AstraZeneca
What science can do

Investor science call: American College of Rheumatology's Annual Meeting 2019

Conference call for investors and analysts

13 November 2019

Forward-looking statements

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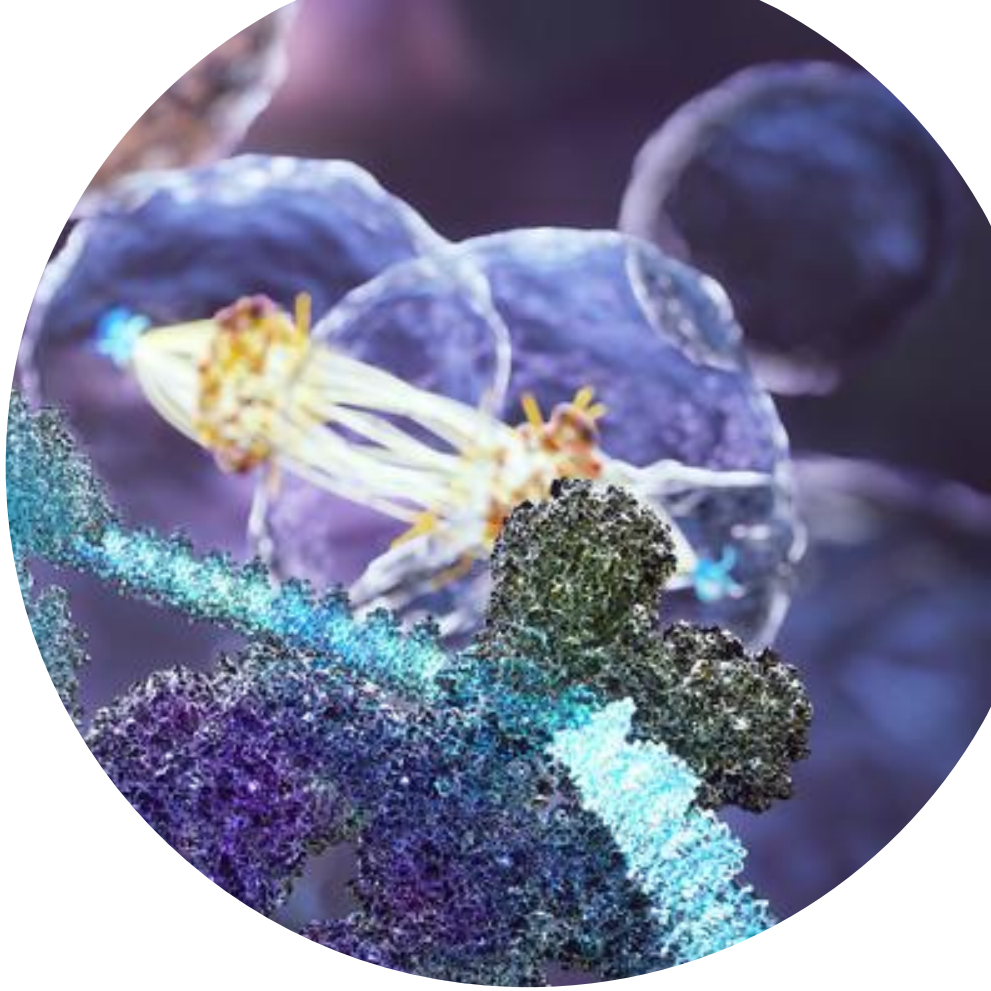
Agenda



Introduction

Anifrolumab Phase III TULIP 1 trial

Anifrolumab Phase III TULIP 2 trial

Next steps

Q&A

2019: a very busy year for the pipeline

Investor science events in each therapy area

Oncology

American Society of Clinical Oncology (Jun)

- Meet AZN management event(s)
- Conference call

European Society of Medical Oncology (Sep)

- Meet AZN management event(s)
- Conference call

Cardiovascular, renal and metabolism

European Society of Cardiology (Sep)

- Conference call

American Society of Nephrology (Nov)

- Conference call

Respiratory (and immunology)

American College of Rheumatology (Nov)

- Conference call

For AstraZeneca investor and analyst events, please visit https://www.astrazeneca.com/investor-relations/results-and-presentations.html.

Speakers

Dr. Richard Furie
Primary Investigator, Phase II MUSE and Phase III TULIP 1 trial and Chief of the Division of Rheumatology at Northwell Health, New York, US

Richard Marshall
Senior Vice President and Head of Late-stage Development, Respiratory, Inflammation and Autoimmunity

Prof. Eric Morand
Primary Investigator, Phase III TULIP 2 trial and Head of the School of Clinical Sciences at Monash Health, Monash University, Australia

Micki Hultquist
Global Medicines Leader, anifrolumab

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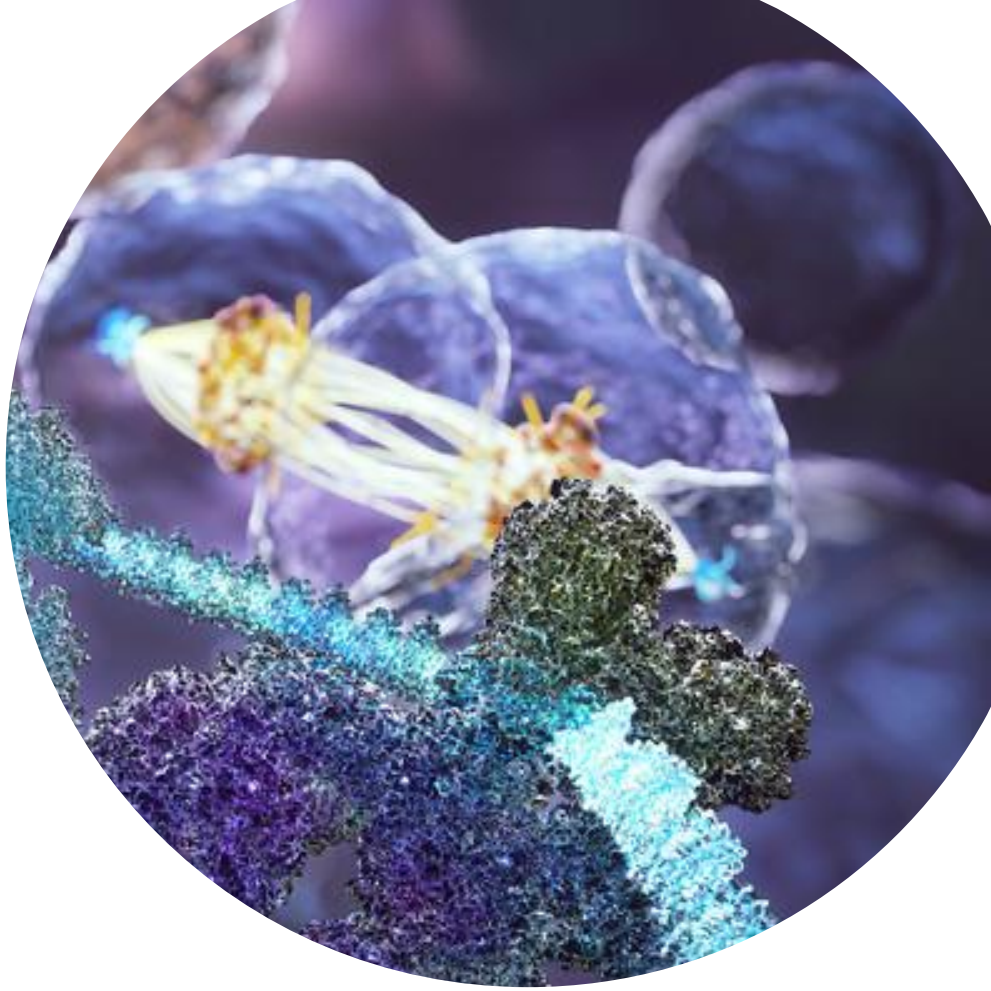
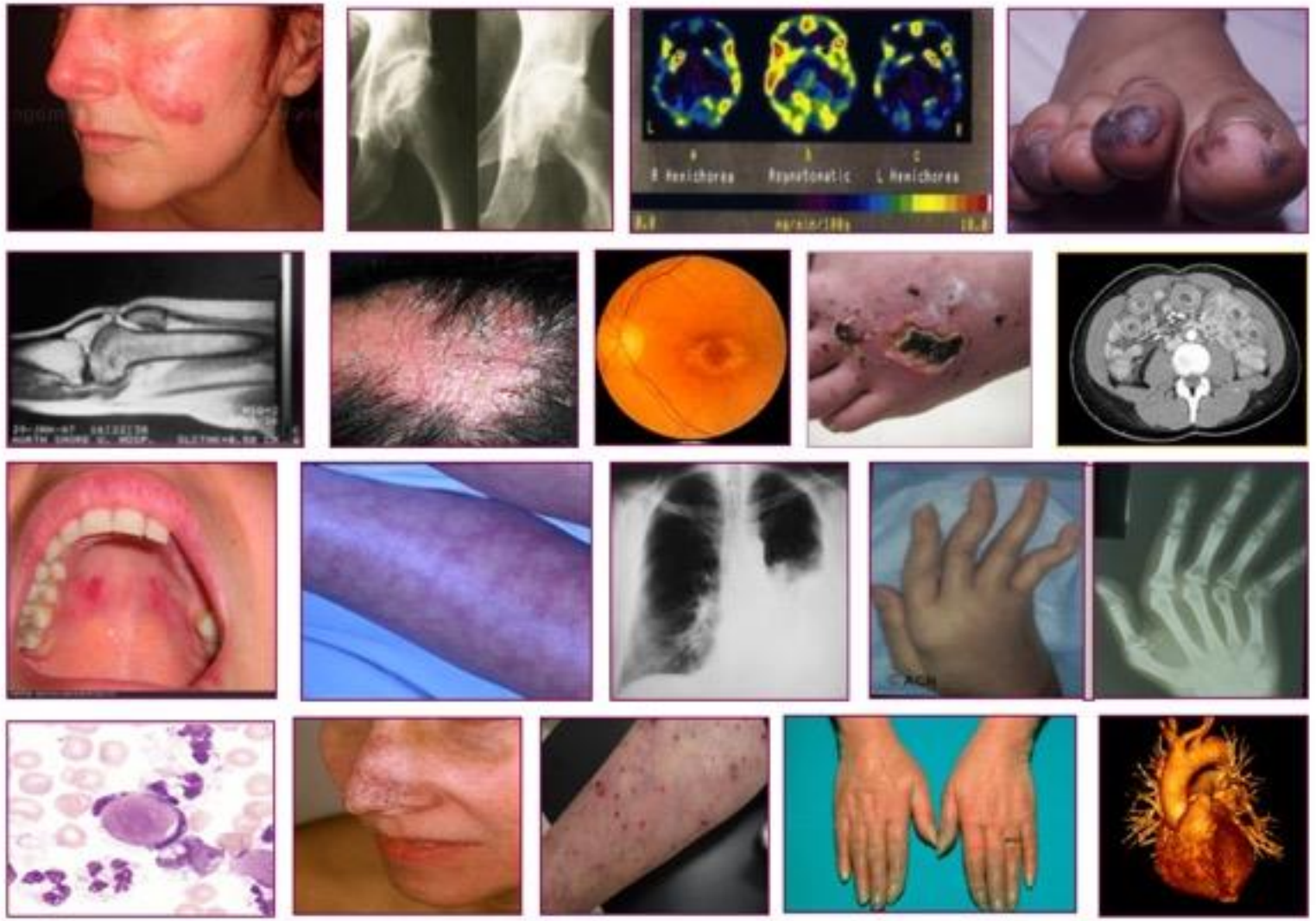


SLE: Clinical Heterogeneity



SLE, systemic lupus erythematosus. Image credit R. Furie /BSIP/ B. Tapper/C. Barry /N.Doss /A.Prohic /ISM

Current SLE Therapies

- NSAIDs*
- Steroids (low dose to “pulse”)*
- Antimalarials (hydroxychloroquine; chloroquine)*
- Immunosuppressives (MMF; AZA, MTX; calcineurin inh)
- Chemotherapy (cyclophosphamide)
- Biologics (belimumab*; rituximab; abatacept)
- Miscellaneous (thalidomide/lenalidomide; quinacrine; dapsone)
- Adjunctive therapies (ACEi; bisphosphonates)

ACEi, angiotensin-converting enzyme inhibitor; AZA, azathioprine; inh, inhibitor; MMF, mycophenolate mofetil; MTX, methotrexate.
*Therapies indicated for use in the treatment of SLE, regional differences apply.

