

SUPPLEMENTARY INFORMATION

Clinical Drug Investigation

Title: Pharmacokinetics, pharmacodynamics and safety of peficitinib (ASP015K) in healthy male Caucasian and Japanese subjects

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Supplementary Table S1. Lymphocyte subsets

	Subset	Cell type
1	CD45+, CD3+, CD4+, CD45RA+, CD28+	Naïve T cells
2	CD45+, CD3+, CD4+, CD45RA+, CD28(-)	Effector T cells
3	CD45+, CD3+, CD4+, CD45RA(-), CD28(-)	Effector memory T cells
4	CD45+, CD3+, CD4+, CD45RA(-), CD28+	Central memory T cells
5	CD45+, CD3+, CD8+, CD45RA+, CD28+	Naïve T cells
6	CD45+, CD3+, CD8+, CD45RA+, CD28(-),	Effector T cells
7	CD45+, CD3+, CD8+, CD45RA(-), CD28(-)	Effector memory T cells
8	CD45+, CD3+, CD8+, CD45RA(-), CD28+	Central memory T cells
9	CD3+, CD4+, CD45RA(-)	Total CD4+ memory
10	CD3+, CD8+, CD45RA(-)	Total CD8+ memory
11	CD3+, CD4+, CD45RA +	Total CD4+ naïve
12	CD3+, CD8+, CD45RA+	Total CD8+ naïve
13	CD3+, CD45RA+	Total naïve
14	CD3+, CD45RA(-)	Total memory
15	CD45+, CD3+, CD4+, CD25+, CD127low	T regulatory cells

Supplementary Table S2. Mean percentage change from baseline in peripheral lymphocyte subsets (single-dose study, Japanese and Caucasian subjects)

	Peficitinib dose			
	Placebo ^a (n=6)	20 mg (n=6)	60 mg (n=6)	200 mg (n=6)
CD45+, CD3+, CD4+, CD45RA+, CD28+, naïve T cells				
Japanese	-2.13	0.80	-1.57	2.35
Caucasian	-1.53	-1.47	-0.68	-1.65
CD45+, CD3+, CD4+, CD45RA+, CD28(-), effector T cells				
Japanese	0	0.05	0.15	-0.05
Caucasian	-0.02	0	0.03	0.05
CD45+, CD3+, CD4+, CD45RA(-), CD28(-), effector memory T cells				
Japanese	0.13	0.07	0.20	-0.33
Caucasian	0.02	0.03	0.02	0.23
CD45+, CD3+, CD4+, CD45RA(-), CD28+, central memory T cells				
Japanese	-1.13	0.02	0.17	1.00
Caucasian	-1.20	-1.28	-0.52	0.08
CD45+, CD3+, CD8+, CD45RA+, CD28+, naïve T cells				
Japanese	-1.92	-0.15	-1.87	0.15
Caucasian	-0.75	-0.50	-0.52	-1.20
CD45+, CD3+, CD8+, CD45RA+, CD28(-), effector T cells				
Japanese	0.52	0.42	0.38	-1.15
Caucasian	0.40	0.23	-0.12	0.47
CD45+, CD3+, CD8+, CD45RA(-), CD28(-), effector memory T cells				
Japanese	0.47	0.03	0.18	-0.43
Caucasian	0.12	0.18	0.33	0.25
CD45+, CD3+, CD8+, CD45RA(-), CD28+, central memory T cells				
Japanese	0.28	-0.32	0.45	0.13
Caucasian	0.17	-0.12	0.93	0.53
CD3+, CD4+, CD45RA(-), total CD4+ memory				
Japanese	-0.97	0.05	0.37	0.62
Caucasian	-1.20	-1.27	-0.50	0.30
CD3+, CD8+, CD45RA(-), total CD8+ memory				
Japanese	0.70	-0.30	0.62	-0.25
Caucasian	0.30	0.07	1.25	0.80
CD3+, CD4+, CD45RA+, total CD4+ naïve				
Japanese	-2.13	0.73	-1.33	2.37
Caucasian	-1.53	-1.48	-0.62	-1.58
CD3+, CD8+, CD45RA+, total CD8+ naïve				
Japanese	-1.42	0.23	-1.43	-0.97

Caucasian	-0.33	-0.28	-0.63	-0.75
CD3+, CD45RA+, total naïve				
Japanese	-2.35	0.50	-2.00	0.02
Caucasian	-1.33	-1.65	-1.07	-2.88
CD3+, CD45RA(-), total memory				
Japanese	-0.48	-0.17	0.83	0.53
Caucasian	-0.63	-1.03	-0.02	1.25
CD45+, CD3+, CD4+, CD25+, CD127 low, T regulatory cells				
Japanese	-0.12	0.57	-0.38	0.48
Caucasian	-0.25	-0.42	-0.38	-0.13

^aData for subjects receiving placebo were pooled

Supplementary Table S3. Mean percentage change from baseline in peripheral lymphocyte subsets (multiple-dose study, Japanese subjects) (PDAS)

