AstraZeneca
What science can do

Investor science conference call: American College of Rheumatology 2015

San Francisco, California, USA

11 November 2015

Forward-looking statements

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This document contains certain forward-looking statements with respect to the operations, performance and financial condition of the Group, including, among other things, statements about expected revenues, margins, earnings per share or other financial or other measures. Although we believe our expectations are based on reasonable assumptions, any forward-looking statements, by their very nature, involve risks and uncertainties and may be influenced by factors that could cause actual outcomes and results to be materially different from those predicted. The forward-looking statements reflect knowledge and information available at the date of preparation of this document and AstraZeneca undertakes no obligation to update these forward-looking statements. We identify the forward-looking statements by using the words 'anticipates', 'believes', 'expects', 'intends' and similar expressions in such statements. Important factors that could cause actual results to differ materially from those contained in forward-looking statements, certain of which are beyond our control, include, among other things: the loss or expiration of, or limitations to, patents, marketing exclusivity or trademarks, or the risk of failure to obtain and enforce patent protection; the risk of substantial adverse litigation/government investigation claims and insufficient insurance coverage; effects of patent litigation in respect of IP rights; exchange rate fluctuations; the risk that R&D will not yield new products that achieve commercial success; the risk that strategic alliances and acquisitions, including licensing and collaborations, will be unsuccessful; the impact of competition, price controls and price reductions; taxation risks; the risk of substantial product liability claims; the impact of any delays in the manufacturing, distribution and sale of any of our products; the impact of any failure by third parties to supply materials or services; the risk of failure of outsourcing; the risks associated with manufacturing biologics; the risk of delay to new product launches; the difficulties of obtaining and maintaining regulatory approvals for products; the risk of failure to adhere to applicable laws, rules and regulations; the risk of failure to adhere to applicable laws, rules and regulations relating to anti-competitive behaviour; the risk that new products do not perform as we expect; failure to achieve strategic priorities or to meet targets or expectations; the risk of an adverse impact of a sustained economic downturn; political and socio-economic conditions; the risk of environmental liabilities; the risk of occupational health and safety liabilities; the risk associated with pensions liabilities; the risk of misuse of social medial platforms and new technology; the risks associated with developing our business in emerging markets; the risk of illegal trade in our products; the risks from pressures resulting from generic competition; the risk of failure to successfully implement planned cost reduction measures through productivity initiatives and restructuring programmes; economic, regulatory and political pressures to limit or reduce the cost of our products; the risk that regulatory approval processes for biosimilars could have an adverse effect on future commercial prospects; the impact of failing to attract and retain key personnel and to successfully engage with our employees; the impact of increasing implementation and enforcement of more stringent anti-bribery and anti-corruption legislation; and the risk of failure of information technology and cybercrime. Nothing in this presentation / webcast should be construed as a profit forecast.

Introduction

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Thomas Kudsk Larsen
Head of Investor Relations

2015 investor science events for each main therapy area

Respiratory, Inflammation & Autoimmunity	Cardiovascular & Metabolic Disease	Oncology
ACR 2015, November	**ACC 2015, March**	**ASCO 2015, June**
• anifrolumab (previously MEDI-546) – Phase II data in lupus – Phase III programme	• *Brilinta*/*Brilique* – Phase III PEGASUS trial – FDA-approval already in September 2015	• Durva + treme combo – Phase Ib in lung cancer and dose selection for Phase II/III • Small-molecule portfolio, including *Lynparza, Iressa,* AZD9291

2015: A great year for science in AstraZeneca

Agenda: Meet the experts

- **Lupus & targeting the interferon pathway**
  - Bing Yao, Head of Respiratory, Inflammation & Autoimmunity iMED, MedImmune
- **Anifrolumab Phase II lupus/SLE**
  - Richard Alan Furie, MD, Chief, Division of Rheumatology, North Shore-LIJ Health System
- **Anifrolumab current & future plans**
  - David J. Chang, MD, VP and Head, Inflammation, Autoimmunity & Neuroscience, Global Medicines Development
- **Q&A**

Total duration ~1 hour

Lupus & targeting the interferon pathway

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Bing Yao
Head of Respiratory, Inflammation & Autoimmunity iMED, MedImmune

High unmet need for systemic lupus erythematosus (SLE)

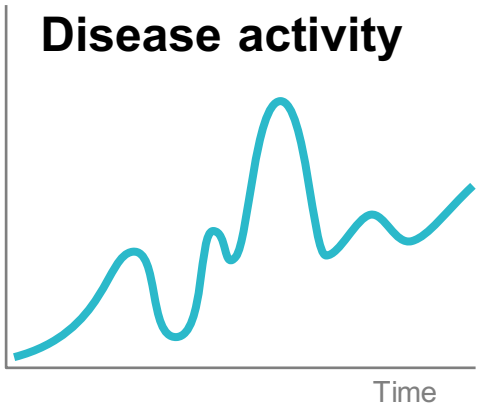
Chronic disease with unpredictable, recurring flares