SLE: Unmet Needs

- Lupus nephritis
- Severe extra-renal disease
- Damage prevention
  - Flare prevention
  - Steroid- and immunosuppressive-sparing
- Remission induction

Importance of Type I Interferons in SLE

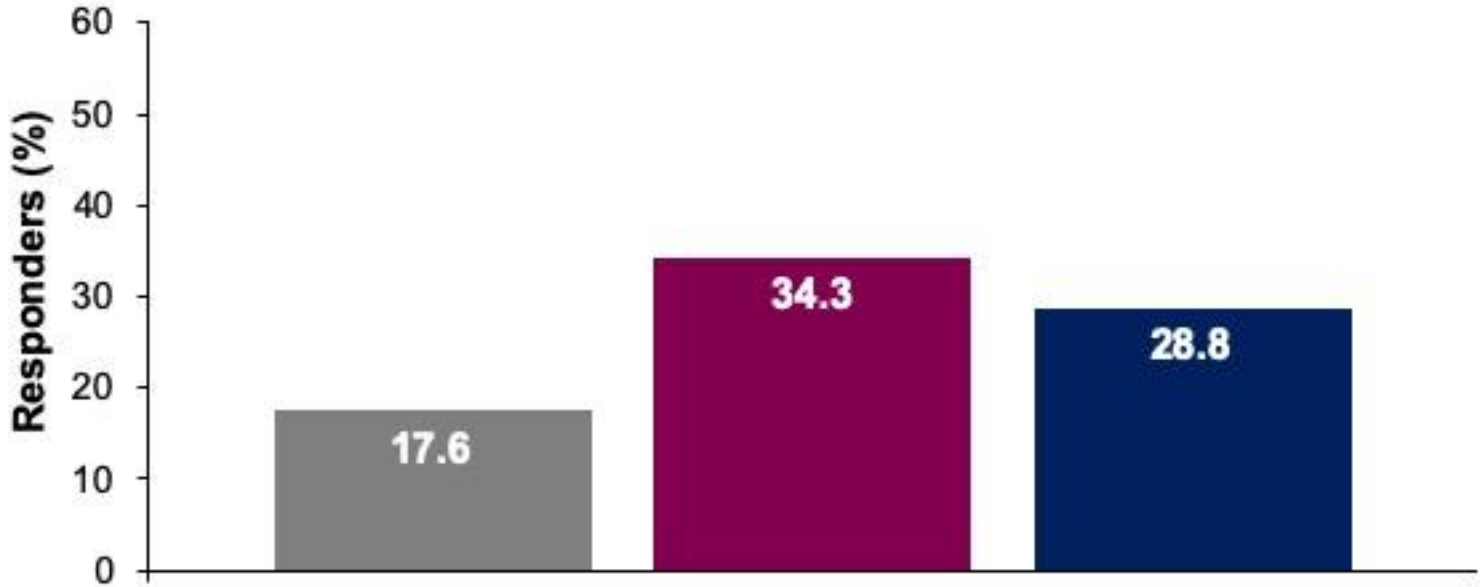
- Elevated IFN-α levels[1]
- SLE sera induce IFN gene signatures[2]
- IFN gene signatures in PBMC of patients with SLE[3]
- Clinical and serologic activity correlate with IFN gene expression[4,5]
- Genetic susceptibility loci in the type I IFN pathway[6]
- Type II IFN (IFN-γ) also plays a role in SLE[7]

Can type I IFN inhibitors reduce SLE clinical activity?

IFN, interferon; PBMC, peripheral blood mononuclear cell.

1. Kim T et al. Clin Exp Immunol. 1987;70:562-9; 2. Porat A et al. Front Immunol. 2018;9:2824; 3. Becker AM et al. PLoS One. 2013;8:e67003; 4. Bengtsson AA et al. Lupus. 2000;9:664-71; 5. Weckerle CE et al. Arthritis Rheum. 2011;63:1044-53; 6. Guerra SG et al. Arthritis Res Ther. 2012;14:211; 7. Pollard KM et al. Discov Med. 2013;16:123-31.

Phase 2 MUSE Study: Primary Endpoint SRI(4) at Week 24, Including Steroid Taper

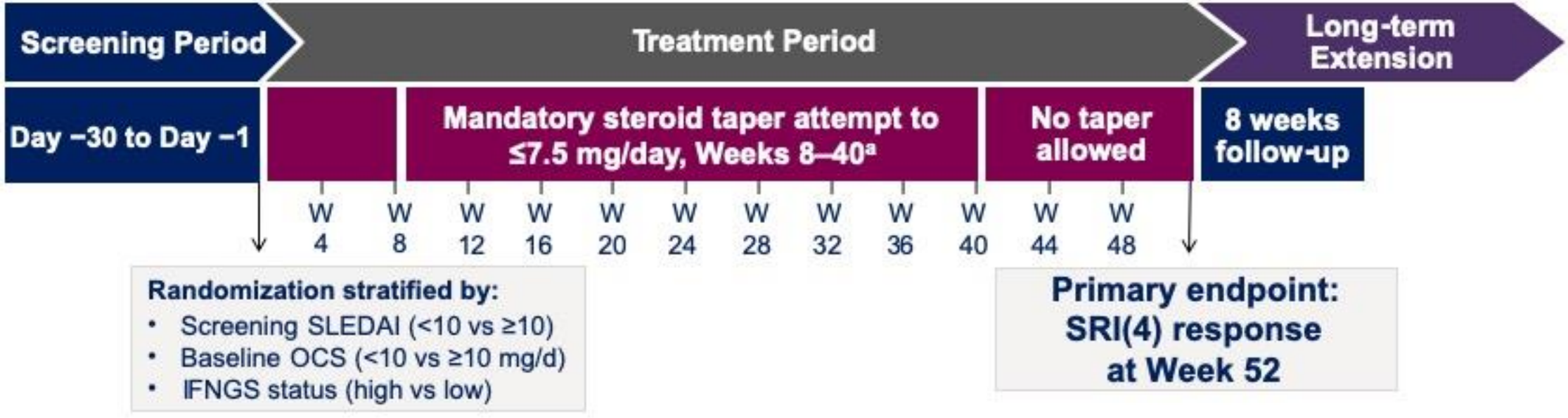


	Placebo	Anifrolumab 300 mg	Anifrolumab 1,000 mg
Delta vs placebo:		16.7	11.2
OR:		2.38	1.94
(90% CI):		(1.33–4.26)	(1.08–3.49)
***P*-value:**		0.014	0.063

CI, confidence interval; OR, odds ratio; SRI, SLE Responder Index.
Furie R et al. Arthritis Rheum. 2017;69:376-86.

TULIP-1 Study Design

Patient population	• Adults with moderately to severely active SLE – SLEDAI ≥6, ≥1 BILAG A or ≥2 B, PGA ≥1 • Seropositive (ANA or anti-dsDNA or anti-Sm) • Receiving standard of care
Treatment (dosing IV, Q4W)	• 2:1:2 randomization ratio – Placebo (n=184) – Anifrolumab 150 mg (n=93) – Anifrolumab 300 mg (n=180)
Sample size	• 123 sites • 457 randomized patients
Geographic distribution	• US/Canada, 40.7% • Europe, 37.9% • Latin America, 13.6% • Asia Pacific, 5.3% • Other, 2.6%



[a]For patients with baseline OCS ≥10 mg/day prednisone or equivalent. ANA, anti-nuclear antibody; BILAG, British Isles Lupus Assessment Group; dsDNA, double-stranded DNA; IFN, interferon; IV, intravenous; OCS, oral corticosteroid; PGA, Physician's Global Assessment; Q4W, every 4 weeks; SLE, systemic lupus erythematosus; SLEDAI, SLE Disease Activity Index; Sm, Smith; SRI(4), SLE Responder Index 4-point reduction. Furie RA et al. Lancet Rheumatol. 2019; doi.org/10.1016/S2665-9913(19)30076-1.

SRI vs BICLA: Composite Disease Activity Measure

- Both measures are binary (responder/nonresponder)
- Both measures consist of 5 components

Responder Definition: SRI(4)

- **≥4-point of SLEDAI-2K from baseline**
- No new organ system affected (BILAG-2004)
- No worsening in PGA
- No use of restricted medications
- No discontinuation of investigational product

Endpoint driven by SLEDAI, which

- Reflects all-or-nothing (partial improvement/worsening of existing symptoms don't count within an item)
- Weighs some organ systems more than others

Responder Definition: BICLA

- **Improvement in all BILAG As and Bs at baseline with no worsening in other organ systems (1 new A or >1 new B)**
- No increase in SLEDAI
- No worsening PGA
- No use of restricted medication
- No discontinuing of investigational product

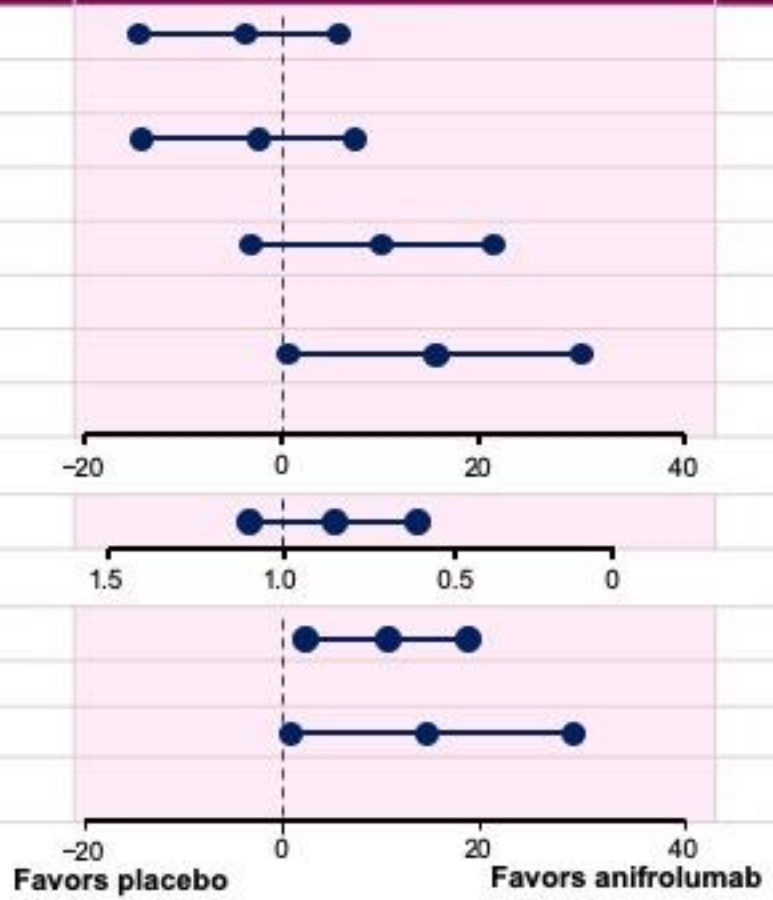
Endpoint driven by BILAG, which

- Captures partial improvement within an organ system
- Weighs organ systems equally
- BUT, BICLA requires improvement in all organ systems of the BILAG with baseline activity

BICLA, BILAG-based Combined Lupus Assessment; PGA, physician's global assessment.

Efficacy: Primary and Key Secondary Endpoints

Primary and Key Secondary Endpoints[a]	Placebo (n=184)	Anifrolumab 300 mg (n=180)	Plot of Treatment Difference (95% CI)	Nominal *P*-Value[b]
Primary: SRI(4) at Week 52, %	40.4	36.2		0.41
SRI(4) at Week 52 in IFNGS test–high patients, %	39.3 (n=151)	35.9 (n=148)		0.55
Sustained OCS reduction to ≤7.5 mg/d Weeks 40–52, %	32.1 (n=102)	41.0 (n=103)		0.18
≥50% reduction in CLASI activity from baseline to Week 12, %	24.9 (n=54)	41.9 (n=58)		0.05
Annualized flare rate to Week 52	0.72	0.60		0.26
BICLA response at Week 52, %	27.0	37.1		N/A
≥50% reduction in active joints from baseline to Week 52, %	32.3	47.0		N/A



[a]For responder rates, the difference in response rates and associated 95% CIs are weighted and calculated using a stratified Cochran–Mantel–Haenszel approach;
[b]Because the primary endpoint was not statistically significant, per the prespecified analysis plan, all other comparisons are nonsignificant.
Furie RA et al. Lancet Rheumatol 2019; doi.org/10.1016/S2665-9913(19)30076-1.

Prespecified and Amended Restricted Medication Rules

Composite efficacy endpoints include nonresponse classification for restricted medication use

- ~8% of patients were misclassified as nonresponders for NSAID use

- This led to a review of all restricted medication responder classification rules
  - After unblinding, SLE experts and sponsor revised restricted medication rules
    - NSAID use prior to Week 50 did not result in nonresponder classification

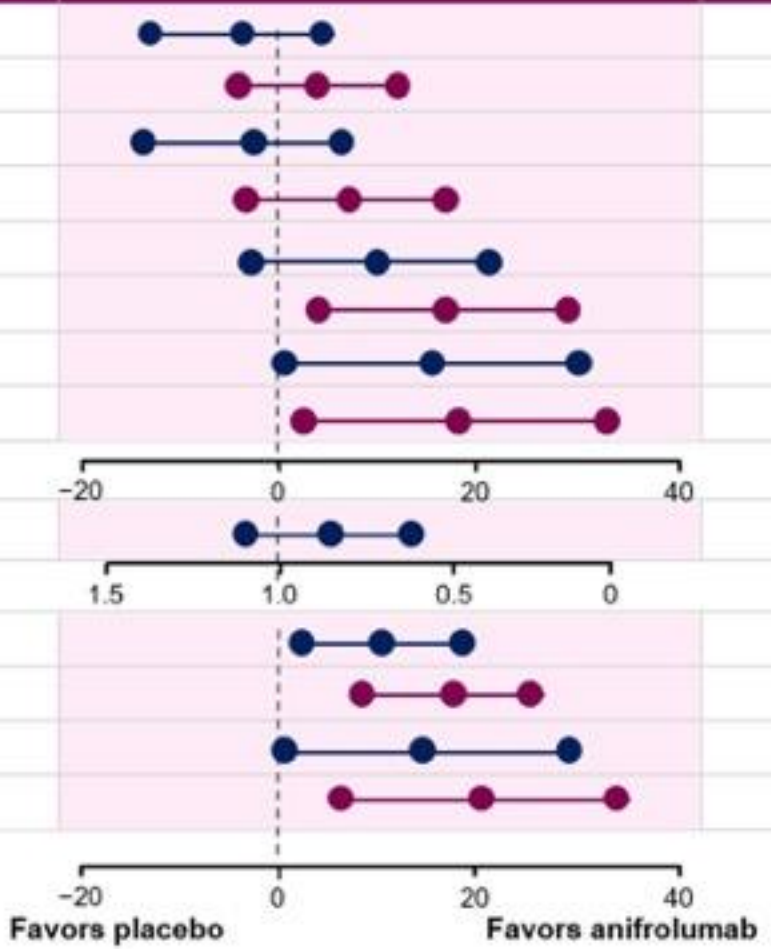
- Key analyses were repeated (post hoc) and are presented alongside the original analyses

NSAID, nonsteroidal anti-inflammatory drug; SLE, systemic lupus erythematosus.

