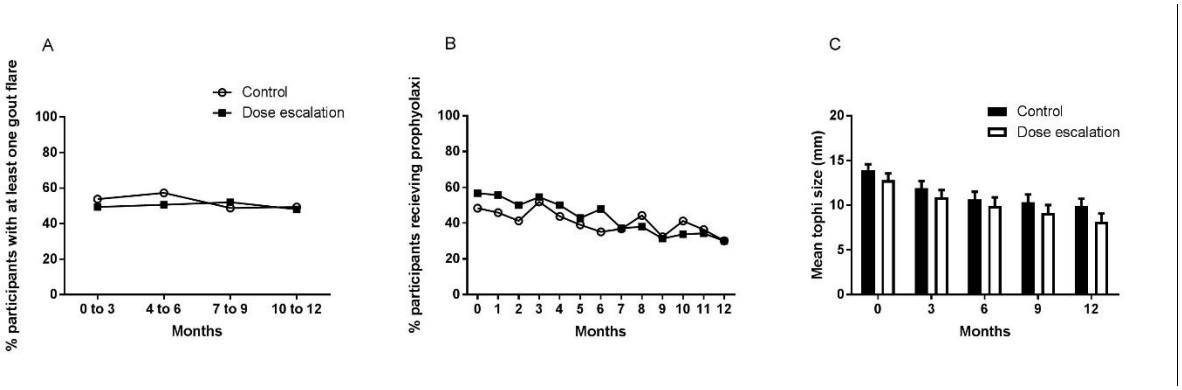
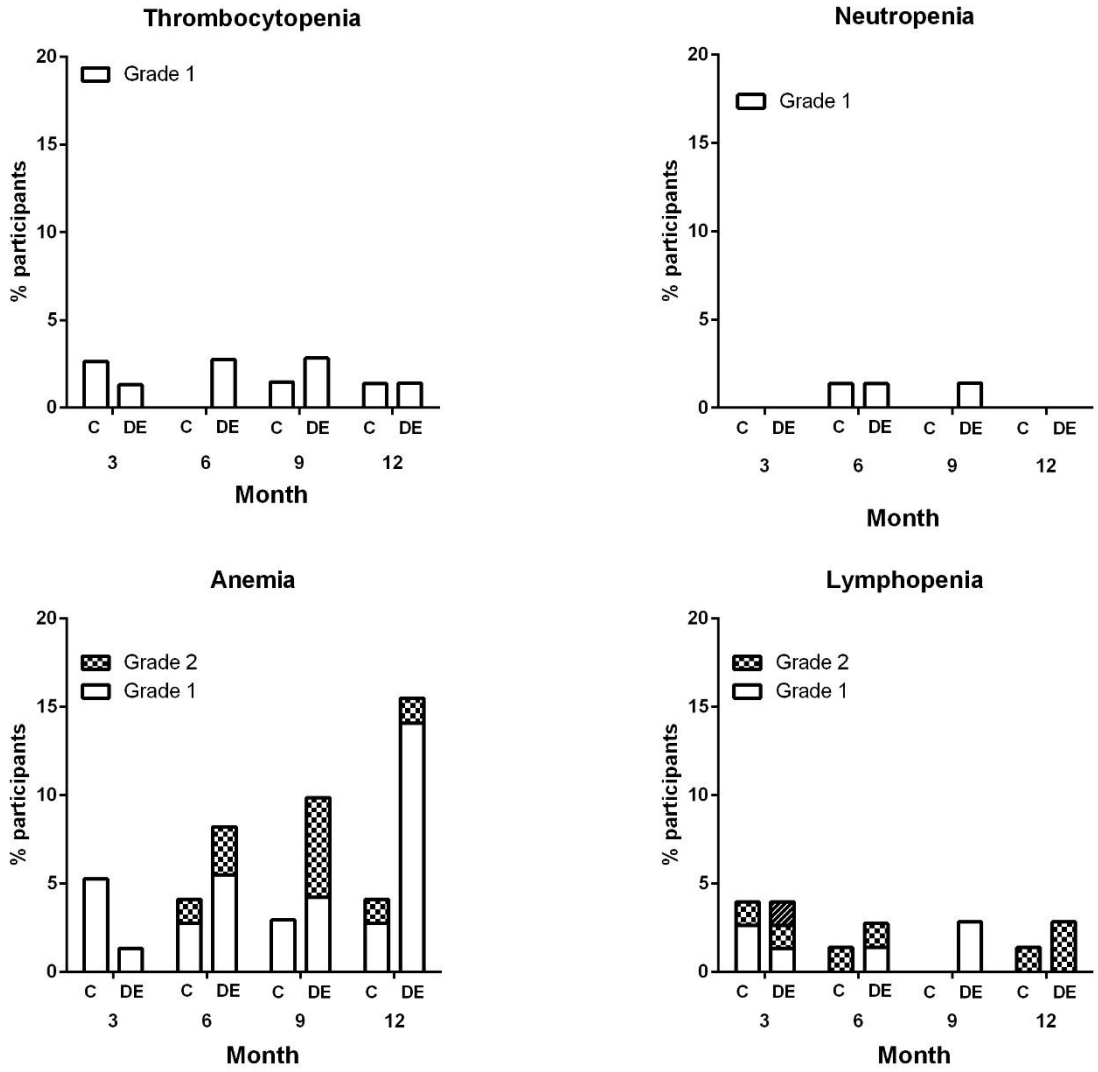
Supplementary Figure 1: Change in gout flares and tophi over study in control and dose escalation groups. A) Percentage of participants reporting at least one gout flare in each time period, B) percentage of participants receiving prophylaxis over the study period and C) Mean (SE) size in tophi at each study visit (for those with measurable tophus at baseline). There were no statistically significant differences between the control and dose escalation groups.



