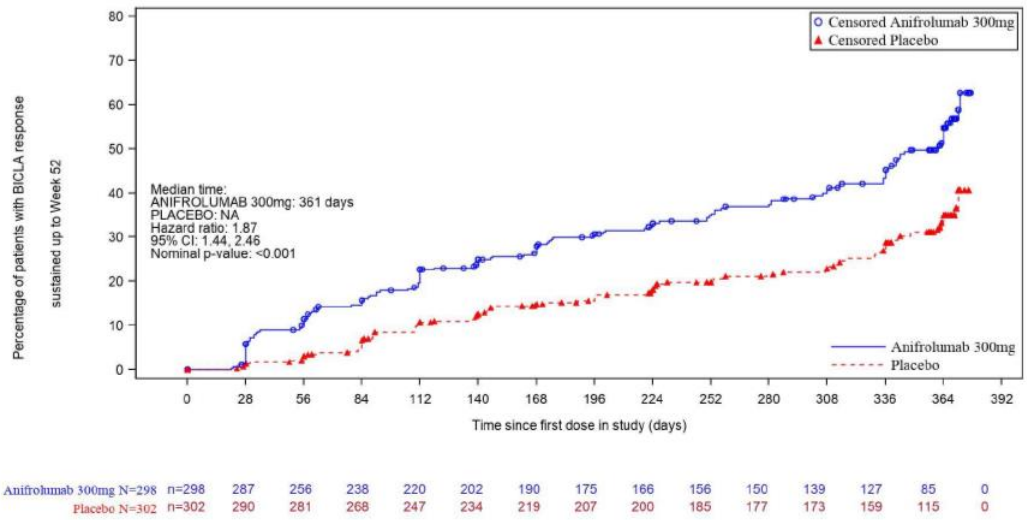
Supplemental Material: Anifrolumab Efficacy and Safety by Type I Interferon Gene Signature and Clinical Subgroups in Patients With SLE: Post Hoc Analysis of Pooled Data From 2 Phase 3 Trials

Contents

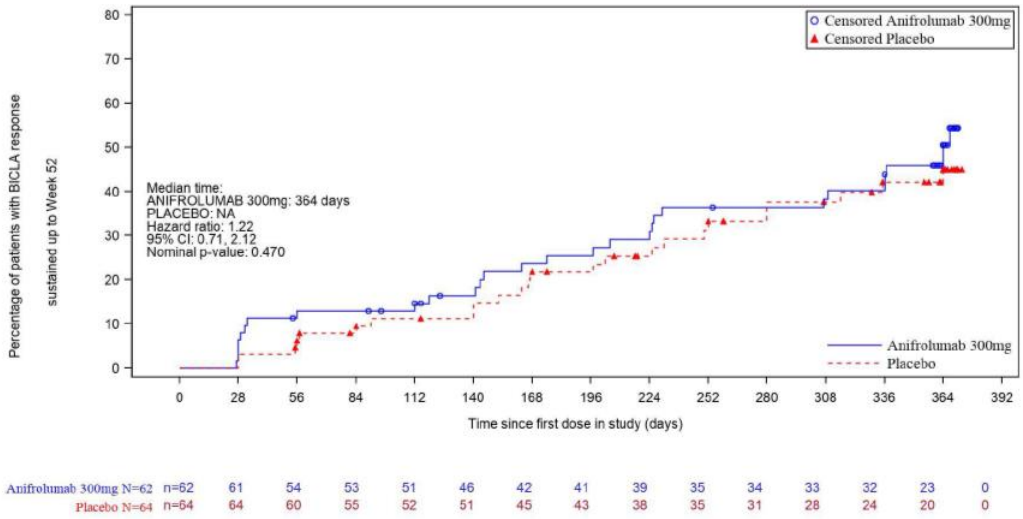
Vital EM, *et al. Ann Rheum Dis* 2022; 81:951–961. doi: 10.1136/annrheumdis-2021-221425

Figure S1. Time to BICLA response sustained to Week 52 in (**A**) type I IFNGS-high and (**B**) IFNGS-low patients in pooled TULIP data

A



B



BICLA, British Isles Lupus Assessment Group–based Composite Lupus Assessment; CI, confidence interval; IFNGS, interferon gene signature.

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Table S1. AEs and adjusted cumulative proportions during study treatment for patients with SLE in pooled data from the TULIP-1 and TULIP-2 trials

Event	**Placebo (n=365)**	**Anifrolumab 300 mg (n=360)**
	n (%)	
Any AE	295 (80.8)	318 (88.3)
Any SAE[a]	60 (16.4)	40 (11.1)
Any AE leading to discontinuation	18 (4.9)	17 (4.9)
Any AESI	36 (9.9)	46 (12.8)
Non-opportunistic serious infections	22 (6.0)	16 (4.4)
Opportunistic infections	0	1 (0.3)
Anaphylaxis	0	0
Malignancy	3 (0.8)	3 (0.8)
Herpes zoster[b]	5 (1.4)	23 (6.4)
Tuberculosis (including latent tuberculosis)[c]	1 (0.3)	2 (0.6)
Tuberculosis[d]	0	0
Influenza[b]	8 (2.2)	6 (1.7)
Vasculitis (non-SLE)	0	0
Major adverse cardiovascular events	0	1 (0.3)

AE, adverse event; AESI, adverse event of special interest; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event; SLE, systemic lupus erythematosus.

Patients with events classified in multiple AESI categories are counted once in each category. AE proportions are adjusted based on the Cochran–Mantel–Haenszel weighting. An AE during treatment is defined as an AE with a date of onset ≥ day of first ever dose of investigational product and ≤ minimum ([last dosing date + 28 days], end of study date, death date). AEs are coded using MedDRA version 22.1. Patients with multiple events in the same category are counted only once in that category.

[a]Including events with outcome of death; [b]Includes serious and nonserious events; [c]Including the preferred terms “latent tuberculosis” and “mycobacterium tuberculosis complex test positive”; [d]Including the preferred term “tuberculosis.”

Table S2. Demographics, clinical characteristics, and SLE medications at baseline in type I IFNGS-high and IFNGS-low patients in pooled data from the TULIP-1 and TULIP-2 trials

Characteristics	IFNGS high			IFNGS low		
	Placebo (n=302)	Anifrolumab 300 mg (n=298)	Total (n=600)	Placebo (n=64)	Anifrolumab 300 mg (n=62)	Total (n=126)
Age, mean (SD), years	40.7 (11.7)	41.5 (11.9)	41.1 (11.8)	42.7 (12.6)	47.6 (11.3)	45.1 (12.2)
≥18–<65 years, n (%)	298 (98.7)	288 (96.6)	586 (97.7)	61 (95.3)	56 (90.3)	117 (92.9)
≥65 years, n (%)	4 (1.3)	10 (3.4)	14 (2.3)	3 (4.7)	6 (9.7)	9 (7.1)
Female, n (%)	280 (92.7)	275 (92.3)	555 (92.5)	61 (95.3)	58 (93.5)	119 (94.4)
Race, n (%)						
White	192 (63.6)	184 (61.7)	376 (62.7)	52 (81.3)	51 (82.3)	103 (81.7)
Black/African American	40 (13.2)	41 (13.8)	81 (13.5)	8 (12.5)	5 (8.1)	13 (10.3)
Asian	33 (10.9)	39 (13.1)	72 (12.0)	2 (3.1)	2 (3.2)	4 (3.2)
Other	27 (8.9)	23 (7.7)	50 (8.3)	2 (3.1)	3 (4.8)	5 (4.0)
Hispanic/Latino ethnic group, n (%)	74 (24.5)	73 (24.5)	147 (24.5)	15 (23.4)	13 (21.0)	28 (22.2)
Geographic region, n (%)						
Asia Pacific	29 (9.6)	35 (11.7)	64 (10.7)	3 (4.7)	3 (4.8)	6 (4.8)
Europe	108 (35.8)	99 (33.2)	207 (34.5)	14 (21.9)	16 (25.8)	30 (23.8)
Latin America	49 (16.2)	54 (18.1)	103 (17.2)	8 (12.5)	5 (8.1)	13 (10.3)
USA/Canada	104 (34.4)	102 (34.2)	206 (34.3)	36 (56.3)	37 (59.7)	73 (57.9)
Rest of world	12 (4.0)	8 (2.7)	20 (3.3)	3 (4.7)	1 (1.6)	4 (3.2)
Time from initial SLE diagnosis to randomization, median (range), months	87.5 (4–503)	97.0 (6–555)	92.0 (4–555)	52.0 (6–389)	77.0 (0–388)	64.5 (0–389)
SLEDAI-2K						
SLEDAI-2K score	11.8 (3.8)	11.6 (4.0)	11.7 (3.9)	10.1 (2.9)	10.2 (3.0)	10.2 (2.9)
Global score, mean (SD)	227 (75.2)	215 (72.1)	442 (73.7)	39 (60.9)	39 (62.9)	78 (61.9)
Score ≥10, n (%)						
Clinical SLEDAI-2K score, mean (SD)	9.0 (2.8)	8.9 (3.0)	8.9 (2.9)	8.8 (2.3)	9.0 (2.4)	8.9 (2.3)