Furie RA et al. Lancet Rheumatol. 2019; doi.org/10.1016/S2665-9913(19)30076-1.

Primary and Key Secondary Endpoints: Prespecified and Amended (Post hoc)

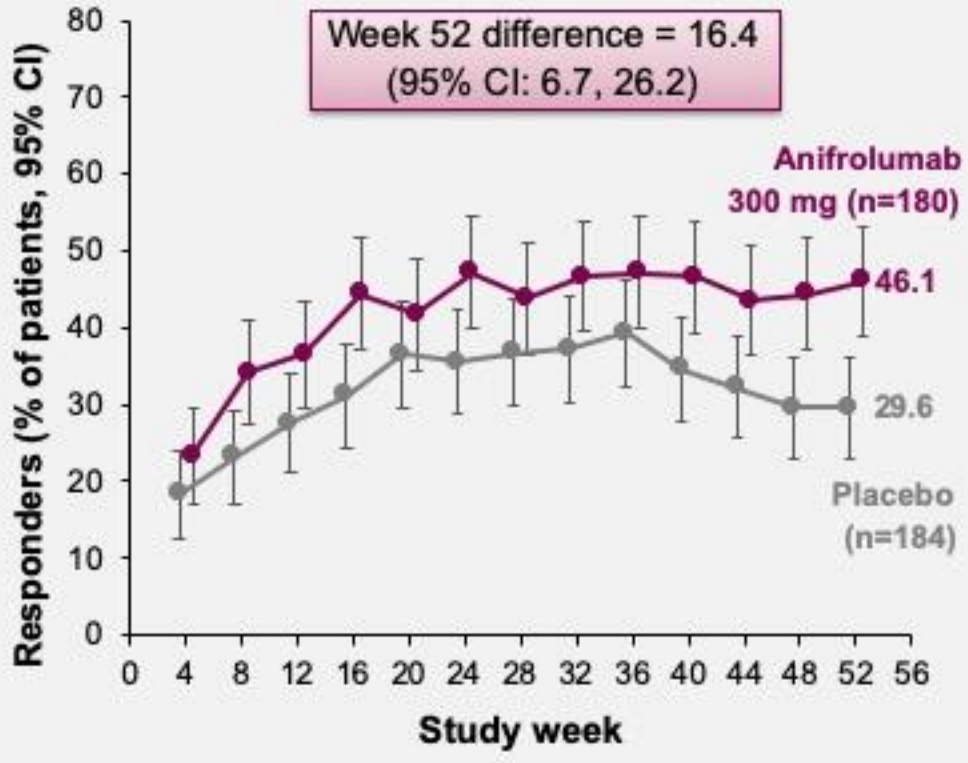
Primary and Key Secondary Endpoints[a]	Analysis[b]	Placebo (n=184)	Anifrolumab 300 mg (n=180)	Plot of Treatment Difference (95% CI)	Nominal *P*-Value[c]
Primary: SRI(4) at Week 52, %	Prespecified	40.4	36.2		0.41
	Amended	43.0	46.9		0.46
SRI(4) at Week 52 in IFNGS test–high patients, %	Prespecified	39.3	35.9		0.55
	Amended	41.8	48.2		0.26
Sustained OCS reduction to ≤7.5 mg/d Weeks 40–52, %	Prespecified	32.1	41.0		0.18
	Amended	32.1	48.8		0.01
≥50% reduction in CLASI activity from baseline to Week 12, %	Prespecified	24.9	41.9		0.05
	Amended	24.9	43.6		0.03
Annualized flare rate to Week 52[d]	N/A	0.72	0.60		0.26
BICLA response at Week 52, %	Prespecified	27.0	37.1		N/A
	Amended	29.6	46.1		N/A
≥50% reduction in active joints from baseline to Week 52, %	Prespecified	32.3	47.0		N/A
	Amended	32.3	53.0		N/A



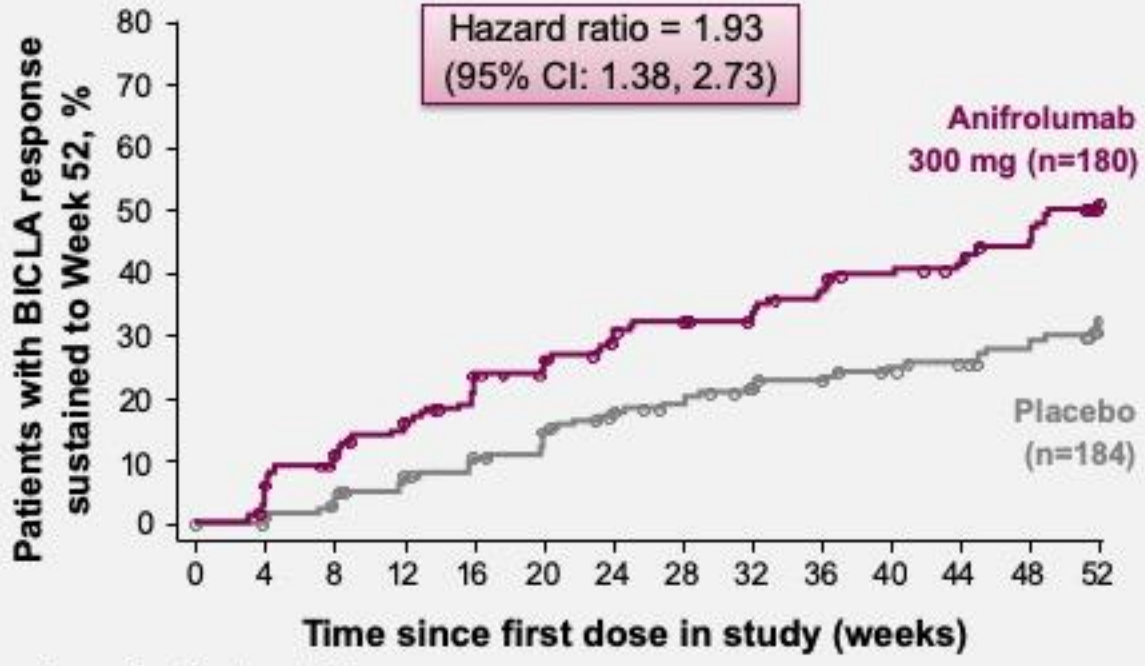
[a]For responder rates, the difference in response rates and associated 95% CIs are weighted and calculated using a stratified Cochran–Mantel–Haenszel approach; [b]Restricted medication rules were amended to correct for misclassified NSAIDs and other medications. [c]Because the primary endpoint was not statistically significant, per the prespecified analysis plan, all other comparisons are nonsignificant; [d]Flare rate calculations did not incorporate amended restricted medication rules; therefore, values for the prespecified and amended analyses are identical. Furie RA et al. Lancet Rheumatol 2019; doi.org/10.1016/S2665-9913(19)30076-1.

BICLA Response: Amended Medication Rules (Post Hoc)[a]

Percentage of Responders



Time to BICLA Response Sustained to 52 weeks



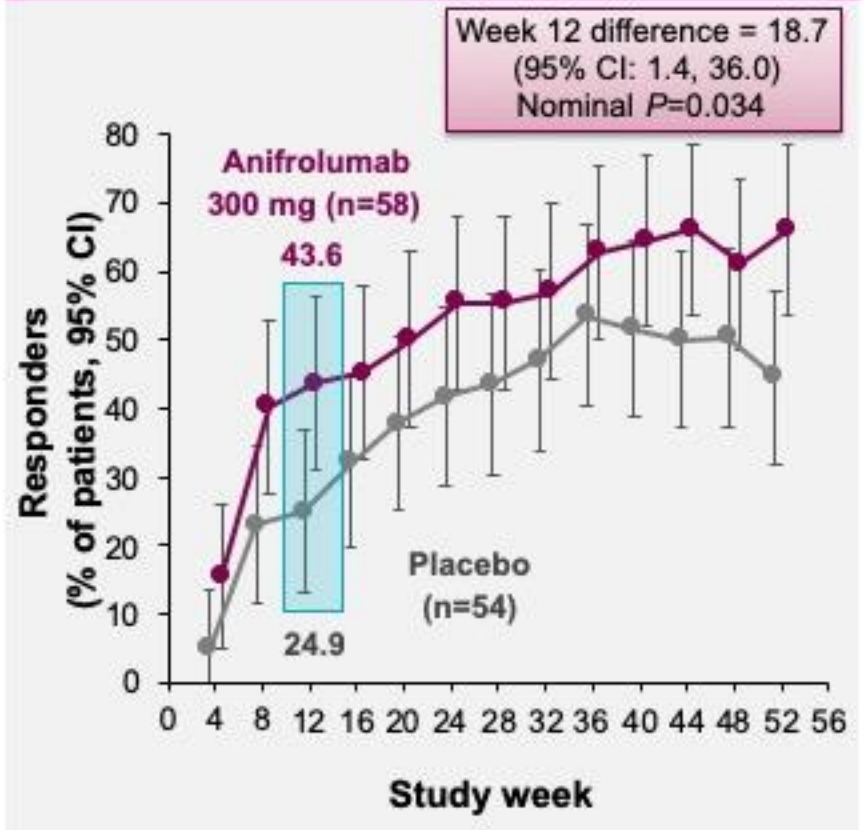
Number of patients at risk

Anifrolumab 300 mg	n =	180	170	153	142	129	119	108	102	99	91	85	81	74	53
Placebo	n =	184	179	171	163	154	147	133	127	120	116	110	106	101	83

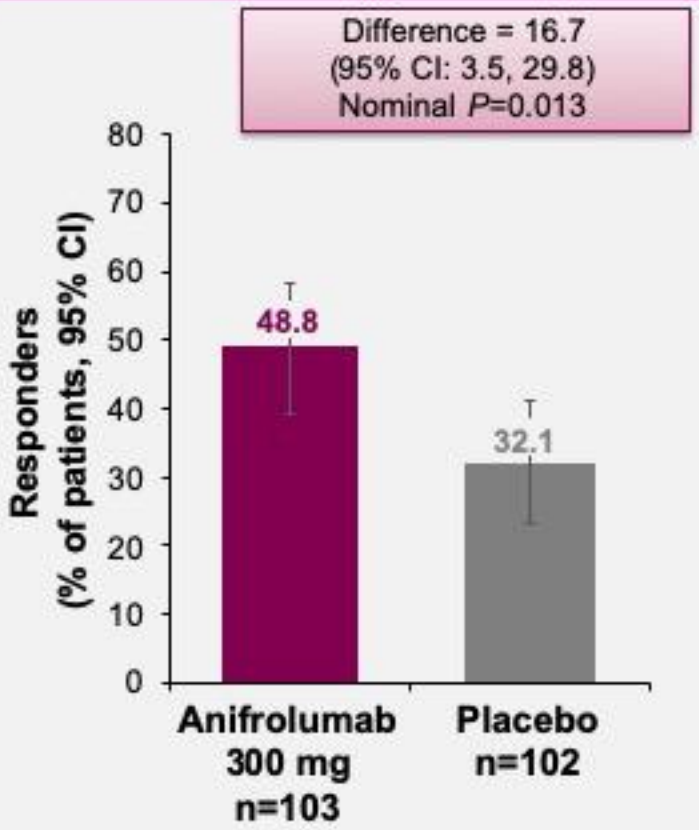
BICLA, British Isles Lupus Assessment Group–based Composite Lupus Assessment; CI, confidence interval.
[a]Restricted medication rules were amended to correct for misclassified NSAIDs and other medications.
Furie RA et al. Lancet Rheumatol. 2019; doi.org/10.1016/S2665-9913(19)30076-1.

