

**Supplementary Table S1:
Safety of SAR245408 (Dose-limiting toxicities and Grade 3/4 adverse events)**

Dose-limiting toxicities according to dose level and treatment regimen			
	Dose (mg)	Days on treatment, median (range)	Dose-limiting toxicity frequency/total patients
21/7 regimen	30	50 (40–224)	0/3
	60	216 (49–392)	0/3
	120	67 (8–330)	0/4
	225	49 (21–616)	0/3
	400	49 (8–106)	1/9 (grade 2 rash)
	600*	57 (10–198)	1/16 (grade 3 rash)
	900†	50 (49–67)	2/3 (grade 3 rash)
CDD regimen	100	107 (15–721)	0/4
	400	109 (44–200)	0/3
	600*	56 (10–230)	0/21#

*Maximum tolerated dose (21/7)/recommended phase 2 dose (CDD); †Maximum administered dose.

#One event of grade 3 hypersensitivity, ultimately deemed unlikely related to SAR245408.

Grade 3/4 adverse events in ≥2% of patients (regardless of relationship with SAR245408)					
	All 21/7 combined n=41 n (%)	21/7 MTD (600mg) n=16 n (%)	All CDD combined n=28 n (%)	CDD MTD (600mg) n=21 n (%)	Total N=69 n (%)
Number of patients with at least one grade 3 or 4 AE	22 (53.7)	8 (50.0)	19 (67.9)	12 (57.1)	41 (59.4)
GGT increased	3 (7.3)	2 (12.5)	2 (7.1)	0	5 (7.2)
Diarrhea	3 (7.3)	1 (6.3)	1 (3.6)	1 (4.8)	4 (5.8)
Dyspnea	2 (4.9)	1 (6.3)	2 (7.1)	2 (9.5)	4 (5.8)
Rash related skin toxicity*	3 (7.3)	1 (6.3)	2 (7.1)	2 (9.5)	5 (7.2)
Abdominal pain	2 (4.9)	1 (6.3)	0	0	2 (2.9)
Dehydration	2 (4.9)	2 (12.5)	0	0	2 (2.9)
Bone pain	2 (4.9)	2 (12.5)	0	0	2 (2.9)
Hyponatremia	2 (4.9)	0	0	0	2 (2.9)
Hypokalemia	0	0	2 (7.1)	1 (4.8)	2 (2.9)
Pelvic pain	0	0	2 (7.1)	1 (4.8)	2 (2.9)
Pulmonary embolism	1 (2.4)	1 (6.3)	2 (7.1)	1 (4.8)	3 (4.3)

CDD = continuous once-daily dosing; CTCAE = Common Terminology Criteria for Adverse Events;

GGT = gamma-glutamyltransferase; MTD = maximum tolerated dose; AE = adverse event; 21/7 = 21 consecutive days on treatment followed by 7 days off treatment. Reported event terms were coded using MedDRA dictionary version 14.0.

At each level of summarization, a patient was counted once for the most severe event if the patient reported one or more events. CTCAE grade: 1 = mild, 2 = moderate, 3 = severe, 4 = life-threatening or disability.

*Includes events coded as rash, macular rash, follicular rash, generalized rash, erythema, skin exfoliation, photosensitivity, eczema and fissuring.