Characteristics	IFNGS high			IFNGS low		
	Placebo (n=302)	**Anifrolumab 300 mg (n=298)**	**Total (n=600)**	**Placebo (n=64)**	**Anifrolumab 300 mg (n=62)**	**Total (n=126)**
BILAG-2004, n (%)						
≥1 A item	146 (48.3)	144 (48.3)	290 (48.3)	33 (51.6)	30 (48.4)	63 (50.0)
No A items and ≥2 B items	135 (44.7)	139 (46.6)	274 (45.7)	27 (42.2)	31 (50.0)	58 (46.0)
PGA score, mean (SD)	1.8 (0.4)	1.8 (0.4)	1.8 (0.4)	1.8 (0.4)	1.8 (0.4)	1.8 (0.4)
CLASI activity score, mean (SD)	7.9 (7.4)	8.8 (8.1)	8.4 (7.8)	7.2 (6.2)	6.5 (4.1)	6.8 (5.3)
SDI global score, mean (SD)	0.6 (0.9)	0.6 (1.1)	0.6 (1.0)	0.5 (1.0)	0.5 (1.0)	0.5 (1.0)
Number of active joints,[a] mean (SD)	6.6 (5.4)	6.0 (5.5)	6.3 (5.4)	7.3 (6.4)	8.3 (6.4)	7.8 (6.4)
Number of swollen joints,[a] mean (SD)	7.0 (5.5)	6.3 (5.6)	6.7 (5.6)	8.2 (6.5)	9.0 (6.2)	8.6 (6.4)
Number of tender joints,[a] mean (SD)	10.6 (7.5)	9.8 (7.3)	10.2 (7.4)	11.7 (7.8)	12.9 (7.4)	12.2 (7.6)
Baseline treatment for SLE						
GC,[b] n (%)	257 (85.1)	251 (84.2)	508 (84.7)	47 (73.4)	40 (64.5)	87 (69.0)
≥10 mg/day, n (%)	160 (53.0)	168 (56.4)	328 (54.7)	25 (39.1)	22 (35.5)	47 (37.3)
Daily dosage, mean (SD), mg/day	11.6 (7.9)	12.1 (10.2)	11.9 (9.1)	9.6 (5.8)	9.4 (5.7)	9.5 (5.7)
Antimalarial, n (%)	214 (70.9)	195 (65.4)	409 (68.2)	53 (82.8)	48 (77.4)	101 (80.2)
Immunosuppressant, n (%)	157 (52.0)	149 (50.0)	306 (51.0)	20 (31.3)	24 (38.7)	44 (34.9)
Biomarkers						
Anti-dsDNA antibody positive,[c] n (%)	139 (46.0)	148 (49.7)	287 (47.8)	16 (25.0)	19 (30.6)	35 (27.8)
Median (range), U/mL	54.1 (15–3790)	53.5 (15–1897)	54.0 (15–3790)	26.3 (16–242)	28.3 (15–92)	27.9 (15–242)
C3, abnormal,[d] n (%)	128 (42.4)	121 (40.6)	249 (41.5)	9 (14.1)	9 (14.5)	18 (14.3)
Mean (SD), g/L	0.70 (0.144)	0.68 (0.152)	0.69 (0.148)	0.71 (0.085)	0.78 (0.103)	0.74 (0.099)
C4, abnormal,[d] n (%)	81 (26.8)	81 (27.2)	162 (27.0)	4 (6.3)	3 (4.8)	7 (5.6)
Mean (SD), g/L	0.072 (0.0142)	0.073 (0.0161)	0.073 (0.0152)	0.071 (0.0244)	0.082 (0.0095)	0.075 (0.0191)

Characteristics	IFNGS high			IFNGS low		
	Placebo (n=302)	**Anifrolumab 300 mg (n=298)**	**Total (n=600)**	**Placebo (n=64)**	**Anifrolumab 300 mg (n=62)**	**Total (n=126)**
Patient-reported outcomes, mean (SD)						
FACIT-F	26.8 (11.7) n=289	26.2 (12.3) n=283	26.5 (12.0) n=572	21.3 (12.2) n=60	23.4 (12.0) n=58	22.3 (12.1) n=118
SF-36 PCS	37.9 (9.2) n=288	38.0 (9.2) n=286	37.9 (9.2) n=574	36.0 (9.6) n=60	34.8 (8.9) n=59	35.4 (9.2) n=119
SF-36 MCS	44.5 (10.8) n=288	43.8 (11.6) n=286	44.1 (11.2) n=574	41.6 (12.4) n=60	45.0 (11.7) n=59	43.3 (12.1) n=119
PtGA	53.9 (21.9) n=289	55.2 (22.5) n=283	54.5 (22.2) n=572	62.0 (23.5) n=60	54.1 (17.6) n=58	58.1 (21.1) n=118

anti-dsDNA, anti–double-stranded DNA; BILAG-2004, British Isles Lupus Assessment Group-2004; C, complement; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; FACIT-F, Functional Assessment of Chronic Illness Therapy–Fatigue; GC, glucocorticoid; IFNGS, interferon gene signature; MCS, mental component summary; PCS, physical component summary; PtGA, Patient's Global Assessment; PGA, Physician's Global Assessment; SD, standard deviation; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; SF-36, Short Form 36 Health Survey, version 2; SLE, systemic lupus erythematosus; SLEDAI-2K, SLE Disease Activity Index 2000; USA, United States of America.

[a]The joint count is based on 28 joints; [b]GC contains prednisone or equivalent; [c]Anti-dsDNA antibody levels were classified as positive (>15 U/mL) or negative (≤15 U/mL) and were measured in a central laboratory using an automated fluoroimmunoassay (EliA dsDNA; Pharmacia, Freiburg, Germany); [d]Complement levels were classified as abnormal (C3 <0.9 g/L; C4 <0.1 g/L) or normal (C3 ≥0.9 g/L; C4 ≥0.1 g/L) and were measured in a central laboratory.

Table S3. Percentage of IFNGS-high and IFNGS-low patients by race and region in pooled data from the TULIP-1 and TULIP-2 trials

	IFNGS-high patients (n=600)	**IFNGS-low patients (n=126)**
Race, n (%)		
White (n=479)	376 (78.5)	103 (21.5)
Black/African American (n=94)	81 (86.2)	13 (13.8)
Asian (n=76)	72 (94.7)	4 (5.3)
Other/missing (n=77)	71 (92.2)	6 (7.8)
Region, n (%)		
Asia Pacific	64 (91.4)	6 (8.6)
Europe	207 (87.3)	30 (12.7)
Latin America	103 (88.8)	13 (11.2)
USA/Canada	206 (73.8)	73 (26.2)
Rest of world	20 (83.3)	4 (16.7)

IFNGS, interferon gene signature; USA, United States of America.