Clinical Endpoints: Amended Medication Rules (Post Hoc)[a]

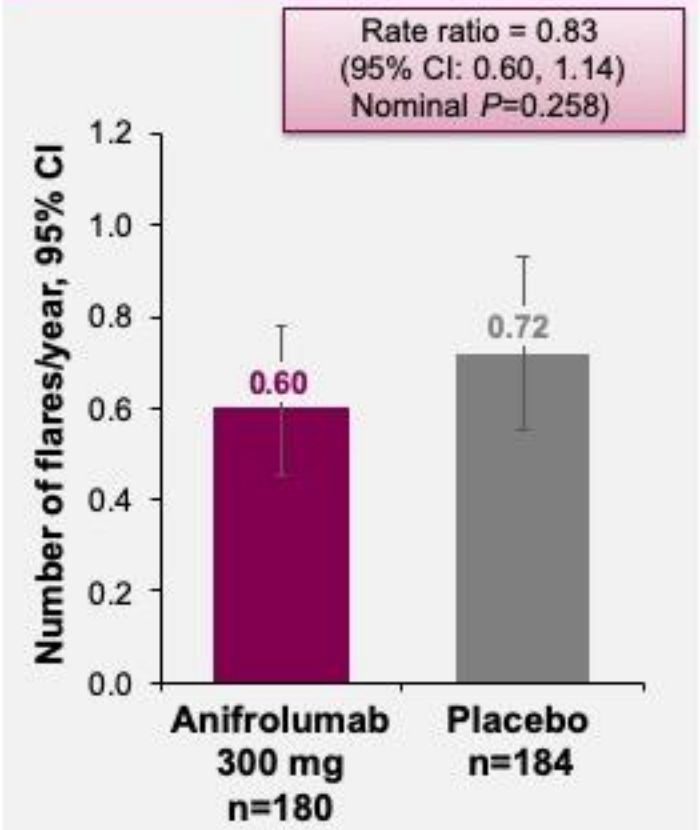
CLASI Response[b]



OCS Reduction to ≤7.5 mg/d Weeks 40 to 52[c]



Annualized Flare Rate Through Week 52[d]



[a]Restricted medication rules were amended to correct for misclassified NSAIDs and other medications; [b]In patients with CLASI score ≥10 at baseline; [c]In patients with baseline OCS ≥10 mg/d (prednisone or equivalent); [d]A flare is defined as either ≥1 new BILAG-2004 A or ≥2 new BILAG-2004 B items compared with the previous visit (ie, a worsening from an E, D, or C score to a B score in at least two organ systems or a worsening from an E, D, C, or B score to an A score in any one organ system compared with the previous visit). BILAG, British Isles Lupus Assessment Group; CI, confidence interval; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity; OCS, oral corticosteroid. Furie RA et al. Lancet Rheumatol. 2019; doi.org/10.1016/S2665-9913(19)30076-1.

Adverse Event Profile During Treatment Period

Adverse Event Category, n (%)[a]	Placebo (n=184)	Anifrolumab 150 mg (n=93)	Anifrolumab 300 mg (n=180)
Any adverse event	144 (78.3)	79 (84.9)	161 (89.4)
Serious adverse event	30 (16.3)	10 (10.8)	25 (13.9)
Serious adverse event in ≥2 patients in either anifrolumab group			
SLE (SLE worsening)	3 (1.6)	2 (2.2)	3 (1.7)
Pneumonia	1 (0.5)	1 (1.1)	3 (1.7)
Asthma	0	0	2 (1.1)
Chest pain	0	0	2 (1.1)
Adverse event with outcome of death	0	0	1 (0.6)[b]
Adverse event leading to discontinuation of study medication	5 (2.7)	5 (5.4)	11 (6.1)
Adverse event of special interest			
Herpes zoster	**3 (1.6)**	**5 (5.4)**	**10 (5.6)**
Nonopportunistic, serious infections	8 (4.3)	2 (2.2)	9 (5.0)
Malignancy	1 (0.5)	1 (1.1)	3 (1.7)
Influenza	2 (1.1)	1 (1.1)	2 (1.1)
Opportunistic infections	1 (0.5)	0	1 (0.6)
Tuberculosis	1 (0.5)	0	1 (0.6)
Anaphylaxis	0	1 (1.1)	0
Major adverse cardiovascular event	0	1 (1.1)	0
Vasculitis	0	0	0

[a]Adverse events are coded using MedDRA version 21.0. An adverse event during treatment was defined as an adverse event with a date of onset on or after the day of the first dose of investigational product and on or before the date of the last dose of investigational product plus 28 days. [b]Death due to pneumonia. SLE, systemic lupus erythematosus.
Furie RA et al. Lancet Rheumatol 2019; doi.org/10.1016/S2665-9913(19)30076-1.

Summary

- The primary endpoint, SRI(4), was not achieved in TULIP-1
- Post hoc analyses suggest potential efficacy of anifrolumab, including steroid reduction, CLASI, BICLA and joints
- Anifrolumab 300 mg suppressed IFNGS and was generally well tolerated
- The totality of data across trials and endpoints is key to understanding effects of SLE treatments

BICLA, British Isles Lupus Assessment Group–based Composite Lupus Assessment; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity; IFNGS, interferon gene signature; SLE, systemic lupus erythematosus; SRI(4), SLE Responder Index 4-point reduction.

Furie RA et al. Lancet Rheumatol. 2019; doi.org/10.1016/S2665-9913(19)30076-1.

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Anifrolumab Phase III TULIP 2 trial

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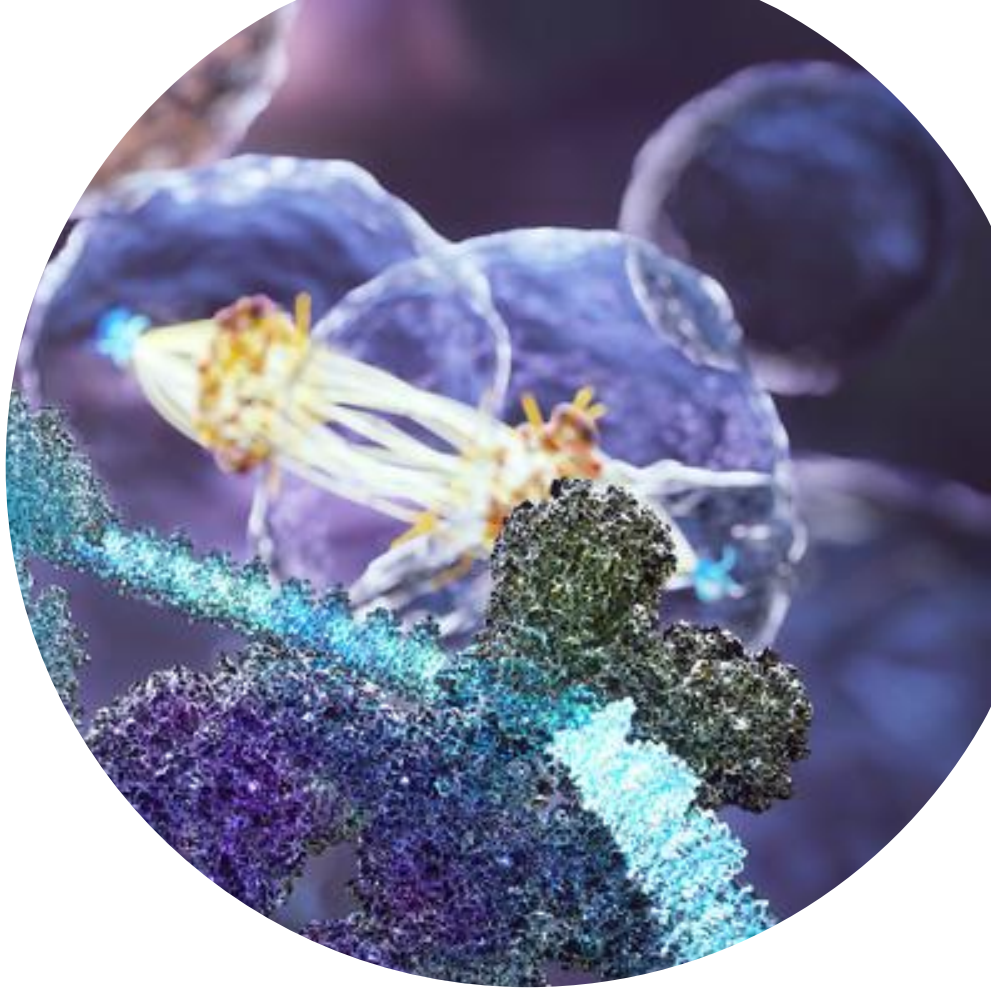
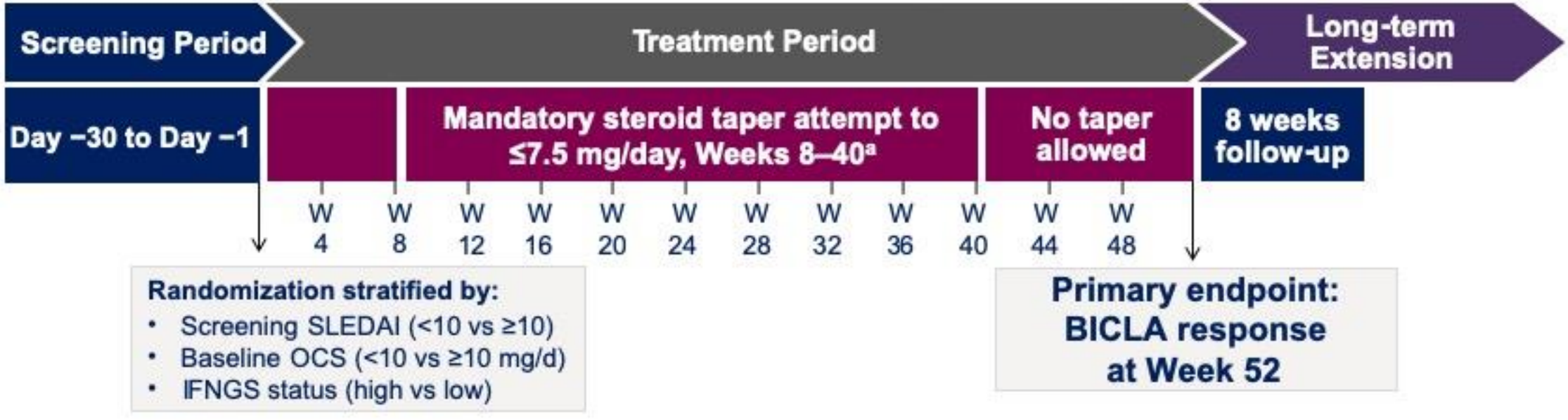


TULIP-2 Study Design

Study population	• Adults with moderately to severely active SLE – SLEDAI ≥6, ≥1 BILAG A or ≥2 B, and PGA ≥1 • Seropositive (ANA or anti-dsDNA or anti-Sm) • Receiving standard of care
Treatment (IV, Q4W)	• 1:1 randomization ratio – Anifrolumab 300 mg (N=180) – Placebo (N=182)
Sample size	• ≈135 sites • 362 patients received therapy
Geographic distribution	• United States/Canada, 36.5% • Europe, 26.8% • Latin America, 18.5% • Asia Pacific, 14.6% • Other, 3.6%



[a]For patients with baseline OCS ≥10 mg/day prednisone or equivalent. ANA, anti-nuclear antibodies; anti-dsDNA, anti–double-stranded DNA antibodies; anti-Sm, anti-Smith antibodies; IFNGS, type I interferon gene signature; SLEDAI, SLE Disease Activity Index.

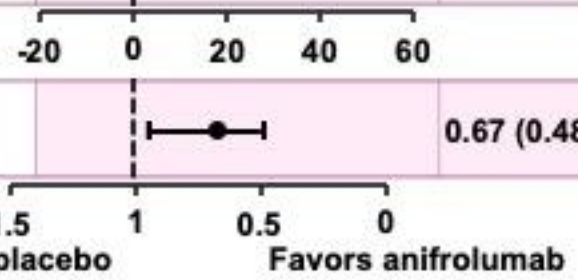
Baseline Patient Characteristics

Patient Characteristic	Placebo (n=182)	Anifrolumab 300 mg (n=180)
Age, mean (SD), years	41.1 (11.47)	43.1 (11.95)
Female, n (%)	170 (93.4)	168 (93.3)
White, n (%)[a]	107 (58.8)	110 (61.1)
Asian, n (%)[a]	30 (16.5)	30 (16.7)
Black/African American, n (%)[a]	25 (13.7)	17 (9.4)
Time from SLE diagnosis to randomization, median (range), months	78.0 (6–494)	94.5(6–555)
BILAG-2004 ≥1 A, n (%)	**95 (52.2)**	**81 (45.0)**
BILAG-2004 no A and ≥2 B, n (%)	**78 (42.9)**	**91 (50.6)**
SLEDAI-2K, mean (SD)	**11.5 (3.88)**	**11.4 (3.64)**
SLEDAI-2K ≥10, n (%)	**131 (72.0)**	**129 (71.7)**
PGA, mean (SD)	1.76 (0.397)	1.68 (0.411)
CLASI activity, mean (SD)	**7.6 (7.75)**	**8.3 (7.94)**
CLASI ≥10, n (%)	**40 (22.0)**	**49 (27.2)**
Swollen joint count, mean (SD)	7.4 (6.55)	6.2 (5.65)
Tender joint count, mean (SD)	11.0 (7.89)	9.0 (7.07)
SDI, mean (SD)	0.5 (0.79)	0.5 (0.91)

SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index. [a]Not all race categories are included in table.

