Supplementary Table S2: Reduction in PI3K pathway signaling in serial hair-sheath samples and skin biopsies

Immunofluorescence quantification of the impact on phosphomarkers of the PIK3 pathway in D1 pre-dose and serial post-dose samples from four patients receiving SAR245408 120mg (n=2), 225mg and 600mg daily on the 21/7 regimen was performed. Modulations shown are significant, except where indicated as non-significant (ns). The statistical analysis employed two-tailed student t test analysis with $p<0.05$ to be considered statistically significant. Bonferroni adjustment was applied when multiple comparisons against a single baseline sample were performed.

Serial Hair Sheath Samples			**Decrease relative to baseline, %**					
Tumor histology	**SAR245408 daily dose, mg, regimen**	**On-study sampling day, time**	**pAKT(T308)**	**pAKT(S473)**	**pPRAS40(T246)**	**p4EBP1(T70)**	**pS6(S240:244)**	**Ki67**
Lymphoma	**120, 21/7**	D1 post	N/A	1 (ns)	-3 (ns)	-2 (ns)	-23 (ns)	29 (ns)
		D8 pre	N/A	57	70	62	60	N/A
		D8 post	N/A	42	52	58	43	-6 (ns)
		D23 pre	N/A	80	81	79	68	N/A
		D23 post	N/A	80	80	77	68	40 (ns)
Breast carcinoma	**120, 21/7**	D1 post	N/A	-4 (ns)	6 (ns)	18 (ns)	10 (ns)	9 (ns)
		D21 pre	N/A	32	74	46	57	7 (ns)
		D21 post	N/A	51	74	59	72	15 (ns)
NSCLC	**225, 21/7**	D1 post	-7 (ns)	0	0	-6	17 (ns)	N/A
		D8 pre	50	43	39	34	18	N/A
		D8 post	51	44	39	49	42	N/A
		D22 pre	75	71	58	59	82	N/A
		D22 post	75	72	59	60	82	N/A
Prostate adenocarcinoma	**600, 21/7**	D1 post	7 (ns)	N/A	N/A	23 (ns)	N/A	33 (ns)
		D8 pre	12 (ns)	N/A	N/A	41	N/A	27 (ns)
		D8 post	46	N/A	N/A	69	N/A	36 (ns)
		D21 pre	47	N/A	N/A	81	N/A	-10 (ns)
		D21 post	48	N/A	N/A	82	N/A	18 (ns)

21/7 = dose administered for the first 21 days of a 28-day cycle; CDD = continuous once-daily dosing; N/A = not available; post = post-dose; pre = pre-dose.

Supplementary Table S2 (con't): Reduction in PI3K pathway signaling in serial hair-sheath samples and skin biopsies

Immunofluorescence quantification of the impact on phosphomarkers of the PIK3 pathway was performed in skin biopsies from nine patients administered SAR245408 and collected on D1 pre-dose and on D20/29 4h post-dose. In the sample collected from the hamartoma (Cowden syndrome) patient, TUNEL was also assessed and no change observed. Modulations shown are significant, except those indicated as non-significant. The statistical analysis employed two-tailed student t test analysis with $p<0.05$ to be considered statistically significant. Bonferroni adjustment was applied when multiple comparisons against a single baseline sample were performed.

		Skin Biopsies	**Decrease relative to baseline, %**							
Tumor histology	**Dose, mg, regimen**	**On-study sampling day**	**pAKT (T308)**	**pAKT (S473)**	**pPRAS40 (T246)**	**P4EBP1 (T70)**	**pS6 (S240/S244)**	**pMEK (S217/S221)**	**pERK (T202/Y204)**	**Ki67**
NSCLC	30, 21/7	D20	50	NA	NA	54	NA	NA	NA	NA
Colon adenocarcinoma	60, 21/7	D21 post	39	35	47	NA	37	NA	17 (ns)	13 (ns)
Cervix carcinoma	225, 21/7	D21 post	30	32	43	53	37	NA	NA	4 (ns)
Prostate adenocarcinoma	600, 21/7	D1 post	34 (ns)	8 (ns)	23 (ns)	8 (ns)	16 (ns)	NA	NA	13 (ns)
		D21 pre	45	28	41	42	51	NA	NA	-4 (ns)
		D21 post	47	40	45	44	53	NA	NA	10 (ns)
Merkel cell carcinoma*	600, 21/7	D1 post	0	NA	NA	3 (ns)	NA	NA	NA	-5 (ns)
		D21 pre	44	NA	NA	41	NA	NA	NA	-1 (ns)
		D21 post	45	NA	NA	43	NA	NA	NA	-1 (ns)
Leiomyosarcoma*	600, 21/7	D1 post	0	NA	NA	1	NA	NA	NA	NA
		D21 pre	41	NA	NA	45	NA	NA	NA	NA
		D21 post	44	NA	NA	54	NA	NA	NA	NA
		D29 pre	45	NA	NA	55	NA	NA	NA	NA
Parotid carcinoma*	900,21/7 (dose halted and reduced)	D8 post	1 (ns)	15 (ns)	13 (ns)	14 (ns)	12 (ns)	12 (ns)	12 (ns)	-5 (ns)
		D10 pre	16 (ns)	32	14 (ns)	16 (ns)	13 (ns)	13 (ns)	13 (ns)	-2 (ns)
		D15	30	42	26	31	23	22 (ns)	22 (ns)	1 (ns)
Pancreatic cancer*	100, CDD	D1 post	3 (ns)	NA	NA	0	NA	NA	NA	NA
		D28 pre	42	NA	NA	55	NA	NA	NA	NA
		D28 post	45	NA	NA	55	NA	NA	NA	NA
Hamartoma (Cowden)*	600, 21/7	D1 post	23 (ns)	NA	NA	13 (ns)	NA	NA	NA	2.1 (ns)
		D21 pre	36	NA	NA	28	NA	NA	NA	15 (ns)
		D21 post	42	NA	NA	35	NA	NA	NA	16 (ns)

*Patients for whom tumor biopsies were also available. NA = data not available; ns = not significant; post = post-dose pre = pre-dose.