SUPPLEMENTAL SECTION

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Scheduling of clinic visits

On day 1 (week 0, investigational site), patients were trained to prepare and self-administer treatment on non-clinic visit days. Thereafter, clinic/home visits were scheduled every other week starting from day 15 (week 2) to day 85 (week 12 – end of treatment (EOT). Home visits, during which blood samples were collected, were carried out on days 43 (week 6) and 71 (week 10). If patients discontinued treatment before week 12, an EOT visit was performed, with a safety follow-up visit 6 weeks after treatment discontinuation.

Supplemental table I Safety and tolerability of sarilumab- safety population

Primary SOC and PT, n (%)	Placebo (n=50)	Sarilumab				
		100 mg q2w (n=49)	150 mg q2w (n=51)	100 mg qw (n=52)	200 mg q2w (n=49)	150 mg qw (n=49)
TEAEs						
Any TEAE	18 (36.0%)	34 (69.4%)	40 (78.4%)	33 (63.5%)	35 (71.4%)	36 (73.5%)
TEAEs by primary SOC and PT (≥5%)*						
Infections and infestations	9 (18.0%)	13 (26.5%)	11 (21.6%)	13 (25.0%)	9 (18.4%)	14 (28.6%)
Upper respiratory tract infection	4 (8.0%)	1 (2.0%)	2 (3.9%)	7 (13.5%)	3 (6.1%)	4 (8.2%)
Nasopharyngitis	1 (2.0%)	2 (4.1%)	2 (3.9%)	1 (1.9%)	2 (4.1%)	3 (6.1%)
Viral infection	0	0	3 (5.9%)	0	0	0
Blood and lymphatic system disorders	0	0	8 (15.7%)	3 (5.8%)	5 (10.2%)	10 (20.4%)
Neutropenia	0	0	7 (13.7%)	2 (3.8%)	4 (8.2%)	8 (16.3%)
Gastrointestinal disorders	6 (12.0%)	16 (32.7%)	15 (29.4%)	6 (11.5%)	11 (22.4%)	5 (10.2%)
Aphthous stomatitis	1 (2.0%)	3 (6.1%)	3 (5.9%)	2 (3.8%)	3 (6.1%)	1 (2.0%)
Diarrhoea	1 (2.0%)	2 (4.1%)	5 (9.8%)	0	2 (4.1%)	0
Abdominal pain	0	3 (6.1%)	3 (5.9%)	1 (1.9%)	0	0
Nervous system disorders	4 (8.0%)	6 (12.2%)	3 (5.9%)	1 (1.9%)	4 (8.2%)	3 (6.1%)

Headache	0	4 (8.2%)	2 (3.9%)	0	2 (4.1%)	1 (2.0%)
Musculoskeletal/connective tissue disorders	2 (4.0%)	7 (14.3%)	17 (13.7%)	6 (11.5%)	9 (18.4%)	7 (14.3%)
Musculoskeletal pain	0	1 (2.0%)	0	0	3 (6.1%)	1 (2.0%)
Investigations	1 (2.0%)	0	3 (5.9%)	7 (13.5%)	6 (12.2%)	2 (4.1%)
ALT increased	0	0	1 (2.0%)	4 (7.7%)	4 (8.2%)	1 (2.0%)
AST increased	0	0	0	3 (5.8%)	1 (2.0%)	0
General disorders and administration site conditions	3 (6.0%)	9 (18.4%)	8 (15.7%)	9 (17.3%)	7 (14.3%)	4 (8.2%)
Injection site reaction	0	3 (6.1%)	2 (3.9%)	2 (3.8%)	1 (2.0%)	1 (2.0%)
Injection site erythema	0	1 (2.0%)	0	3 (5.8%)	1 (2.0%)	4 (8.2%)
Injection site pruritus	0	0	1 (2.0%)	3 (5.8%)	0	1 (2.0%)
Fatigue	0	3 (6.1%)	2 (3.9%)	0	0	0
Pain	0	0	3 (5.9%)	0	0	0
Injury, poisoning and procedural complications	3 (6.0%)	6 (12.2%)	3 (5.9%)	3 (5.8%)	5 (10.2%)	1 (2.0%)
Accidental overdose	2 (4.0%)	2 (4.1%)	2 (3.9%)	2 (3.8%)	3 (6.1%)	1 (2.0%)
TEAEs leading to permanent treatment discontinuation						
Any TEAE leading to discontinuation	0	2 (4.1%)	5 (9.8%)	5 (9.6%)	2 (4.1%)	6 (12.2%)
TEAEs leading to permanent treatment discontinuation by PT						
Helicobacter gastritis	0	0	0	1 (1.9%)	0	0

Ear infection	0	0	0	1 (1.9%)	0	0
Anaemia	0	0	1 (2.0%)	0	0	0
Neutropenia	0	0	2 (3.9%)	2 (3.8%)	0	2 (4.1%)
Aphthous stomatitis	0	0	1 (2.0%)	0	0	1 (2.0%)
Epilepsy	0	1 (2.0%)	0	0	0	0
Crohn’s disease	0	0	0	0	0	1 (2.0%)
Abdominal pain	0	1 (2.0%)	0	0	0	0
Gastrooesophageal reflux disease	0	0	0	1 (1.9%)	0	0
Hepatitis alcoholic	0	0	0	0	0	1 (2.0%)
ALT increased	0	0	1 (2.0%)	1 (1.9%)	2 (4.1%)	0
False positive tuberculosis test	0	0	0	0	0	1 (2.0%)

n (%) = number and percentage of patients. Summary of TEAEs was based on Medical Dictionary for Regulatory Activities coding of verbatim terms reported by investigators.

*Only SOC with at least one PT with a frequency ≥5% in at least one group are presented.

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; PT, preferred term; SOC, system organ class; TEAE, treatment-emergent adverse event

Supplemental table 2 Serious adverse events - safety population

	Placebo (n=50)	Sarilumab				
		100 mg q2w (n=49)	150 mg q2w (n=51)	100 mg qw (n=52)	200 mg q2w (n=49)	150 mg qw (n=49)
Serious adverse events, n (%)						
Any serious TEAE	0	1 (2.0%)	4 (7.8%)	1 (1.9%)	0	1 (2.0%)
Serious adverse events by PT, n (%)						
Neutropenia	0	0	1 (2.0%)	0	0	0
ALT increased	0	0	1 (2.0%)	0	0	0
Helicobacter gastritis	0	0	0	1 (1.9%)	0	0
False positive tuberculosis test	0	0	0	0	0	1 (2.0%)
Epileptic seizure	0	1 (2.0%)	0	0	0	0
Myocardial ischaemia	0	0	1 (2.0%)	0	0	0
Pain	0	0	1 (2.0%)	0	0	0

ALT, alanine aminotransferase; PT, preferred term; TEAE, treatment-emergent adverse event