Table S4. BILAG-2004 organ domain scores for IFNGS-high and IFNGS-low patients in pooled data from the TULIP-1 and TULIP-2 trials

Organ domain, n (%)	IFNGS high			IFNGS low		
	Placebo (n=302)	Anifrolumab 300 mg (n=298)	Total (n=600)	Placebo (n=64)	Anifrolumab 300 mg (n=62)	Total (n=126)
Musculoskeletal						
A	89 (29.5)	89 (29.9)	178 (29.7)	26 (40.6)	25 (40.3)	51 (40.5)
B	179 (59.3)	168 (56.4)	347 (57.8)	34 (53.1)	35 (56.5)	69 (54.8)
C, D, or E	34 (11.3)	41 (13.8)	75 (12.5)	4 (6.3)	2 (3.2)	6 (4.8)
Mucocutaneous						
A	63 (20.9)	71 (23.8)	134 (22.3)	12 (18.8)	13 (21.0)	25 (19.8)
B	196 (64.9)	190 (63.8)	386 (64.3)	41 (64.1)	41 (66.1)	82 (65.1)
C, D, or E	43 (14.2)	37 (12.4)	80 (13.3)	11 (17.2)	8 (12.9)	19 (15.1)
Renal						
A	7 (2.3)	2 (0.7)	9 (1.5)	0	0	0
B	22 (7.3)	21 (7.0)	43 (7.2)	3 (4.7)	2 (3.2)	5 (4.0)
C, D, or E	273 (90.4)	275 (92.3)	548 (91.3)	61 (95.3)	60 (96.8)	121 (96.0)
Cardiorespiratory						
A	3 (1.0)	3 (1.0)	6 (1.0)	1 (1.6)	0	1 (0.8)
B	14 (4.6)	19 (6.4)	33 (5.5)	9 (14.1)	8 (12.9)	17 (13.5)
C, D, or E	285 (94.4)	276 (92.6)	561 (93.5)	54 (84.4)	54 (87.1)	108 (85.7)
Neuropsychiatric						
A	1 (0.3)	1 (0.3)	2 (0.3)	0	0	0
B	2 (0.7)	5 (1.7)	7 (1.2)	2 (3.1)	3 (4.8)	5 (4.0)
C, D, or E	299 (99.0)	292 (98.0)	591 (98.5)	62 (96.9)	59 (95.2)	121 (96.0)
Constitutional						
A	0	1 (0.3)	1 (0.2)	0	0	0
B	13 (4.3)	21 (7.0)	34 (5.7)	4 (6.3)	3 (4.8)	7 (5.6)
C, D, or E	289 (95.7)	276 (92.6)	565 (94.2)	60 (93.8)	59 (95.2)	119 (94.4)
Gastrointestinal						
A	1 (0.3)	0	1 (0.2)	0	0	0
B	3 (1.0)	1 (0.3)	4 (0.7)	0	0	0
C, D, or E	298 (98.7)	297 (99.7)	595 (99.2)	62 (100)	64 (100)	126 (100)

Organ domain, n (%)	IFNGS high			IFNGS low		
	Placebo (n=302)	Anifrolumab 300 mg (n=298)	Total (n=600)	Placebo (n=64)	Anifrolumab 300 mg (n=62)	Total (n=126)
Ophthalmic						
A	0	1 (0.3)	1 (0.2)	0	0	0
B	1 (0.3)	0	1 (0.2)	0	0	0
C, D, or E	301 (99.7)	297 (99.7)	598 (99.7)	62 (100)	64 (100)	126 (100)
Hematologic						
A	0	0	0	0	0	0
B	1 (0.3)	2 (0.7)	3 (0.5)	0	0	0
C, D, or E	301 (99.7)	296 (99.3)	597 (99.5)	62 (100)	64 (100)	126 (100)

BILAG-2004, British Isles Lupus Assessment Group-2004; IFNGS, interferon gene signature.

Table S5. Past and current relevant medical history for IFNGS-high patients with SLE in pooled data from the TULIP-1 and TULIP-2 trials

n (%)	**Placebo (n=302)**	**Anifrolumab 300 mg (n=298)**	**Total (n=600)**
Any current medical history	270 (89.4)	262 (87.9)	532 (88.7)
Current relevant medical history occurring in >5% of patients in either arm			
Infections and manifestations	28 (9.3)	34 (11.4)	62 (10.3)
Neoplasms benign, malignant, and unspecified (including cysts and polyps)	27 (8.9)	22 (7.4)	49 (8.2)
Neoplasms occurring in >2% of patients in either treatment arm			
Uterine leiomyoma	11 (3.6)	10 (3.4)	21 (3.5)
Blood and lymphatic system disorders	56 (18.5)	46 (15.4)	102 (17.0)
Disorders occurring in >2% of patients in either treatment arm			
Anemia	19 (6.3)	17 (5.7)	36 (6.0)
Antiphospholipid syndrome	10 (3.3)	11 (3.7)	21 (3.5)
Iron deficiency anemia	17 (5.6)	9 (3.0)	26 (4.3)
Immune system disorders	43 (14.2)	49 (16.4)	92 (15.3)
Disorders occurring in >2% of patients in either treatment arm			
Drug hypersensitivity	24 (7.9)	27 (9.1)	51 (8.5)
Seasonal allergy	25 (8.3)	27 (9.1)	52 (8.7)
Endocrine disorders	47 (15.6)	47 (15.8)	94 (15.7)
Disorders occurring in >2% of patients in either treatment arm			
Hypothyroidism	28 (9.3)	29 (9.4)	56 (9.3)
Goiter	4 (1.3)	10 (3.4)	14 (2.3)
Autoimmune thyroiditis	7 (2.3)	5 (1.7)	12 (2.0)
Metabolism and nutrition disorders	74 (24.5)	68 (22.8)	142 (23.7)
Disorders occurring in >2% of patients in either treatment arm			
Vitamin D deficiency	10 (3.3)	21 (7.0)	31 (5.2)

n (%)	**Placebo (n=302)**	**Anifrolumab 300 mg (n=298)**	**Total (n=600)**
Hyperlipidemia	21 (7.0)	13 (4.4)	34 (5.7)
Obesity	13 (4.3)	10 (3.4)	23 (3.8)
Hypercholesterolemia	12 (4.0)	9 (3.0)	21 (3.5)
Dyslipidemia	10 (3.3)	6 (2.0)	16 (2.7)
Psychiatric disorders	87 (28.8)	83 (27.9)	170 (28.3)
Disorders occurring in >2% of patients in either treatment arm			
Depression	40 (13.2)	45 (15.1)	85 (14.2)
Insomnia	39 (12.9)	33 (11.1)	72 (12.0)
Anxiety	29 (9.6)	31 (10.4)	60 (10.0)
Bipolar disorder	3 (1.0)	8 (2.7)	11 (1.8)
Nervous system disorders	71 (23.5)	78 (26.2)	149 (24.8)
Disorders occurring in >2% of patients in either treatment arm			
Migraine	20 (6.6)	29 (9.7)	49 (8.2)
Headache	20 (6.6)	27 (9.1)	47 (7.8)
Restless leg syndrome	6 (2.0)	7 (2.3)	13 (2.2)
Neuropathy peripheral	5 (1.7)	6 (2.0)	11 (1.8)
Eye disorders	33 (10.9)	37 (12.4)	70 (11.7)
Disorders occurring in >2% of patients in either treatment arm			
Dry eye	7 (2.3)	9 (3.0)	16 (2.7)
Cataract	11 (3.6)	6 (2.0)	17 (2.8)
Ear and labyrinth disorders	16 (5.3)	12 (4.0)	28 (4.7)
Cardiac disorders	35 (11.6)	30 (10.1)	65 (10.8)
Disorders occurring in >2% of patients in either treatment arm			
Mitral valve incompetence	6 (2.0)	7 (2.3)	13 (2.2)
Vascular disorders	120 (39.7)	123 (41.3)	243 (40.5)
Disorders occurring in >2% of patients in either treatment arm			
Hypertension	91 (30.1)	87 (29.2)	178 (29.7)