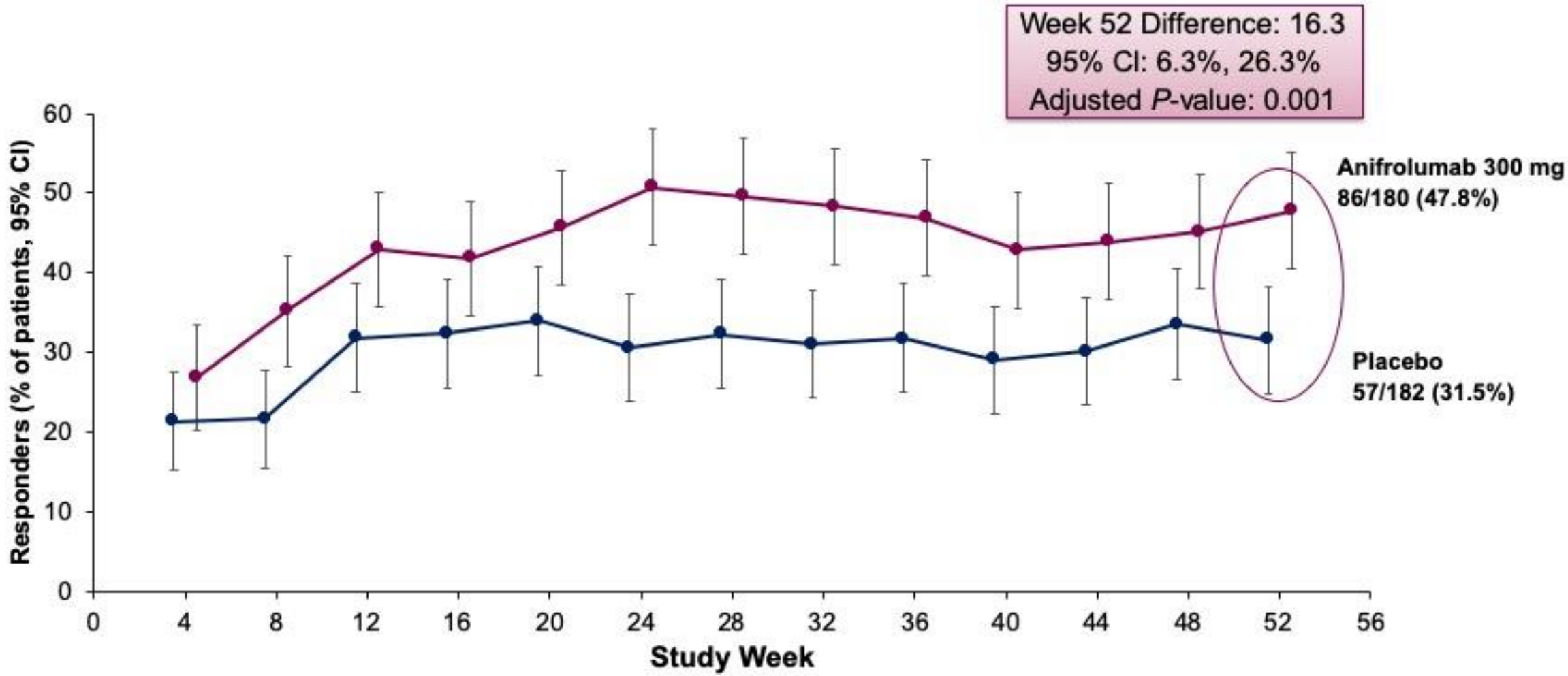
Primary and Key Secondary Endpoints

Endpoint[a]	Placebo n/N (%)	Anifrolumab 300 mg n/N (%)	Treatment Difference Plot (95% CI)	Treatment Difference (95% CI)	Adjusted *P*-Value	Significant Following Multiplicity[b]
Primary: BICLA response at Week 52	57/182 (**31.5**)	86/180 (**47.8**)		**16.3 (6.3, 26.3)**	0.0013	**Yes**
Key secondary						
BICLA response in IFNGS test–high patients at Week 52	46/151 (**30.7**)	72/150 (**48.0**)		**17.3 (6.5, 28.2)**	0.0022	**Yes**
Sustained OCS reduction[c]	25/83 (**30.2**)	45/87 (**51.5**)		**21.2 (6.8, 35.7)**	0.0135	**Yes**
CLASI response at Week 12[d]	10/40 (**25.0**)	24/49 (**49.0**)		**24.0 (4.3, 43.6)**	0.0392	**Yes**
Joint count response at Week 52[e]	34/90 (**37.5**)	30/71 (**42.2**)		**4.7(-10.6, 20.0)**	0.5469	**No**
Annualized flare rate[f]	**0.64**	**0.43**		**0.67 (0.48, 0.94)**	0.0809	**No**

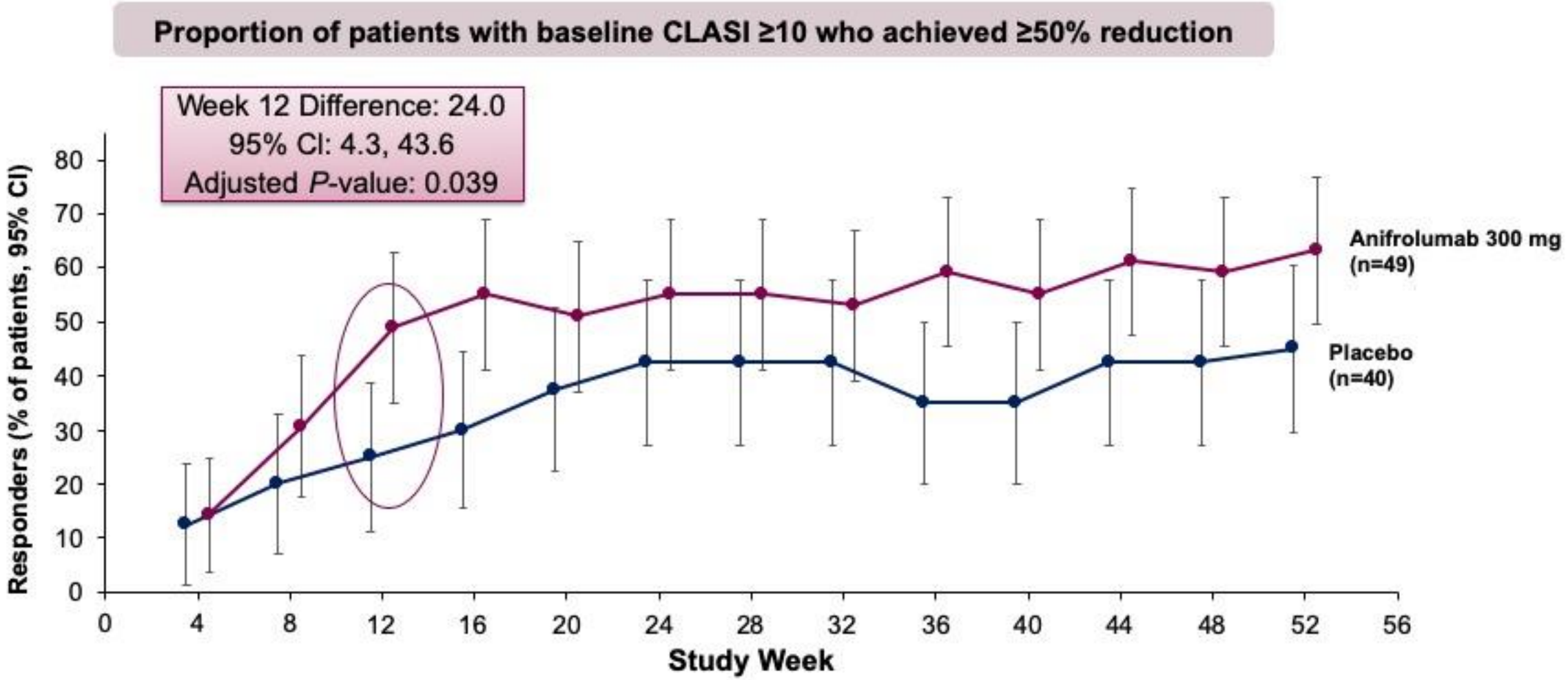


[a]For responder rates, the difference in response rates and associated 95% CIs are weighted and calculated using a stratified Cochran–Mantel–Haenszel approach; [b]Treatment comparison using a stratified Cochran–Mantel–Haenszel method; *P*-values adjusted per weighted Holm procedure; [c]In patients with baseline OCS ≥10 mg/d prednisone or equivalent; [d]In patients with CLASI activity score ≥10 at baseline; [e]In patients with ≥6 swollen and ≥6 tender joints at baseline; [f]Values are annualized flare rates rather than responder percentages; treatment difference for flare rate calculated as a rate ratio (anifrolumab/placebo).

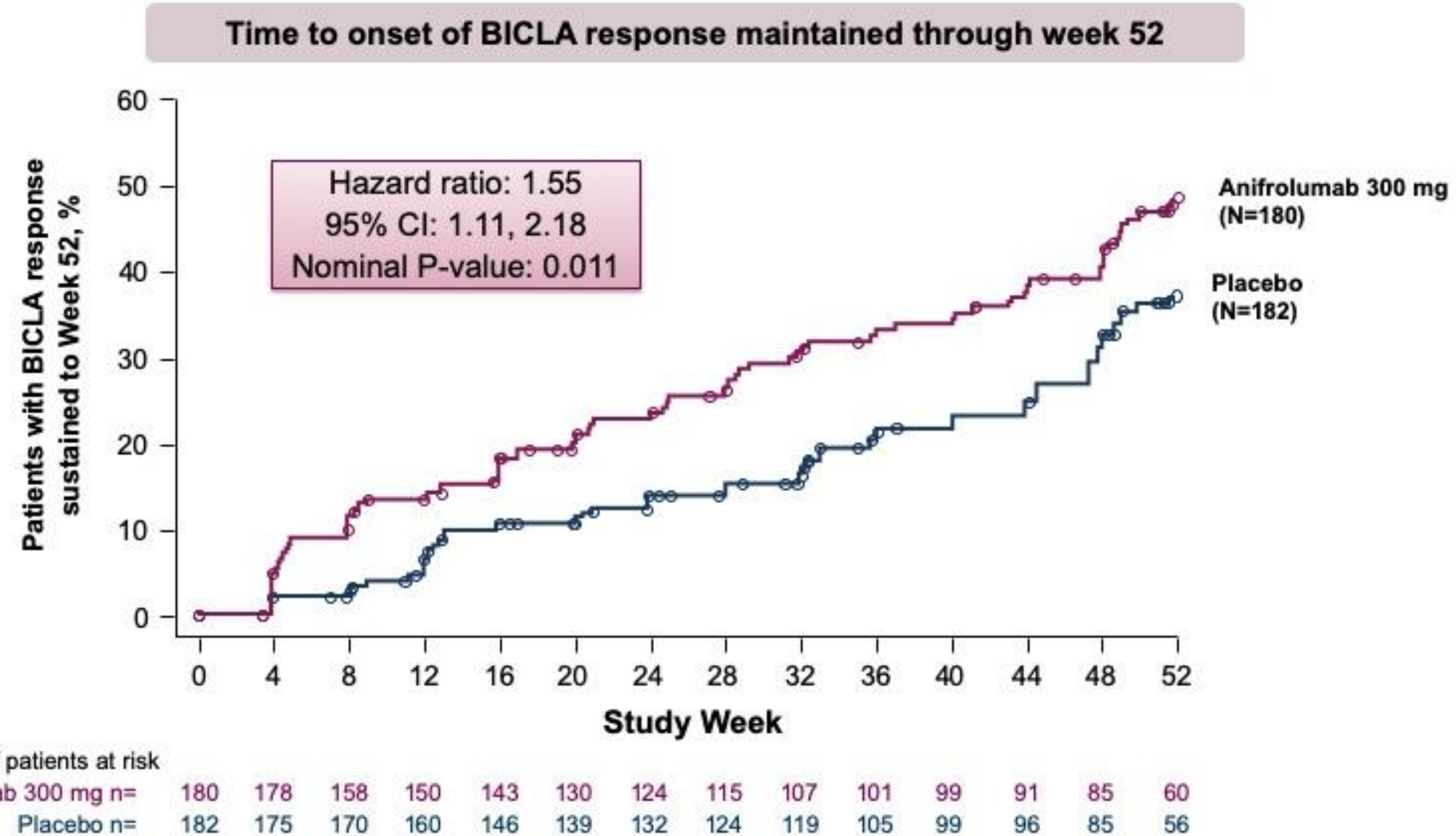
Primary Outcome Measure: BICLA Response at Week 52