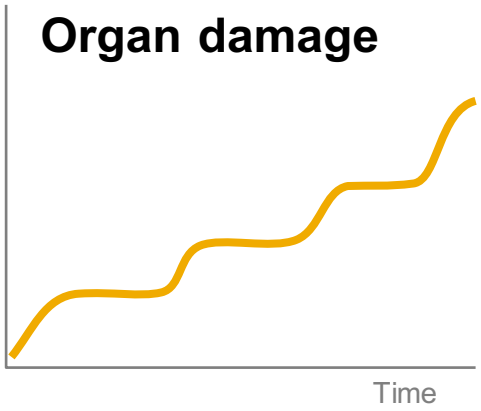
Widespread organ and tissue damage: Any part of the body, including skin, joints, heart, lungs, blood, liver, kidneys, and brain

About 90% women, usually of childbearing age

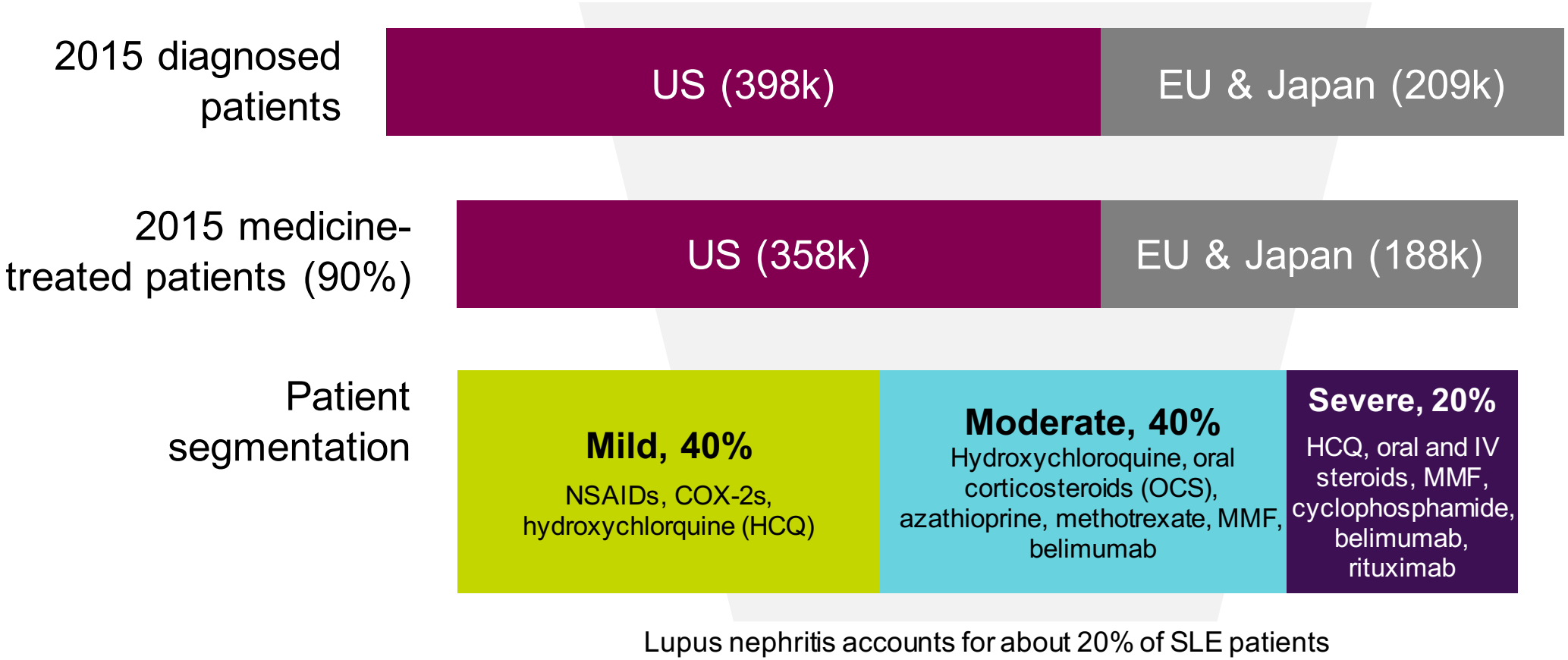
Limited efficacy and poor tolerability of standard of care

Need more effective therapies to reduce disease activity, steroids use, and flares





Lupus epidemiology in select countries



Lupus nephritis accounts for about 20% of SLE patients

Source: Decision Resources 2014 and primary market research
NSAID = Non-Steroidal Anti-Inflammatory Drugs MMF = Mycophenolate Mofetil