n (%)	**Placebo (n=302)**	**Anifrolumab 300 mg (n=298)**	**Total (n=600)**
Raynaud's phenomenon	34 (11.3)	38 (12.8)	72 (12.0)
Respiratory, thoracic, and mediastinal disorders	55 (18.2)	57 (19.1)	112 (18.7)
Disorders occurring in >2% of patients in either treatment arm			
Asthma	26 (8.6)	29 (9.7)	55 (9.2)
Allergic rhinitis	10 (3.3)	5 (1.7)	15 (2.5)
Gastrointestinal disorders	86 (28.5)	106 (35.6)	192 (32.0)
Disorders occurring in >2% of patients in either treatment arm			
Gastroesophageal reflux disease	38 (12.6)	51 (17.1)	89 (14.8)
Constipation	12 (4.0)	12 (4.0)	24 (4.0)
Nausea	5 (1.7)	12 (4.0)	17 (2.8)
Chronic gastritis	9 (3.0)	10 (3.4)	19 (3.2)
Gastritis	9 (3.0)	9 (3.0)	18 (3.0)
Diarrhea	1 (0.3)	7 (2.3)	8 (1.3)
Irritable bowel syndrome	6 (2.0)	7 (2.3)	13 (2.2)
Dyspepsia	11 (3.6)	4 (1.3)	15 (2.5)
Hepatobiliary disorders	19 (6.3)	18 (6.0)	37 (6.2)
Disorders occurring in >2% of patients in either treatment arm			
Hepatic steatosis	10 (3.3)	6 (2.0)	16 (2.7)
Skin and subcutaneous tissue disorders	34 (11.3)	39 (13.1)	73 (12.2)
Musculoskeletal and connective tissue disorders	130 (43.0)	122 (40.9)	252 (42.0)
Disorders occurring in >2% of patients in either treatment arm			
Sjogren's syndrome	31 (10.3)	34 (11.4)	65 (10.8)
Osteoporosis	28 (9.3)	26 (8.7)	54 (9.0)
Fibromyalgia	23 (7.6)	22 (7.4)	45 (7.5)
Osteoarthritis	17 (5.6)	22 (7.4)	39 (6.5)

n (%)	**Placebo (n=302)**	**Anifrolumab 300 mg (n=298)**	**Total (n=600)**
Back pain	15 (5.0)	13 (4.4)	28 (4.7)
Osteopenia	6 (2.0)	13 (4.4)	19 (3.2)
Spinal osteoarthritis	12 (4.0)	11 (3.7)	23 (3.8)
Arthralgia	7 (2.3)	10 (3.4)	17 (2.8)
Osteonecrosis	3 (1.0)	9 (3.0)	12 (2.0)
Rheumatoid arthritis	6 (2.0)	9 (3.0)	15 (2.5)
Muscle spasms	7 (2.3)	6 (2.0)	13 (2.2)
Renal and urinary disorders	33 (10.9)	33 (11.1)	66 (11.0)
Disorders occurring in >2% of patients in either treatment arm			
Chronic kidney disease	7 (2.3)	4 (1.3)	11 (1.8)
Reproductive system and breast disorders	27 (8.9)	34 (11.4)	61 (10.2)
General disorders and administration site conditions	25 (8.3)	28 (9.4)	53 (8.8)
Disorders occurring in >2% of patients in either treatment arm			
Fatigue	13 (4.3)	15 (5.0)	28 (4.7)
Investigations	15 (5.0)	19 (6.4)	34 (5.7)

IFNGS, interferon gene signature; SLE, systemic lupus erythematosus.

Table S6. Past and current relevant medical history for IFNGS-low patients with SLE in pooled data from the TULIP-1 and TULIP-2 trials

	Placebo (n=64)	**Anifrolumab 300 mg (n=62)**	**Total (n=126)**
Any current medical history	55 (85.9)	60 (96.8)	115 (91.3)
Current relevant medical history occurring in >5% of patients in either arm			
Infections and manifestations	5 (7.8)	9 (14.5)	14 (11.1)
Infections and manifestations occurring in >2% of patients in either treatment arm			
Chronic tonsillitis	1 (1.6)	2 (3.2)	3 (2.4)
Herpes simplex	0	2 (3.2)	2 (1.6)
Urinary tract infection	2 (3.1)	0	2 (1.6)
Blood and lymphatic system disorders	11 (17.2)	8 (12.9)	19 (15.1)
Disorders occurring in >2% of patients in either treatment arm			
Antiphospholipid syndrome	4 (6.3)	5 (8.1)	9 (7.1)
Anemia	3 (4.7)	2 (3.2)	5 (4.0)
Iron deficiency anemia	1 (1.6)	2 (3.2)	3 (2.4)
Immune system disorders	12 (18.8)	17 (27.4)	29 (23.0)
Disorders occurring in >2% of patients in either treatment arm			
Drug hypersensitivity	7 (10.9)	9 (14.5)	16 (12.7)
Seasonal allergy	8 (12.5)	6 (9.7)	14 (11.1)
Multiple allergies	0	2 (3.2)	2 (1.6)
Endocrine disorders	15 (23.4)	19 (30.6)	34 (27.0)
Disorders occurring in >2% of patients in either treatment arm			
Hypothyroidism	9 (14.1)	15 (24.2)	24 (19.0)
Goiter	3 (4.7)	3 (4.8)	6 (4.8)
Autoimmune thyroiditis	2 (3.1)	1 (1.6)	3 (2.4)
Metabolism and nutrition disorders	22 (34.4)	23 (37.1)	45 (35.7)
Disorders occurring in >2% of patients in either treatment arm			

	Placebo (n=64)	**Anifrolumab 300 mg (n=62)**	**Total (n=126)**
Vitamin D deficiency	10 (15.6)	7 (11.3)	17 (13.5)
Type 2 diabetes mellitus	3 (4.7)	5 (8.1)	8 (6.3)
Diabetes mellitus	1 (1.6)	4 (6.5)	5 (4.0)
Hypercholesterolemia	3 (4.7)	4 (6.5)	7 (5.6)
Obesity	4 (6.3)	3 (4.8)	7 (5.6)
Hypokalemia	1 (1.6)	2 (3.2)	3 (2.4)
Hyperlipidemia	6 (9.4)	1 (1.6)	7 (5.6)
Psychiatric disorders	29 (45.3)	27 (43.5)	56 (44.4)
Disorders occurring in >2% of patients in either treatment arm			
Depression	14 (21.9)	14 (22.6)	28 (22.2)
Anxiety	12 (18.8)	13 (21.0)	25 (19.8)
Insomnia	18 (28.1)	13 (21.0)	31 (24.6)
Sleep disorder	2 (3.1)	2 (3.2)	4 (3.2)
Adjustment disorder with depressed mood	2 (3.1)	1 (1.6)	3 (2.4)
Bipolar disorder	4 (6.3)	1 (1.6)	5 (4.0)
Attention deficit/hyperactivity disorder	2 (3.1)	0	2 (1.6)
Nervous system disorders	26 (40.6)	22 (35.5)	48 (38.1)
Disorders occurring in >2% of patients in either treatment arm			
Migraine	13 (20.3)	11 (17.7)	24 (19.0)
Headache	5 (7.8)	3 (4.8)	8 (6.3)
Carpal tunnel syndrome	1 (1.6)	2 (3.2)	3 (2.4)
Peripheral neuropathy	1 (1.6)	2 (3.2)	3 (2.4)
Restless leg syndrome	2 (3.1)	2 (3.2)	4 (3.2)
Memory impairment	2 (3.1)	1 (1.6)	3 (2.4)
Tension headache	2 (3.1)	1 (1.6)	3 (2.4)
Epilepsy	2 (3.1)	0	2 (1.6)
Hypoesthesia	3 (4.7)	0	3 (2.4)
Eye disorders	9 (14.1)	14 (22.6)	23 (18.3)
Disorders occurring in >2% of patients in either			