Lymphocyte subset/ time point	Placebo bid ^a (n=6)	Peficitinib dose		
		10 mg bid (n=6)	30 mg bid (n=6)	100 mg bid (n=6)
CD45+, CD3+, CD4+, CD45RA+, CD28+, naïve T cells				
Day 4, pre-dose	-1.87	-1.57	-0.72	-2.77
Day 7, pre-dose	0.48	-3.72	-1.35	-3.32
Day 7, 72 h post-dose	-2.13	-4.67	-0.77	-4.82
CD45+, CD3+, CD4+, CD45RA+, CD28(-), effector T cells				
Day 4, pre-dose	0.20	0.00	-0.02	-0.08
Day 7, pre-dose	0.82	0.12	-0.05	-0.18
Day 7, 72 h post-dose	0.38	0.10	0.02	0.02
CD45+, CD3+, CD4+, CD45RA(-), CD28(-), effector memory T cells				
Day 4, pre-dose	0.17	0.08	0.08	0.38
Day 7, pre-dose	0.23	0.35	0.05	0.13
Day 7, 72 h post-dose	0.22	0.42	0.03	0.18
CD45+, CD3+, CD4+, CD45RA(-), CD28+, central memory T cells				
Day 4, pre-dose	0.62	0.10	-1.07	-1.40
Day 7, pre-dose	-1.18	0.55	0.32	-0.80
Day 7, 72 h post-dose	-0.87	-0.43	-0.92	-0.75
CD45+, CD3+, CD8+, CD45RA+, CD28+, naïve T cells				
Day 4, pre-dose	0.27	0.75	-0.83	-3.20
Day 7, pre-dose	0.35	-0.98	-1.33	-3.87
Day 7, 72 h post-dose	-0.63	-1.87	-1.07	-4.38
CD45+, CD3+, CD8+, CD45RA+, CD28(-), effector T cells				
Day 4, pre-dose	-0.18	0.03	-0.15	0.57
Day 7, pre-dose	-0.77	0.28	-0.13	0.05
Day 7, 72 h post-dose	0.77	0.43	0.33	0.27
CD45+, CD3+, CD8+, CD45RA(-), CD28(-), effector memory T cells				
Day 4, pre-dose	-0.27	-0.17	0.13	0.18
Day 7, pre-dose	-0.10	-0.03	0.22	0.18
Day 7, 72 h post-dose	0.02	0.03	0.32	0.18
CD45+, CD3+, CD8+, CD45RA(-), CD28+, central memory T cells				
Day 4, pre-dose	0.17	-0.48	0.42	-0.12
Day 7, pre-dose	0.55	-0.28	1.15	0.38
Day 7, 72 h post-dose	0.48	-0.33	0.27	-0.33
CD3+, CD4+, CD45RA(-), total CD4+ memory				
Day 4, pre-dose	0.83	0.18	-1.02	-1.03
Day 7, pre-dose	-0.92	0.95	0.38	-0.72

Day 7, 72 h post-dose	-0.57	0.02	-0.83	-0.57
CD3+, CD8+, CD45RA(-), total CD8+ memory				
Day 4, pre-dose	-0.08	-0.62	0.52	0.05
Day 7, pre-dose	0.48	-0.32	1.37	0.53
Day 7, 72 h post-dose	0.50	-0.25	0.57	-0.15
CD3+, CD4+, CD45RA+, total CD4+ naïve				
Day 4, pre-dose	-1.65	-1.47	-0.65	-2.73
Day 7, pre-dose	1.25	-3.47	-1.37	-3.42
Day 7, 72 h post-dose	-1.68	-4.38	-0.70	-4.65
CD3+, CD8+, CD45RA+, total CD8+ naïve				
Day 4, pre-dose	0.08	0.75	-1.05	-2.60
Day 7, pre-dose	-0.42	-0.70	-1.48	-3.80
Day 7, 72 h post-dose	0.13	-1.45	-0.77	-4.07
CD3+, CD45RA+, total naïve				
Day 4, pre-dose	-1.53	-1.55	-1.25	-4.68
Day 7, pre-dose	0.15	-5.35	-2.52	-6.47
Day 7, 72 h post-dose	-0.80	-6.30	-1.30	-7.50
CD3+, CD45RA(-), total memory T cells				
Day 4, pre-dose	1.90	1.02	-0.37	-0.93
Day 7, pre-dose	2.23	2.72	1.93	-0.02
Day 7, 72 h post-dose	0.33	1.70	-0.42	-0.93
CD45+, CD3+, CD4+, CD25+, CD127 low, T regulatory cells				
Day 4, pre-dose	-0.23	-1.08	-0.17	-0.52
Day 7, pre-dose	-0.12	-1.20	-0.18	-0.68
Day 7, 72 h post-dose	-0.30	-1.27	-0.28	-0.48

Bid, twice daily; PDAS, pharmacodynamic analysis set
^aData for subjects receiving placebo were pooled