Early Onset of Action - CLASI Response at Week 12

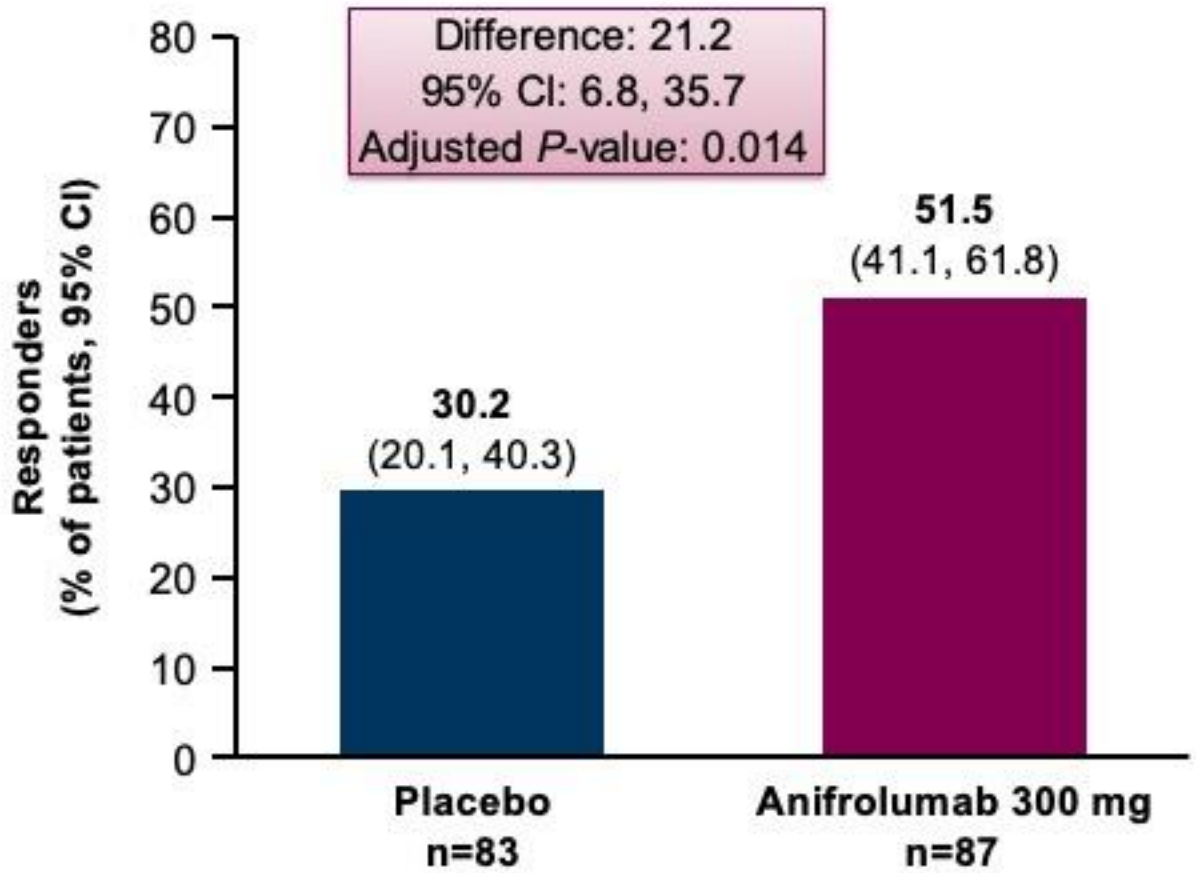


Early and Sustained BICLA Response



Sustained OCS Reduction to ≤7.5 mg/d

Proportion of patients with baseline OCS ≥10 mg/d who achieved reduction to ≤7.5 mg/d from Weeks 40 to 52



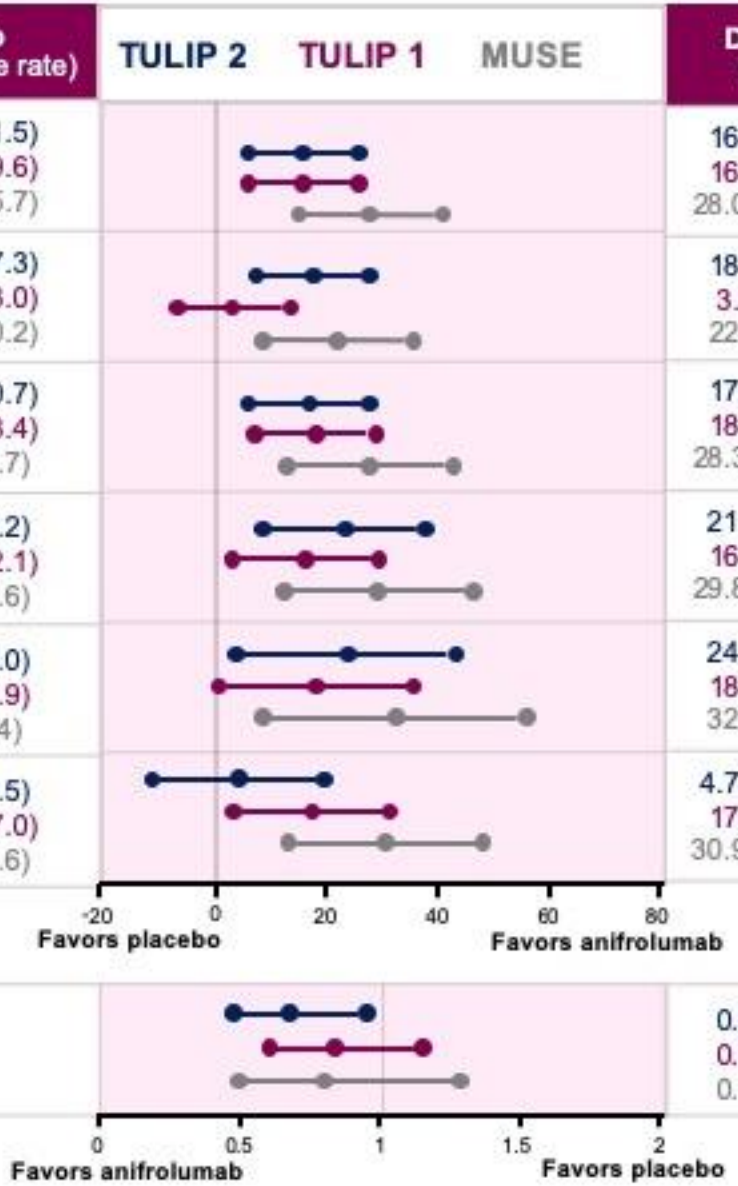
Adverse Event Profile During Treatment Period

Adverse Event Category, n (%)[a]	Placebo (n=182)	Anifrolumab 300 mg (n=180)
Any adverse event	153 (84.1)	159 (88.3)
Serious adverse event	**31 (17.0)**	**15 (8.3)**
Serious adverse event in ≥2 patients in the study		
Pneumonia	7 (3.8)	3 (1.7)
Gastroenteritis viral	0	2 (1.1)
SLE (SLE worsening)	6 (3.3)	1 (0.6)
Radius fracture	2 (1.1)	0
Adverse event with outcome of death	**0**	**1 (0.6)[b]**
Adverse event leading to discontinuation of study medication	13 (7.1)	5 (2.8)
Adverse event of special interest[c]	**18 (9.9)**	**25 (13.9)**
Herpes zoster[d]	**2 (1.1)**	**13 (7.2)**
Nonopportunistic, serious infections	10 (5.5)	5 (2.8)
Influenza	6 (3.3)	4 (2.2)
Tuberculosis (latent)	0	3 (1.7)
Major adverse cardiovascular event	0	1 (0.6)
Malignancy	1 (0.5)	0

[a]An adverse event during treatment was defined as an adverse event with a date of onset on or after the day of the first dose of investigational product and on or before the date of the last dose of investigational product plus 28 days; [b]Death due to pneumonia; [c]Other adverse events of special interest that were not reported in any patients were opportunistic infections, anaphylaxis, and vasculitis (n=0); [d]All were cutaneous manifestations and resolved without discontinuation of investigational product.

Overall Efficacy Results Were Highly Consistent Between TULIP 1, TULIP 2 and MUSE

		Anifrolumab 300 mg n/N (response rate)	Placebo n/N (response rate)	Difference (95% CI)	Nominal P-value	Statistical Significance in TULIP2
Primary endpoints	BICLA week 52 *primary endpoint TULIP2*	86/180 (47.8) 83/180 (46.1) 53/99 (53.5)	57/182 (31.5) 54/184 (29.6) 26/101 (25.7)	16.3 (6.3, 26.3) 16.4 (6.7, 26.2) 28.0 (15.1, 41.0)	0.001 0.001 <0.001	Yes
	SRI(4) week 52 *primary endpoint TULIP1*	100/180 (55.5) 84/180 (46.9) 62/99 (62.6)	68/182 (37.3) 79/184 (43.0) 41/102 (40.2)	18.2 (8.1, 28.3) 3.9 (-6.3, 14.1) 22.4 (9.0, 35.9)	<0.001 0.455 0.002	
Secondary endpoints in TULIP 2	BICLA IFN test-high week 52	72/150 (48.0) 68/148 (45.9) 39/75 (52.0)	46/151 (30.7) 41/151 (18.4) 18/76 (23.7)	17.3 (6.5, 28.2) 18.4 (7.7, 29.1) 28.3 (13.5, 43.1)	0.002 <0.001 <0.001	Yes
	Sustained OCS reduction	45/87 (51.5) 50/103 (48.8) 31/55 (56.4)	25/83 (30.2) 33/102 (32.1) 17/64 (26.6)	21.2 (6.8, 35.7) 16.7 (3.5, 29.8) 29.8 (12.8, 46.8)	0.004 0.013 0.001	Yes
	CLASI week 12	24/49 (49.0) 25/58 (43.6) 13/27 (48.1)	10/40 (25.0) 14/54 (24.9) 4/26 (15.4)	24.0 (4.3, 43.6) 18.7 (1.4, 36.0) 32.8 (9.4, 52.2)	0.017 0.034 0.011	Yes
	Joint Count week 52	30/71 (42.2) 50/93 (54.1) 42/58 (72.5)	34/90 (37.5) 37/100 (37.0) 24/58 (41.6)	4.7 (-10.6, 20.0) 17.8 (3.9, 31.7) 30.9 (13.6, 48.2)	0.547 0.019 < 0.001	No
	Annualized flare rate	0.43 0.60 0.53	0.64 0.72 0.72	0.67 (0.48, 0.94) 0.83 (0.60, 1.14) 0.80 (0.49, 1.31)	0.020 0.258 0.373	No



*Analytic methods and definitions differ across trials

Clinical Implications– Anifrolumab in Active SLE

- Unmet need in SLE demands better treatments
  - IFN pathway is active in 60%-80% of SLE patients
- Robust response vs. placebo across 3 studies
  - Overall disease activity – highly significant BICLA responses, early and sustained
  - Skin disease –early and sustained benefit
  - Steroid taper – key driver of long term damage, accepted treat-to-target goal
- Well tolerated
  - Incidence of herpes zoster was increased

Cumulative evidence identifies anifrolumab as a potential novel treatment option for SLE

Agenda

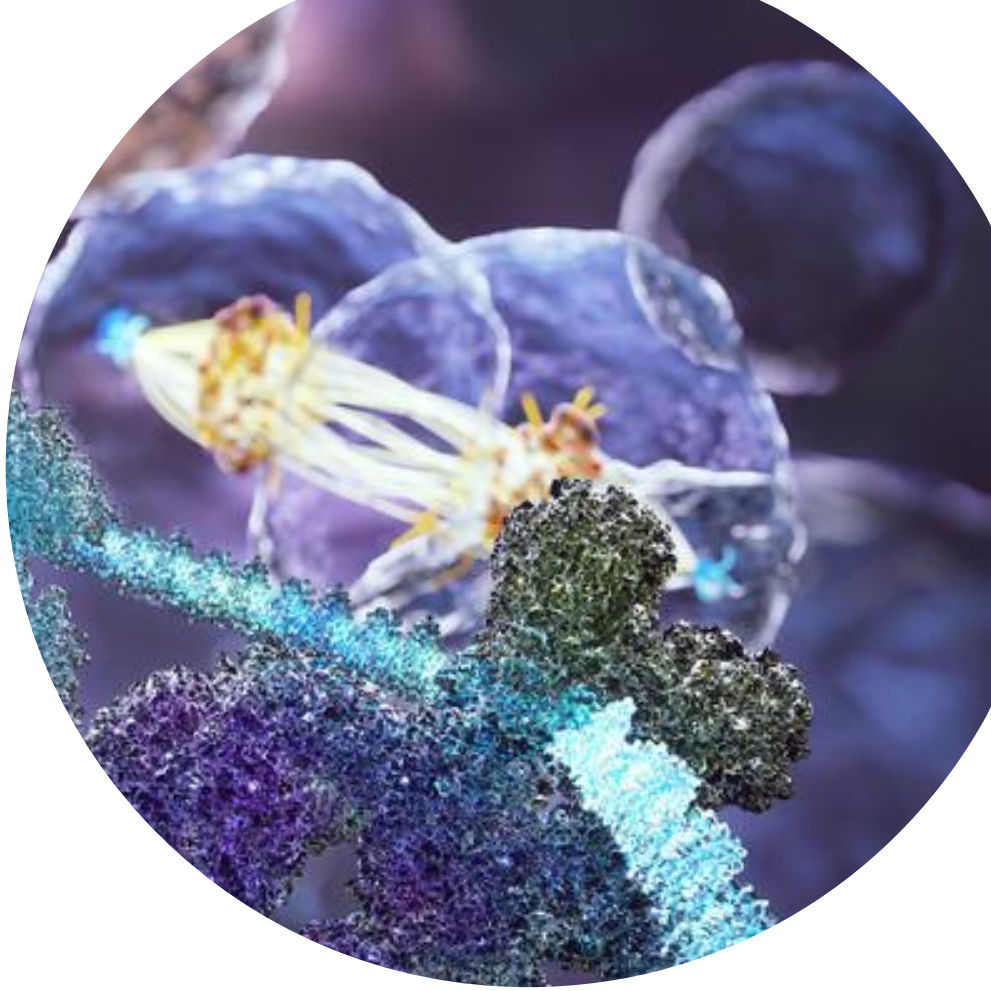
Introduction

Anifrolumab Phase III TULIP 1 trial

Anifrolumab Phase III TULIP 2 trial

Next steps

Q&A



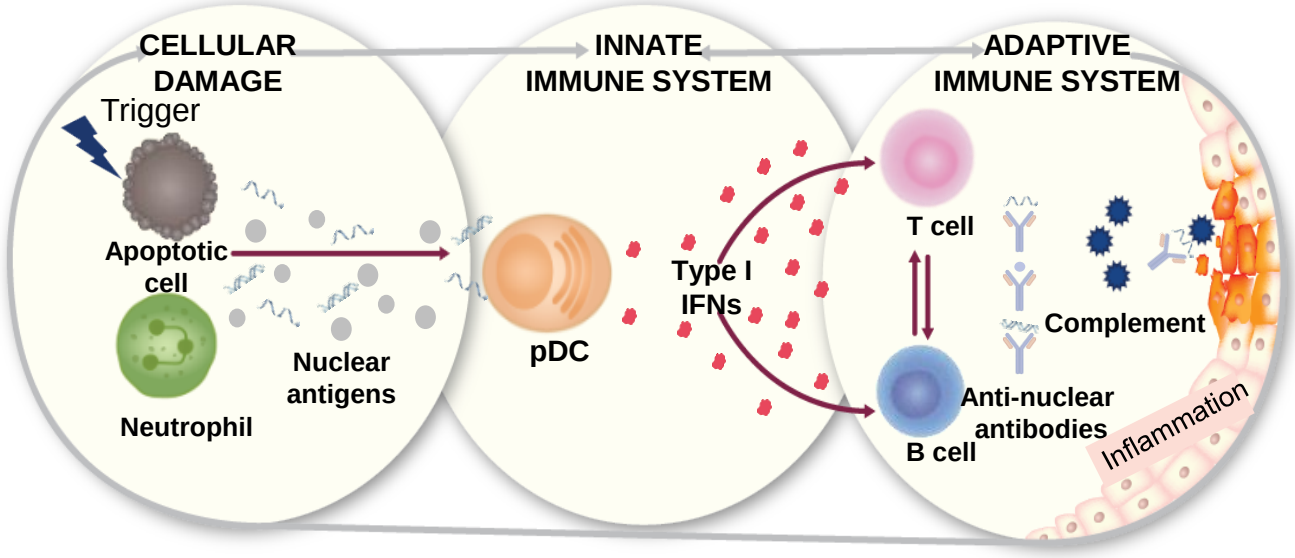
Anifrolumab: potential first-in-class treatment for SLE