	Placebo (n=64)	**Anifrolumab 300 mg (n=62)**	**Total (n=126)**
treatment arm			
Glaucoma	0	5 (8.1)	5 (4.0)
Astigmatism	0	3 (4.8)	3 (2.4)
Dry eye	4 (6.3)	3 (4.8)	7 (5.6)
Cataract	2 (3.1)	1 (1.6)	3 (2.4)
Myopia	2 (3.1)	1 (1.6)	3 (2.4)
Cardiac disorders	11 (17.2)	8 (12.9)	19 (15.1)
Disorders occurring in >2% of patients in either treatment arm			
Mitral valve prolapse	4 (6.3)	1 (1.6)	5 (4.0)
Bundle branch block right	2 (3.1)	0	2 (1.6)
Vascular disorders	25 (39.1)	31 (50.0)	56 (44.4)
Disorders occurring in >2% of patients in either treatment arm			
Hypertension	19 (29.7)	26 (41.9)	45 (35.7)
Raynaud's phenomenon	3 (4.7)	3 (4.8)	6 (4.8)
Peripheral venous disease	0	2 (3.2)	2 (1.6)
Respiratory, thoracic, and mediastinal disorders	13 (20.3)	17 (27.4)	30 (23.8)
Disorders occurring in >2% of patients in either treatment arm			
Asthma	5 (7.8)	9 (14.5)	14 (11.1)
Dyspnea	2 (3.1)	2 (3.2)	4 (3.2)
Chronic obstructive pulmonary disease	2 (3.1)	1 (1.6)	3 (2.4)
Sleep apnea syndrome	4 (6.3)	1 (1.6)	5 (4.0)
Gastrointestinal disorders	24 (37.5)	25 (40.3)	49 (38.9)
Disorders occurring in >2% of patients in either treatment arm			
Gastroesophageal reflux disease	14 (21.9)	11 (17.7)	25 (19.8)
Gastritis	1 (1.6)	3 (4.8)	4 (3.2)
Hiatus hernia	2 (3.1)	3 (4.8)	5 (4.0)
Irritable bowel syndrome	3 (4.7)	3 (4.8)	6 (4.8)

	Placebo (n=64)	**Anifrolumab 300 mg (n=62)**	**Total (n=126)**
Nausea	1 (1.6)	3 (4.8)	4 (3.2)
Dyspepsia	1 (1.6)	2 (3.2)	3 (2.4)
Constipation	3 (4.7)	1 (1.6)	4 (3.2)
Hepatobiliary disorders	3 (4.7)	5 (8.1)	8 (6.3)
Disorders occurring in >2% of patients in either treatment arm			
Hepatic steatosis	3 (4.7)	2 (3.2)	5 (4.0)
Skin and subcutaneous tissue disorders	7 (10.9)	7 (11.3)	14 (11.1)
Disorders occurring in >2% of patients in either treatment arm			
Rosacea	2 (3.1)	0	2 (1.6)
Musculoskeletal and connective tissue disorders	37 (57.8)	36 (58.1)	73 (57.9)
Disorders occurring in >2% of patients in either treatment arm			
Fibromyalgia	17 (26.6)	13 (21.0)	30 (23.8)
Osteoarthritis	5 (7.8)	10 (16.1)	15 (11.9)
Back pain	2 (3.1)	7 (11.3)	9 (7.1)
Osteoporosis	4 (6.3)	6 (9.7)	10 (7.9)
Intervertebral disc degeneration	2 (3.1)	4 (6.5)	6 (4.8)
Sjogren's syndrome	5 (7.8)	4 (6.5)	9 (7.1)
Arthralgia	2 (3.1)	3 (4.8)	5 (4.0)
Osteopenia	1 (1.6)	3 (4.8)	4 (3.2)
Rheumatoid arthritis	0	3 (4.8)	3 (2.4)
Bursitis	1 (1.6)	2 (3.2)	3 (2.4)
Exostosis	0	2 (3.2)	2 (1.6)
Intervertebral disc protrusion	3 (4.7)	2 (3.2)	5 (4.0)
Musculoskeletal pain	1 (1.6)	2 (3.2)	3 (2.4)
Osteochondrosis	1 (1.6)	2 (3.2)	3 (2.4)
Spinal osteoarthritis	6 (9.4)	2 (3.2)	8 (6.3)
Temporomandibular joint syndrome	0	2 (3.2)	2 (1.6)
Muscle spasms	2 (3.1)	1 (1.6)	3 (2.4)

	Placebo (n=64)	**Anifrolumab 300 mg (n=62)**	**Total (n=126)**
Osteonecrosis	2 (3.1)	0	2 (1.6)
Renal and urinary disorders	7 (10.9)	8 (12.9)	15 (11.9)
Disorders occurring in >2% of patients in either treatment arm			
Hypertonic bladder	0	2 (3.2)	2 (1.6)
Nephrolithiasis	2 (3.1)	2 (3.2)	4 (3.2)
Renal impairment	0	2 (3.2)	2 (1.6)
Pollakiuria	2 (3.1)	0	2 (1.6)
Reproductive system and breast disorders	9 (14.1)	5 (8.1)	14 (11.1)
Disorders occurring in >2% of patients in either treatment arm			
Polycystic ovaries	0	2 (3.2)	2 (1.6)
Ovarian cyst	2 (3.1)	0	2 (1.6)
General disorders and administration site conditions	5 (7.8)	4 (6.5)	9 (7.1)
Disorders/conditions occurring in >2% of patients in either treatment arm			
Fatigue	2 (3.1)	1 (1.6)	3 (2.4)
Investigations	4 (6.3)	6 (9.7)	10 (7.9)
Investigations occurring in >2% of patients in either treatment arm			
Irregular heart rate	1 (1.6)	2 (3.2)	3 (2.4)
Cardiac murmur	2 (3.1)	0	2 (1.6)
Surgical and medical procedures	7 (10.9)	3 (4.8)	10 (7.9)
Disorders occurring in >2% of patients in either treatment arm			
Female sterilization	2 (3.1)	1 (1.6)	3 (2.4)
Cholecystectomy	2 (3.1)	0	2 (1.6)
Hysterectomy	2 (3.1)	0	2 (1.6)
Social circumstances	6 (9.4)	6 (9.7)	12 (9.5)

	Placebo (n=64)	**Anifrolumab 300 mg (n=62)**	**Total (n=126)**
Disorders occurring in >2% of patients in either treatment arm			
Menopause	0	4 (6.5)	4 (3.2)
Post menopause	4 (6.3)	2 (3.2)	6 (4.8)

IFNGS, interferon gene signature; SLE, systemic lupus erythematosus.

Table S7. Percentage change from baseline to Week 52 in complement C3, C4, and anti-dsDNA levels by IFNGS in pooled data from the TULIP-1 and TULIP-2 trials

	IFNGS high		**IFNGS low**	
	Placebo (n=302)	**Anifrolumab 300 mg (n=298)**	**Placebo (n=64)**	**Anifrolumab 300 mg (n=62)**
C3[a]				
n	98	104	9	8
Estimated change from baseline,[b] LS mean (SE)	11.9 (2.7)	21.0 (2.6)	−0.6 (6.8)	2.8 (7.0)
Comparison with placebo, LS mean difference (SE)	9.2 (3.5)		3.4 (9.3)	
Nominal *P*-value	0.009		0.721	
C4[a]				
n	59	68	4	3
Estimated change from baseline,[b] LS mean (SE)	23.5 (6.4)	34.3 (6.2)	4.7 (202.5)	27.7 (143.1)
Comparison with placebo, LS mean difference (SE)	10.8 (8.6)		23.0 (244.6)	
Nominal *P*-value	0.209		0.936	
Anti-dsDNA[a]				
n	99	117	12	16
Estimated change from baseline,[b] LS mean (SE)	113.4 (97.6)	−43.4 (87.1)	13.4 (37.2)	−6.6 (32.1)
Comparison with placebo, LS mean difference (SE)	−156.8 (108.7)		−20.0 (45.1)	
Nominal *P*-value	0.150		0.658	

anti-dsDNA, anti–double-stranded DNA; C, complement; GC, glucocorticoid; IFNGS, interferon gene signature; LS, least squares; SE, standard error; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000.