Supplementary Figure 2: Percentage of participants with laboratory hematological variables. C: control, DE: dose escalation.



Supplementary Table 1: Number (%) of participants with laboratory abnormalities at baseline by CTCAE grade

	Grade 1		Grade 2		Grade 3		Grade 4	
	Control	**Dose escalation**	**Control**	**Dose escalation**	**Control**	**Dose escalation**	**Control**	**Dose escalation**
GGT*	25 (27%)	32 (36%)	6 (7%)	7 (8%)	2 (2%)	0	0	0
ALP*	6 (7%)	11 (12%)	1 (1%)	0	0	0	0	0
ALT^	11 (12%)	15 (17%)	0	0	0	0	0	0
AST^	4 (4%)	3 (3%)	0	0	0	0	0	0
Creatinine#	29 (31%)	34 (38%)	10 (11%)	15 (17%)	5 (5%)	1 (1%)	0	2 (2%)
Anemia**	15 (16%)	21 (23%)	3 (3%)	0	0	0	0	0
Neutropenia^^	0 (0%)	1 (1%)	0	0	0	0	0	0
Eosinophilia##	10 (11%)	6 (7%)	2 (2%)	0	0	0	0	0

GGT – gamma glutamyl transferase, ALP – alkaline phosphatase, ALT – alanine transferase, AST – aspartate transaminase
*GGT/ALP – grade 1: >1 – 2.5xULN, grade 2: >2.5 – 5xULN, grade 3: >5-20xULN; grade 4: >20xULN
^ALT/AST - grade 1: >1 - 3xULN, grade 2: >3 – 5xULN, grade 3: >5-20xULN; grade 4 >20xULN
#Creatinine - grade 1: >1 – 1.5xbaseline, grade 2: >1.5 – 3xbaseline, grade 3: >3-6xbaseline; grade >6xbaseline
**Anemia – grade 1:HB <LLN -10g/dl, grade 2 : HB<10 – 8.0 g/dl, grade 3:<8.0g/dl
^^Neutropenia – grade 1: <LLN – 1.5x10^9/l, grade 2: <1.5-1.0x10^9/l
##Eosinophilia – grade 1: 0.5-1.0x10^9/l; grade 2: 1.1-1.9x10^9/l; grade 3 2.3-3.0 x10^9/l

Supplementary Table 2: Primary and secondary efficacy endpoints

Endpoint	**Control**	**Dose escalation**	**P value**
Primary endpoint			
Reduction in serum urate at final visit (mg/dl)	-0.34	-1.5	<0.001
Secondary endpoints			
Serum urate <6mg/dl at last 3 monthly visits n (%)	10/73 (14%)	42/71 (59%)	<0.001
Serum urate <6mg/dl at final visit n (%)	30 (32%)	62 (69%)	<0.001
Percentage change in serum urate from baseline to final visit mean (SE)	-3.3 (2.2)	-17.8 (2.3)	<0.001
HAQ mean (SE)	N=73	N=70	
Baseline	0.53 (0.07)	0.57 (0.07)	0.51
Month 12	0.51 (0.09)	0.62 (0.09	
Pain VAS mean (SE)			
Baseline	1.73 (0.27)	1.97 (0.27)	0.42
Month 12	2.04 (0.31)	1.93 (0.32)	
SJC mean (SE)			
Baseline	1.92 (0.60)	1.42 (0.60)	0.93
Month 12	1.58 (0.69)	1.01 (0.70)	
TJC mean (SE)			
Baseline	3.43 (0.78)	2.11 (0.79)	0.39
Month 12	2.07 (0.86)	1.73 (0.86)	

HAQ – health assessment questionnaire, VAS – visual analogue scale, SJC – swollen joint count, TJC – tender joint count

Supplementary Table 3: Number of non-laboratory adverse events within each CTCAE category

	Number of events										
	Not related	Possibly related	Probably related	Definitely related	Total		Not related	Possibly related	Probably related	Definitely related	Total
Group 1: Control	329		7		336	Group 2: Immediate dose escalation	309	8	21	1	339
Blood and lymphatic system disorders					0		1				1
Cardiac disorders	17				17		7				7
Ear and labarynth disorders	3				3		2		9		11
Endocrine disorders					0		1				1
Eye disorders	5				5		4				4
Gastrointestinal disorders	39				39		28		6		34
General disorders	78				78		73	1			74
Hepatobiliary disorders					0		2				2
Immune system disorders	1				1		0		1		1
Infections and infestations	25				25		19				19
Injury, poisoning and procedural complications	15				15		28			1	29
Metabolism and nutrition disorders	5				5		1				1
Musculoskeletal and connective tissue disorders	50				50		43		1		44
Neoplasms benign, malignant and unspecified	5				5		4				4
Nervous system disorders	16				16		14	2			16
Psychiatric disorders	6				6		5				5
Renal and urinary disorders					0		2				2
Reproductive and breast disorders	2				2		0				
Respiratory, thoracic and mediastinal disorders	22				22		19				19
Skin and subcutaneous disorders	28		7		35		39	5	4		48
Surgical and medical procedures	2				2		2				2
Vascular disorders	9				9		15				15
Venous disorders	1				1		0				0

Supplementary Table 4: Number (%) of participants with hematological laboratory adverse events in the control and dose escalation groups during the study period.

	Control (n=93)	Dose escalation (n=90)
Eosinophilia	15 (16%)	14 (16%)
Thrombocytopenia	2 (2%)	4 (4%)
Neutropenia	1 (1%)	1 (1%)
Lymphopenia	3 (3%)	6 (7%)
Anemia	8 (9%)	14 (16%)
Any	25 (27%)	30 (33%)