Important new mode of action validated

- Multiple lines of evidence indicated the role of type 1 IFNs in SLE[1-3]
- Anifrolumab data has now validated targeting the type 1 IFN receptor[4]
- Only molecule targeted against type 1 receptor[5]

Only one new treatment in SLE in the last 60 years[6]

Anifrolumab blocks type 1 interferon

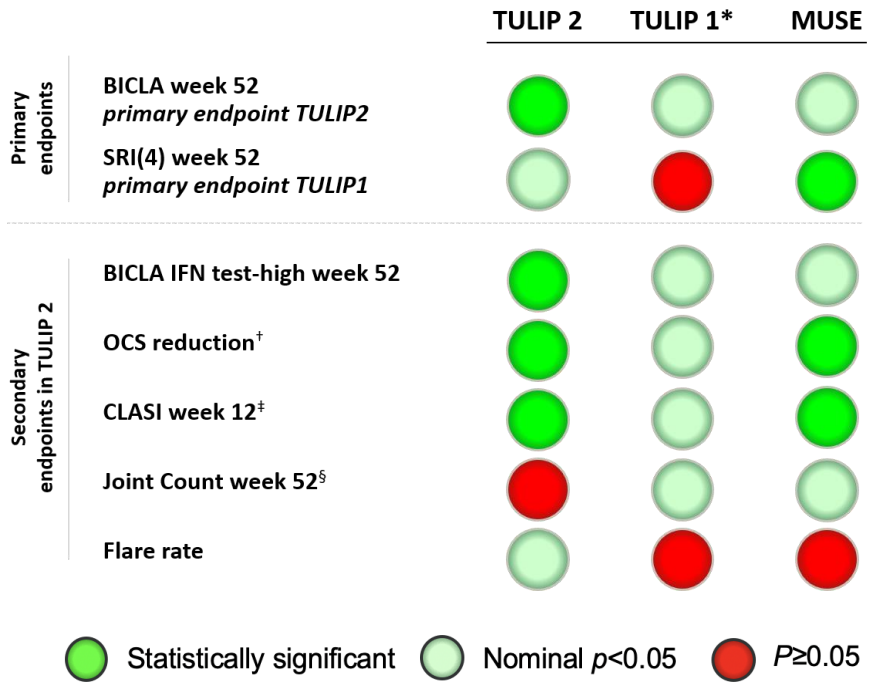


Anifrolumab blocks all type 1 interferons, suppressing multiple steps in downstream activation of B & T cells contribute to the cycle of tissue inflammation and destruction seen in lupus[5, 7-9]

Source: 1. Crow MK, *J Immunol* (192):5459-5468 (2014). 2. Furie R et al, *Arthritis Rheum* (69):376–86 (2017). 3. Furie RA et al, *Lancet Rheumatol* (2019). 4. Morand E et al, ACR 2019; Late breaking abstract L17. 5. Riggs JM et al, *Lupus Sci Med* (5):e000261 (2018). 6. Mahieu MA et al, *Lupus* 25:1122–1140 (2016). 7. Crow MK. *Curr Opin Rheumatol* (26):467-474 (2014). 8. Rönnblom L. *Ups J Med Sci* (116):227-237 (2011). 9. Dennis GJ. *Clin Pharmacol Ther* (91):143-14 (2012).

Anifrolumab results indicate important clinical potential

Trials exhibited consistency across multiple clinical endpoints at 300mg dose[1-3]



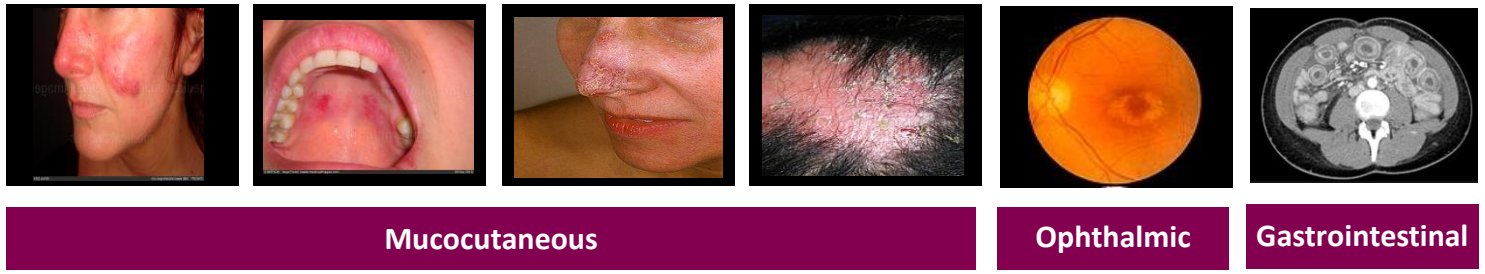
Data strengths should be compelling for clinicians and patients[1]

- BICLA results – improvement in all organ systems
- Response seen early
- OCS use reduced and sustained
- Skin disease activity reduced and seen as early as week 12
- Opportunity to identify predictors of response

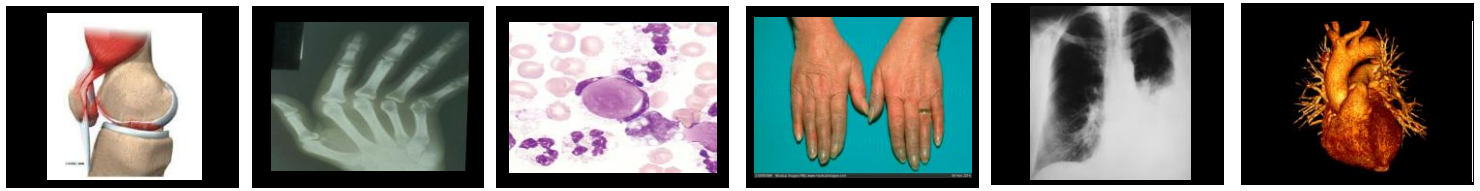
Source: 1. Morand E et al, ACR 2019; Late breaking abstract L17. 2. Furie R et al, *Arthritis Rheum* (69):376–86 (2017). 3. Furie RA et al, *Lancet Rheumatol* (2019). *Data generated using the revised restriction medication rules. †In patients with OCS ≥10 mg/d at baseline. ‡CLASI analysis includes patients with baseline CLASI score ≥10. §In TULIP-1 and MUSE joint activity was assessed in patients with ≥8 swollen and ≥8 tender joints. In TULIP-1 joint activity was assessed in patients with ≥6 swollen and ≥6 tender joints. OCS = oral corticosteroid

Improvement in BICLA means all organ systems with moderate to severe disease improved from baseline

Examples of organ systems measured by BICLA in the TULIP trials[1]

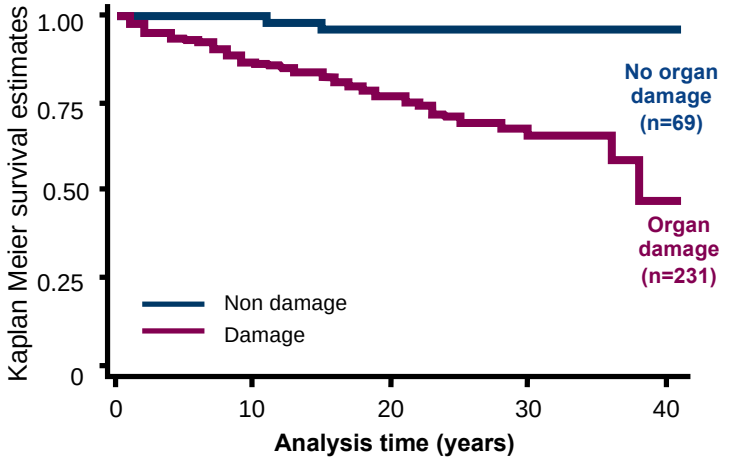


Mucocutaneous | Ophthalmic | Gastrointestinal



Musculoskeletal | Hematologic | Cardiorespiratory

Survival probability in patients with and without organ damage[2]



In a retrospective chart review of patients attending the Lupus Clinic of University College Hospital London:

35%

of patients with SLE who exhibited organ damage died over the follow-up period compared with

8.7%

who had no organ damage

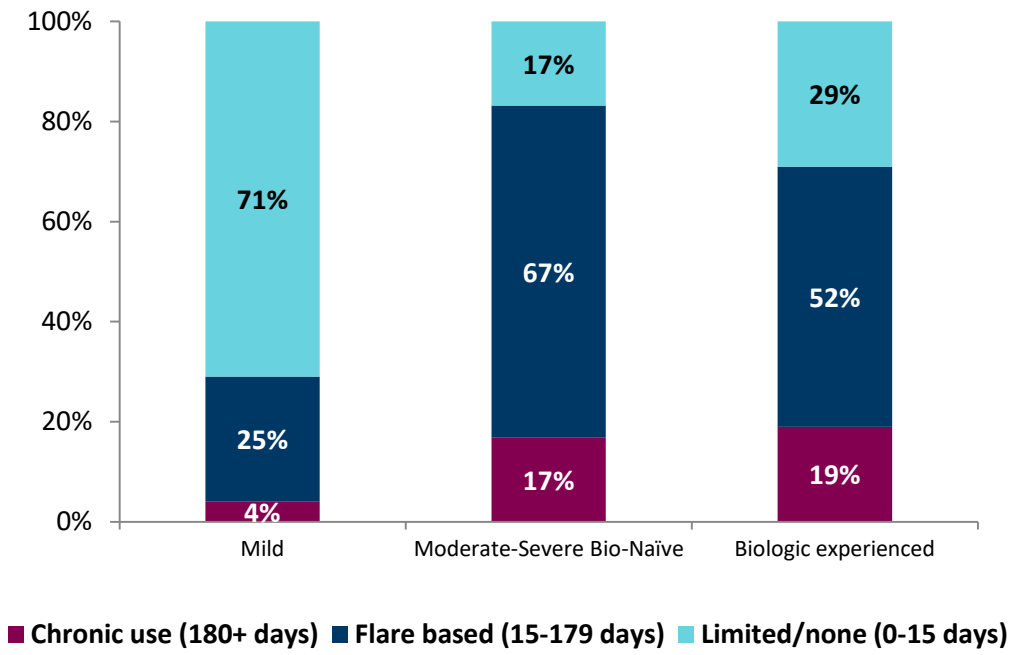
Source:1. Furie RA et al, *Lancet Rheumatol* (2019). Images credit: BSIP/ B. Tapper/C. Barry /N.Doss /A.Prohic /ISM

Source: 2. Segura BT, et al. *Rheumatology (Oxford).* 2019.