[a]Only patients with abnormal anti-dsDNA, low complement C3 and low C4, respectively, are included in the analysis; [b]A repeated measures model with fixed effects for baseline value, treatment group, visit, including study for the pooled analysis, and stratification factors (SLEDAI-2K score at screening (<10 points vs ≥10 points) and Day 1 GC dosage (<10 mg/day vs ≥10 mg/day prednisone or equivalent) was used. An interaction term for visit and treatment group will also be included in the model to allow the relationship to differ across groups. Visit will be fitted as a repeated variable in the model.

Table S8. AEs and adjusted cumulative proportions during study treatment for patients with SLE by IFNGS subgroup in pooled data from the TULIP-1 and TULIP-2 trials

Event	IFNGS high		IFNGS low	
	Placebo (n=301)	**Anifrolumab 300 mg (n=298)**	**Placebo (n=64)**	**Anifrolumab 300 mg (n=62)**
	n (%)		**n (%)**	
Any AE	246 (81.7)	263 (88.3)	49 (76.6)	55 (88.7)
Any SAE[a]	53 (17.6)	34 (11.4)	7 (10.9)	6 (9.7)
Any AE leading to discontinuation	15 (5.0)	14 (4.7)	3 (4.7)	3 (4.8)
Any AESI	31 (10.3)	37 (12.4)	5 (7.8)	9 (14.5)
Non-opportunistic serious infections	20 (6.7)	13 (4.4)	2 (3.1)	3 (4.8)
Opportunistic infections	0	1 (0.3)	0	0
Anaphylaxis	0	0	0	0
Malignancy	3 (1.0)	2 (0.7)	0	1 (1.6)
Herpes zoster[b]	4 (1.3)	19 (6.4)	1 (1.6)	4 (6.5)
Tuberculosis (including latent tuberculosis)[c]	1 (0.3)	2 (0.7)	0	0
Tuberculosis[d]	0	0	0	0
Influenza[b]	6 (2.0)	4 (1.3)	2 (3.1)	2 (3.2)
Vasculitis (non-SLE)	0	0	0	0
Major adverse cardiovascular events	0	1 (0.3)	0	0

AE, adverse event; AESI, adverse event of special interest; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event; SLE, systemic lupus erythematosus.

Patients with events classified in multiple AESI categories are counted once in each category. AE proportions are adjusted based on the Cochran–Mantel–Haenszel weighting. An AE during treatment is defined as an AE with a date of onset ≥ day of first ever dose of investigational product and ≤ minimum ([last dosing date + 28 days], end of study date, death date). AEs are coded using MedDRA version 22.1. Patients with multiple events in the same category are counted only once in that category.

[a]Including events with outcome of death; [b]Includes serious and nonserious events; [c]Including the preferred terms "latent tuberculosis" and "mycobacterium tuberculosis complex test positive"; [d]Including the preferred term "tuberculosis."

Table S9. AEs and adjusted cumulative proportions during study treatment for patients with SLE by age and sex subgroups in pooled data from the TULIP-1 and TULIP-2 trials

Event	Age				Sex			
	≥18–<65 years		≥65 years		Female		Male	
	Placebo (n=358)	Anifrolumab 300 mg (n=344)	Placebo (n=7)	Anifrolumab 300 mg (n=16)	Placebo (n=340)	Anifrolumab 300 mg (n=333)	Placebo (n=25)	Anifrolumab 300 mg (n=27)
	n (%)		n (%)		n (%)		n (%)	
Any AE	288 (80.5)	304 (88.4)	7 (100)	14 (89.0)	276 (81.2)	296 (88.9)	19 (75.8)	22 (81.3)
Any SAE[a]	57 (15.9)	36 (10.5)	3 (41.2)	4 (26.0)	56 (16.5)	36 (10.8)	4 (16.0)	4 (14.9)
Any AE leading to discontinuation	18 (5.0)	15 (4.4)	0	2 (15.0)	18 (5.3)	17 (5.1)	0	0
Any AESI	36 (10.1)	44 (12.8)	0	2 (11.0)	33 (9.7)	42 (12.6)	3 (11.8)	4 (14.6)
Non-opportunistic serious infections	22 (6.1)	14 (4.1)	0	2 (11.0)	20 (5.9)	15 (4.5)	2 (8.0)	1 (3.6)
Opportunistic infections	0	1 (0.3)	0	0	0	1 (0.3)	0	0
Anaphylaxis	0	0	0	0	0	0	0	0
Malignancy	3 (0.8)	3 (0.9)	0	0	3 (0.9)	3 (0.9)	0	0
Herpes zoster[b]	5 (1.4)	23 (6.7)	0	0	5 (1.5)	20 (6.0)	0	3 (11.0)
Tuberculosis (including latent tuberculosis)[c]	1 (0.3)	2 (0.6)	0	0	1 (0.3)	2 (0.6)	0	0
Tuberculosis[d]	0	0	0	0	0	0	0	0
Influenza[b]	8 (2.2)	6 (1.7)	0	0	7 (2.1)	6 (1.8)	1 (3.9)	0
Vasculitis (non-SLE)	0	0	0	0	0	0	0	0
Major adverse cardiovascular events	0	1 (0.3)	0	0	0	1 (0.3)	0	0

AE, adverse event; AESI, adverse event of special interest; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event; SLE, systemic lupus erythematosus.

Patients with events classified in multiple AESI categories are counted once in each category. AE proportions are adjusted based on the Cochran–Mantel–Haenszel weighting. An AE during treatment is defined as an AE with a date of onset ≥ day of first ever dose of investigational product and ≤ minimum ([last dosing date + 28 days], end of study date, death date). AEs are coded using MedDRA version 22.1. Patients with multiple events in the same category are counted only once in that category.

[a]Including events with outcome of death; [b]Includes serious and nonserious events; [i]Including the preferred terms "latent tuberculosis" and "mycobacterium tuberculosis complex test positive"; [d]Including the preferred term "tuberculosis."

Table S10. AEs and adjusted cumulative proportions during study treatment for patients with SLE by BMI subgroup in pooled data from the TULIP-1 and TULIP-2 trials

Event	BMI			
	≤28 kg/m^2		>28 kg/m^2	
	Placebo (n=223)	Anifrolumab 300 mg (n=205)	Placebo (n=142)	Anifrolumab 300 mg (n=155)
	n (%)		n (%)	
Any AE	177 (79.5)	179 (87.3)	118 (83.1)	139 (89.7)
Any SAE[a]	37 (16.6)	20 (9.8)	23 (16.2)	20 (12.9)
Any AE leading to discontinuation	12 (5.4)	13 (6.4)	6 (4.2)	4 (2.6)
Any AESI	18 (8.0)	26 (12.7)	18 (12.7)	20 (12.9)
Non-opportunistic serious infections	12 (5.4)	7 (3.4)	10 (7.0)	9 (5.8)
Opportunistic infections	0	1 (0.5)	0	0
Anaphylaxis	0	0	0	0
Malignancy	2 (0.9)	3 (1.5)	1 (0.7)	0
Herpes zoster[b]	3 (1.3)	13 (6.3)	2 (1.4)	10 (6.5)
Tuberculosis (including latent tuberculosis)[c]	0	0	1 (0.7)	2 (1.3)
Tuberculosis[d]	0	0	0	0
Influenza[b]	3 (1.3)	6 (2.9)	5 (3.5)	0
Vasculitis (non-SLE)	0	0	0	0
Major adverse cardiovascular events	0	0	0	1 (0.6)

AE, adverse event; AESI, adverse event of special interest; BMI, body mass index; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event; SLE, systemic lupus erythematosus.

