
	25104	1	5.2
		365	5.5
	26101	1	5.9
		260	6.3
	26105	1	5.7
		85	5.8
	26106	1	5.6
		229	7.1
	26110	1	5.5
		63	5.7
	26111	1	6.8
		102	6.9
800	10601	1	5.7
		28	6.8
	10603	1	4.5
		59	6.2
	10604	1	4.7
		78	4.6
	10605	1	5.3
		21	5.5
	10606	1	5.5
		71	6.4
	10607	1	5.9
		183	6.4

Supplementary Table S8. Summary data for patients with best radiographic stable disease (SD) by RECIST version 1.0 criteria.

Stage	Ipatasertib Dose (mg)	Days on Study	Best RECIST Response	Cancer Diagnosis	PTEN H-score [a]	*PIK3CA*/*AKT* mutation [a]
1	100	65	SD	Ovarian	0	MND
	200	122	SD	Chondrosarcoma	NE	NE
	400	232	SD	Colorectal	100	*PIK3CA* H1047R
	600	77	SD	Colorectal	150	MND
		245	SD	Chondrosarcoma	NE	NE
	800	28	SD	Colorectal	100	MND
		183	SD	Colorectal	200	MND
2	600	169	IR/SD [b]	Prostate	300	MND
		1072	IR/SD [b]	Prostate	0	MND
		85	IR/SD [b]	Prostate	NE	NE
		260	SD	Breast	115	*PIK3CA* H1047R
		55	SD	Breast	0	MND
		85	SD	Breast	200	MND
		229	SD	Breast	300	*AKT1* E17K
		102	SD	Breast	NE	NE
3	600	249	SD	Lung	NE	NE

IR = incomplete response, mg = milligrams, MND = mutation not detected, NE = not evaluable, RECIST = Response Evaluation Criteria in Solid Tumors, SD = stable disease.

[a] PI3K/Akt pathway alteration was determined by central Genentech assessment. PTEN status was assessed by immunohistochemistry (H-score). *PIK3CA* or *AKT1* mutations were assessed by RT-PCR analysis.

[b] Patients with metastatic castration-resistant prostate cancer who had no measurable target lesion at screening and had a best RECIST response of IR/SD.