Around 70-80% of moderate to severe SLE patients use OCS

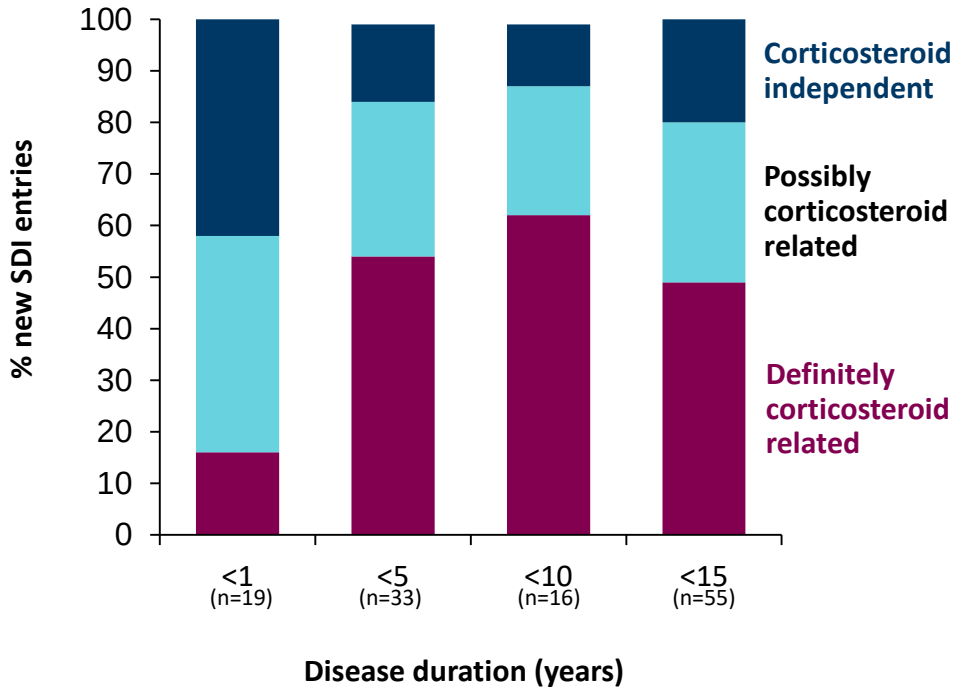
OCS is major contributor to organ damage

Significant corticosteroid use in SLE patients



Source: C1 Consulting SLE Integrated Insights study 2017; MarketScan Truven US claims data analysis 2010-2015.

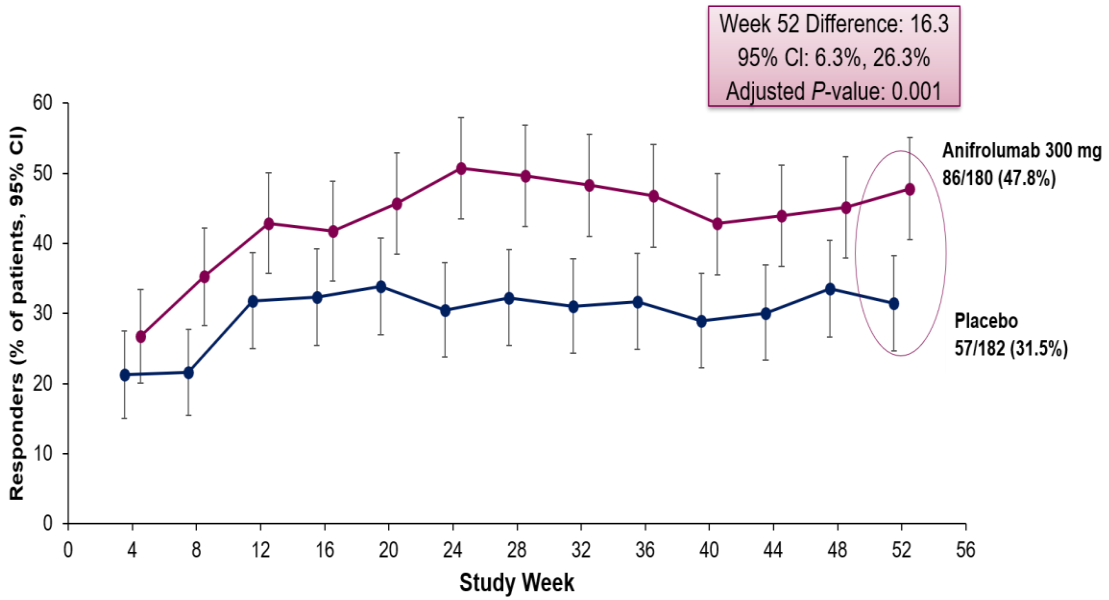
Corticosteroid-mediated organ damage



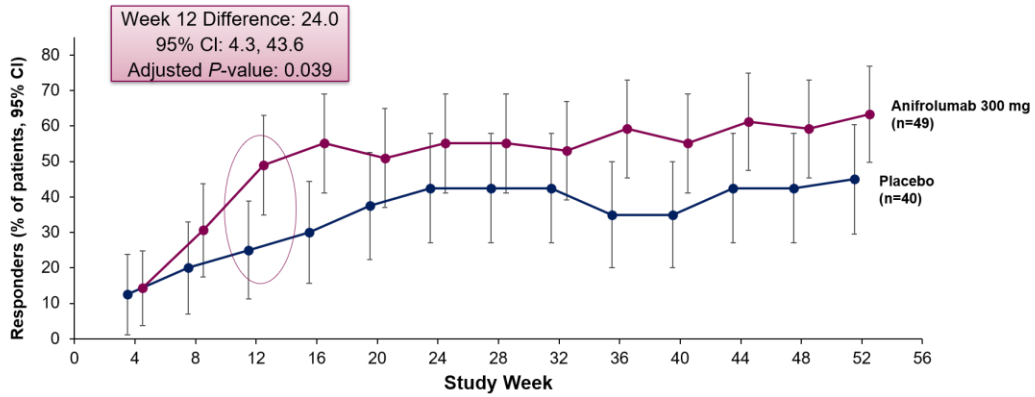
Source: Gladman et al. *J Rheumatol*. 2003;30:1955-1959. SDI = Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.

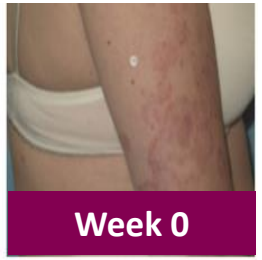
Anifrolumab led to early onset of response

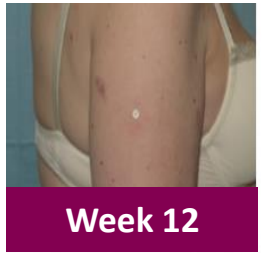
BICLA response over time in TULIP 2[1]



CLASI response seen at pre-specified measure of 12 weeks in TULIP 2*




Week 0


Week 12

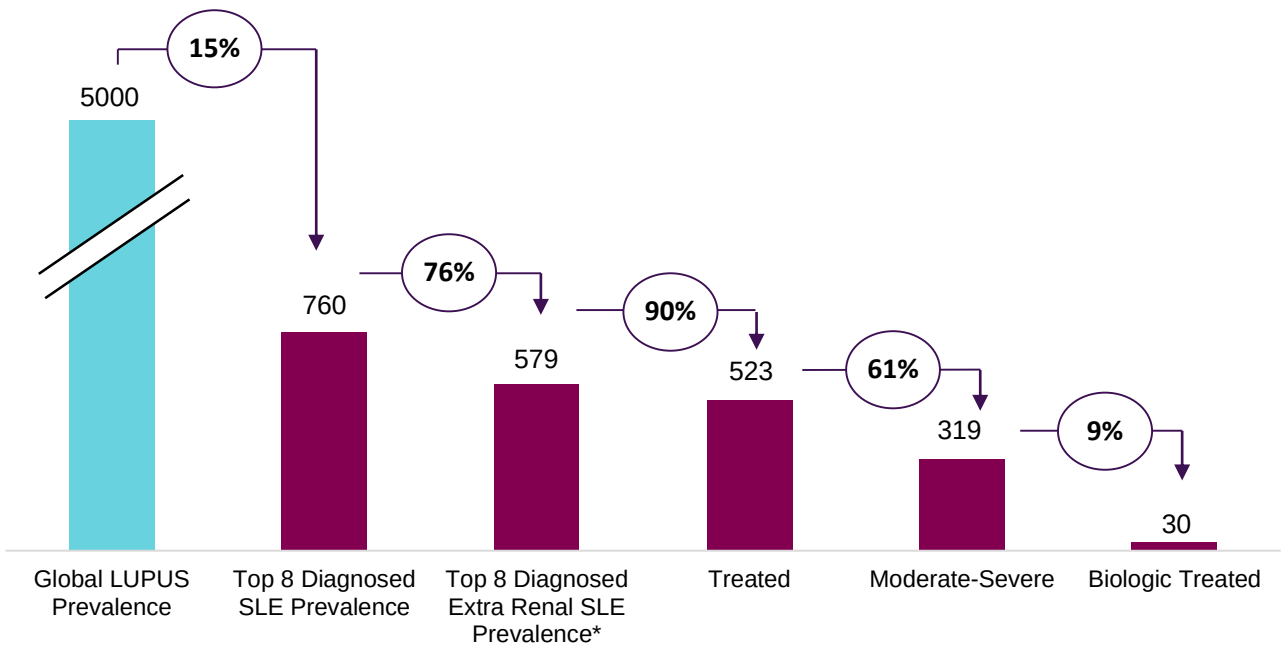
Source: 1. Morand E et al, ACR 2019; Late breaking abstract L17.

*In patients with CLASI activity score ≥10 at baseline.

Significant healthcare burden and clear unmet need

New modalities will drive the SLE market

SLE Patients (000s), Top 8 Countries (US, UK, ES, IT, DE, FR, JP, CN)



SLE prevalence outlook

SLE, rates	2016	2018	2025E
Diagnosed prevalence	556k	579k	↑
Treated	90%	90%	↔
Biologic treated	6%	9%	↑

Source: AstraZeneca analysis supported by Decision Resources, KantarHealth, Epi Literature Review and other market feedback.

Next steps for anifrolumab

Anifrolumab is a potential first-in-class treatment that blocks type 1 interferon for patients with SLE

- TULIP 2 demonstrated superiority across multiple endpoints vs. placebo[1]
- Overall efficacy results were highly consistent between TULIP 1, TULIP 2 and MUSE
- US FDA Fast Track attained based on MUSE data
- Data strengths should be compelling for clinicians and patients[1-3]
  - Efficacy as measured by BICLA
  - Early treatment response
  - OCS reduction, skin disease activity reduction
  - Consistent safety profile across trials

Important news flow

Trial/milestone	Phase	Status
Subcutaneous use trial	II	Detailed results announced at ACR 2019[4]
Regulatory submissions in moderate-to-severe SLE	-	Anticipated H2 2020
TULIP LTE (long-term extension)	III	Data anticipated 2021+
TULIP-LN1 (lupus nephritis)	II	Data anticipated 2021

Regulatory submission anticipated H2 2020

Source: 1. Morand E et al, ACR 2019; Late breaking abstract L17. 2. Furie R et al, *Arthritis Rheum* (69):376–86 (2017). 3. Furie RA et al, *Lancet Rheumatol* (2019). 4. Bruce I et al, ACR 2019 abstract 2563.

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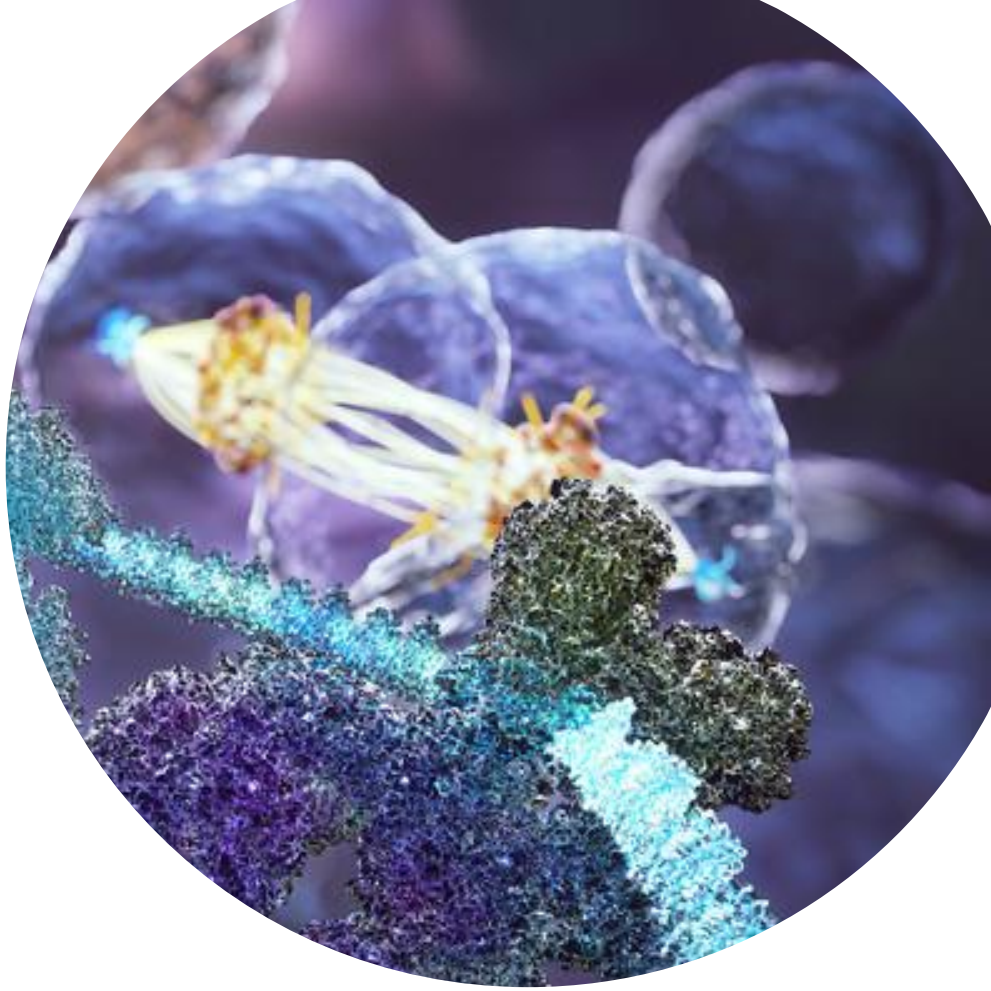


Q&A

Use of AstraZeneca conference call, webcast and presentation slides