Patients with events classified in multiple AESI categories are counted once in each category. AE proportions are adjusted based on the Cochran–Mantel–Haenszel weighting. An AE during treatment is defined as an AE with a date of onset ≥ day of first ever dose of investigational product and ≤ minimum ([last dosing date + 28 days], end of study date, death date). AEs are coded using MedDRA version 22.1. Patients with multiple events in the same category are counted only once in that category.

[a]Including events with outcome of death; [b]Includes serious and nonserious events; [c]Including the preferred terms "latent tuberculosis" and "mycobacterium tuberculosis complex test positive"; [d]Including the preferred term "tuberculosis."

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Table S11. AEs and adjusted cumulative proportions during study treatment for patients with SLE by racial subgroup in pooled data from the TULIP-1 and TULIP-2 trials

Event	White		Black/African American		Asian		Other	
	Placebo (n=243)	**Anifrolumab 300 mg (n=235)**	**Placebo (n=48)**	**Anifrolumab 300 mg (n=46)**	**Placebo (n=35)**	**Anifrolumab 300 mg (n=41)**	**Placebo (n=31)**	**Anifrolumab 300 mg (n=30)**
	n (%)		**n (%)**		**n (%)**		**n (%)**	
Any AE	186 (76.7)	204 (86.9)	39 (82.1)	40 (86.4)	35 (100)	38 (93.9)	27 (88.3)	28 (93.3)
Any SAE[a]	35 (14.4)	27 (11.6)	12 (25.8)	4 (7.7)	8 (23.7)	4 (9.8)	5 (16.2)	3 (11.1)
Any AE leading to discontinuation	12 (5.0)	12 (5.1)	1 (1.8)	1 (1.9)	4 (10.8)	1 (1.7)	1 (2.9)	2 (7.4)
Any AESI	21 (8.7)	29 (12.4)	7 (15.0)	1 (1.9)	4 (11.9)	6 (14.2)	3 (10.3)	7 (23.0)
Non-opportunistic serious infections	12 (5.0)	10 (4.2)	4 (9.1)	1 (1.9)	4 (11.9)	3 (7.1)	2 (6.6)	2 (7.4)
Opportunistic infections	0	0	0	0	0	1 (1.7)	0	0
Anaphylaxis	0	0	0	0	0	4 (9.8)	0	0
Malignancy	3 (1.3)	3 (1.3)	0	0	0	0	0	0
Herpes zoster[b]	4 (1.6)	13 (5.6)	1 (1.8)	0	0	4 (9.8)	0	4 (12.6)
Tuberculosis (including latent tuberculosis)[c]	1 (0.4)	1 (0.4)	0	0	0	0	0	1 (3.0)
Tuberculosis[d]	0	0	2 (4.2)	0	0	0	0	0
Influenza[b]	2 (0.9)	4 (1.7)	0	0	2 (6.4)	0	1 (3.7)	1 (3.0)
Vasculitis (non-SLE)	0	0	0	0	0	0	0	0
Major adverse cardiovascular events	0	1 (0.4)	0	0	0	0	0	0

AE, adverse event; AESI, adverse event of special interest; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event; SLE, systemic lupus erythematosus.

Patients with events classified in multiple AESI categories are counted once in each category. AE proportions are adjusted based on the Cochran–Mantel–Haenszel weighting. An AE during treatment is defined as an AE with a date of onset ≥ day of first ever dose of investigational product and ≤ minimum ([last dosing date + 28 days], end of study date, death date). AEs are coded using MedDRA version 22.1. Patients with multiple events in the same category are counted only once in that category.

[a]Including events with outcome of death; [b]Includes serious and nonserious events; [c]Including the preferred terms "latent tuberculosis" and "mycobacterium tuberculosis complex test positive"; [d]Including the preferred term "tuberculosis."

Table S12. AEs and adjusted cumulative proportions during study treatment for patients with SLE by geographic region subgroup in pooled data from the TULIP-1 and TULIP-2 trials

Event	Asia Pacific		Europe		Latin America		USA/Canada		Rest of world	
	Placebo (n=32)	Anifrolumab 300 mg (n=38)	Placebo (n=122)	Anifrolumab 300 mg (n=115)	Placebo (n=57)	Anifrolumab 300 mg (n=59)	Placebo (n=139)	Anifrolumab 300 mg (n=139)	Placebo (n=15)	Anifrolumab 300 mg (n=9)
	n (%)		n (%)		n (%)		n (%)		n (%)	
Any AE	32 (100)	36 (95.9)	86 (71.0)	93 (81.0)	43 (75.3)	54 (91.6)	120 (86.4)	126 (90.6)	14 (95.4)	9 (100)
Any SAE[a]	8 (25.4)	5 (12.7)	18 (14.8)	12 (10.4)	4 (7.0)	4 (6.9)	27 (19.4)	17 (12.1)	3 (20.0)	2 (18.1)
Any AE leading to discontinuation	4 (11.9)	2 (4.1)	5 (4.2)	5 (4.5)	3 (5.2)	1 (1.8)	5 (3.5)	8 (5.8)	1 (4.6)	1 (9.0)
Any AESI	4 (12.7)	6 (15.6)	12 (9.9)	11 (9.7)	3 (5.3)	8 (13.5)	16 (11.5)	20 (14.4)	1 (4.6)	1 (15.3)
Non-opportunistic serious infections	4 (12.7)	3 (7.8)	5 (4.1)	1 (0.9)	3 (5.3)	3 (5.2)	9 (6.5)	9 (6.5)	1 (4.6)	0
Opportunistic infections	0	1 (2.1)	0	0	0	0	0	0	0	0
Anaphylaxis	0	0	0	0	0	0	0	0	0	0
Malignancy	0	0	2 (1.7)	2 (1.8)	0	0	1 (0.7)	1 (0.7)	0	0
Herpes zoster[b]	0	4 (10.7)	2 (1.6)	5 (4.4)	0	4 (6.7)	3 (2.1)	9 (6.5)	0	1 (15.3)
Tuberculosis (including latent tuberculosis)[c]	0	0	1 (0.8)	0	0	2 (3.4)	0	0	0	0
Tuberculosis[d]	0	0	0	0	0	0	0	0	0	0
Influenza[b]	2 (6.8)	0	2 (1.8)	2 (1.7)	0	1 (1.6)	4 (2.8)	3 (2.2)	0	0
Vasculitis (non-SLE)	0	0	0	0	0	0	0	0	0	0
Major adverse cardiovascular events	0	0	0	1 (0.8)	0	0	0	0	0	0

AE, adverse event; AESI, adverse event of special interest; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event; SLE, systemic lupus erythematosus.

Patients with events classified in multiple AESI categories are counted once in each category. AE proportions are adjusted based on the Cochran–Mantel–Haenszel weighting. An AE during treatment is defined as an AE with a date of onset ≥ day of first ever dose of investigational product and ≤ minimum ([last dosing date + 28 days], end of study date, death date). AEs are coded using MedDRA version 22.1. Patients with multiple events in the same category are counted only once in that category.

[a]Including events with outcome of death; [b]Includes serious and nonserious events; [c]Including the preferred terms "latent tuberculosis" and "mycobacterium tuberculosis complex test positive"; [d]Including the preferred term "tuberculosis."

Table S13. AEs and adjusted cumulative proportions during study treatment for patients with SLE by glucocorticoid dosage at baseline and by SLEDAI-2K at screening subgroups in pooled data from the TULIP-1 and TULIP-2 trials

Event	GC dosage at baseline				SLEDAI-2K at screening			
	<10 mg/day		≥10 mg/day		<10 points		≥10 points	
	Placebo (n=180)	Anifrolumab 300 mg (n=170)	Placebo (n=185)	Anifrolumab 300 mg (n=190)	Placebo (n=106)	Anifrolumab 300 mg (n=109)	Placebo (n=259)	Anifrolumab 300 mg (n=251)
	n (%)		n (%)		n (%)		n (%)	
Any AE	153 (85.0)	155 (91.2)	142 (76.8)	163 (85.8)	88 (83.0)	98 (89.9)	207 (79.9)	220 (87.7)
Any SAE[a]	28 (15.6)	15 (8.8)	32 (17.3)	25 (13.2)	11 (10.4)	8 (7.4)	49 (18.9)	32 (12.8)
Any AE leading to discontinuation	7 (3.9)	6 (3.5)	11 (6.0)	11 (5.8)	4 (3.8)	4 (3.7)	14 (5.4)	13 (5.2)
Any AESI	18 (10.0)	22 (12.9)	18 (9.7)	24 (12.6)	9 (8.5)	9 (8.3)	27 (10.4)	37 (14.7)
Non-opportunistic serious infections	12 (6.7)	6 (3.5)	10 (5.4)	10 (5.3)	5 (4.7)	3 (2.8)	17 (6.6)	13 (5.2)
Opportunistic infections	0	0	0	1 (0.5)	0	0	0	1 (0.4)
Anaphylaxis	0	0	0	0	0	0	0	0
Malignancy	0	2 (1.2)	3 (1.6)	1 (0.5)	0	1 (0.9)	3 (1.2)	2 (0.8)
Herpes zoster[b]	2 (1.1)	11 (6.5)	3 (1.6)	12 (6.3)	2 (1.9)	3 (2.8)	3 (1.2)	20 (8.0)
Tuberculosis (including latent tuberculosis)[c]	0	1 (0.6)	1 (0.5)	1 (0.5)	0	0	1 (0.4)	2 (0.8)
Tuberculosis[d]	0	0	0	0	0	0	0	0
Influenza[b]	6 (3.3)	4 (2.4)	2 (1.1)	2 (1.0)	2 (1.9)	3 (2.7)	6 (2.3)	3 (1.2)
Vasculitis (non-SLE)	0	0	0	0	0	0	0	0
Major adverse cardiovascular events	0	0	0	1 (0.5)	0	0	0	1 (0.4)

AE, adverse event; AESI, adverse event of special interest; GC, glucocorticoid; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event; SLE, systemic lupus erythematosus; SLEDAI-2K, SLE Disease Activity Index 2000.

Patients with events classified in multiple AESI categories are counted once in each category. AE proportions are adjusted based on the Cochran–Mantel–Haenszel weighting. An AE during treatment is defined as an AE with a date of onset ≥ day of first ever dose of investigational product and ≤ minimum ([last

dosing date + 28 days], end of study date, death date). AEs are coded using MedDRA version 22.1. Patients with multiple events in the same category are counted only once in that category.

[a]Including events with outcome of death; [b]Includes serious and nonserious events; [c]Including the preferred terms "latent tuberculosis" and "mycobacterium tuberculosis complex test positive"; [d]Including the preferred term "tuberculosis."

Table S14. AEs and adjusted cumulative proportions during study treatment for patients with SLE by age of disease onset subgroups in pooled data from the TULIP-1 and TULIP-2 trials

Event	Pediatric		Adult	
	Placebo (n=24)	**Anifrolumab 300 mg (n=26)**	**Placebo (n=342)**	**Anifrolumab 300 mg (n=334)**
	n (%)		**n (%)**	
Any AE	22 (92.0)	25 (96.3)	274 (80.1)	293 (87.7)
Any SAE[a]	6 (24.7)	7 (26.5)	55 (16.1)	33 (9.9)
Any AE leading to discontinuation	2 (8.0)	2 (7.7)	16 (4.7)	15 (4.5)
Any AESI	3 (12.3)	7 (26.9)	33 (9.6)	39 (11.7)
Non-opportunistic serious infections	3 (12.3)	4 (15.4)	19 (5.6)	12 (3.6)
Opportunistic infections	0	0	0	1 (0.3)
Anaphylaxis	0	0	0	0
Malignancy	0	0	3 (0.9)	3 (0.9)
Herpes zoster[b]	0	5 (19.4)	5 (1.5)	18 (5.4)
Tuberculosis (including latent tuberculosis)[c]	0	0	1 (0.3)	2 (0.6)
Tuberculosis[d]	0	0	0	0
Influenza[b]	0	0	8 (2.3)	6 (1.8)
Vasculitis (non-SLE)	0	0	0	0
Major adverse cardiovascular events	0	0	0	1 (0.3)

AE, adverse event; AESI, adverse event of special interest; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event; SLE, systemic lupus erythematosus.

Patients with events classified in multiple AESI categories are counted once in each category. AE proportions are adjusted based on the Cochran–Mantel–Haenszel weighting. An AE during treatment is defined as an AE with a date of onset ≥ day of first ever dose of investigational product and ≤ minimum ([last dosing date + 28 days], end of study date, death date). AEs are coded using MedDRA version 22.1. Patients with multiple events in the same category are counted only once in that category.

[a]Including events with outcome of death; [b]Includes serious and nonserious events; [c]Including the preferred terms "latent tuberculosis" and "mycobacterium tuberculosis complex test positive"; [d]Including the preferred term "tuberculosis."

Table S15. AEs and adjusted cumulative proportions during study treatment for patients with SLE by baseline anti–dsDNA/C3/C4 subgroup in pooled data from the TULIP-1 and TULIP-2 trials

Event	All negative/normal		≥1 positive/abnormal	
	Placebo (n=157)	**Anifrolumab 300 mg (n=138)**	**Placebo (n=209)**	**Anifrolumab 300 mg (n=222)**
	n (%)		**n (%)**	
Any AE	130 (82.8)	122 (88.2)	166 (79.8)	196 (88.3)
Any SAE[a]	15 (9.3)	16 (11.6)	46 (21.9)	24 (11.1)
Any AE leading to discontinuation	6 (3.7)	6 (4.3)	12 (5.9)	11 (5.1)
Any AESI	10 (6.3)	18 (13.2)	26 (12.5)	28 (12.6)
Non-opportunistic serious infections	4 (2.4)	6 (4.5)	18 (8.6)	10 (4.7)
Opportunistic infections	0	0	0	1 (0.5)
Anaphylaxis	0	0	0	0
Malignancy	1 (0.6)	2 (1.3)	2 (1.0)	1 (0.5)
Herpes zoster[b]	3 (2.0)	6 (4.3)	2 (1.0)	17 (7.6)
Tuberculosis (including latent tuberculosis)[c]	0	1 (0.8)	1 (0.4)	1 (0.5)
Tuberculosis[d]	0	0	0	0
Influenza[b]	3 (1.9)	5 (3.7)	5 (2.5)	1 (0.4)
Vasculitis (non-SLE)	0	0	0	0
Major adverse cardiovascular events	0	0	0	1 (0.4)

AE, adverse event; AESI, adverse event of special interest; anti-dsDNA, anti–double-stranded DNA; C3, complement 3; C4, complement 4; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event; SLE, systemic lupus erythematosus.

Patients with events classified in multiple AESI categories are counted once in each category. AE proportions are adjusted based on the Cochran–Mantel–Haenszel weighting. An AE during treatment is defined as an AE with a date of onset ≥ day of first ever dose of investigational product and ≤ minimum ([last dosing date + 28 days], end of study date, death date). AEs are coded using MedDRA version 22.1. Patients with multiple events in the same category are counted only once in that category. Positive anti-dsDNA is defined as value >15 U/mL. Abnormal C3 is defined as value <0.9 g/L. Abnormal C4 is defined as value <0.1 g/L.

[a]Including events with outcome of death; [b]Includes serious and nonserious events; [c]Including the preferred terms "latent tuberculosis" and "mycobacterium tuberculosis complex test positive"; [d]Including the preferred term "tuberculosis.