Many challenges to medicine development in lupus

Waxing and waning nature of disease

Disease assessments not sensitive to changes

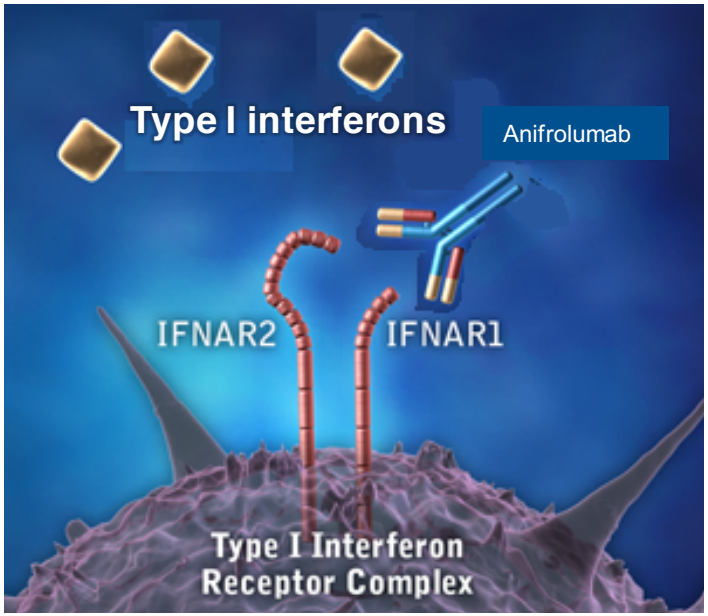
Evolving knowledge of underlying pathophysiology

Heterogeneity of organ manifestations

Only one new medicine approval in close to 60 years and multiple failures since

Target critical pathways; diagnostics to select right patients; multiple global disease activity and organ specific disease activity measures

Anifrolumab mechanism of action



Interferons drive multiple pathways central to pathogenesis

Maturation of monocytes which enhances the **function of effector T cells**

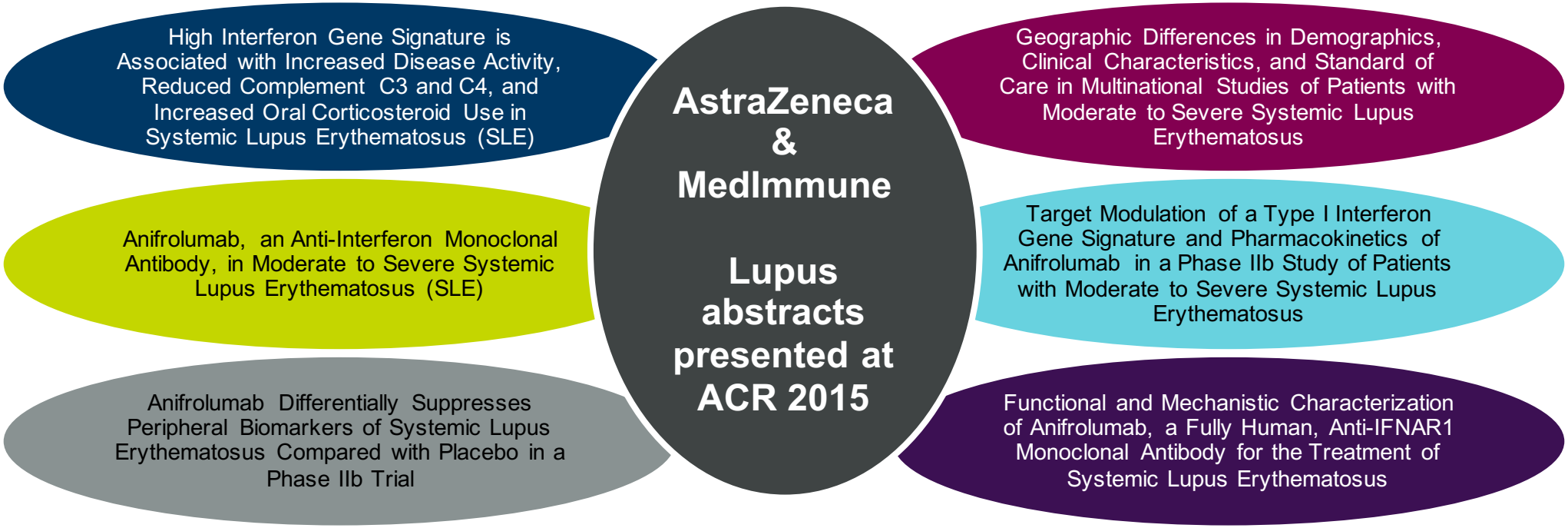
Expression of BLyS from dendritic cells which **enhances survival of B cells**

Expansion of plasma cells and **production of autoantibodies**

T cell and B cell release of cytokines **causing tissue damage**

Anifrolumab suppresses interferon gene signature to normal level
Gene signature used as a potential predictor of responders

Mounting evidence and support for anifrolumab as a potential future medicine



Sifalimumab (previously MEDI-545)**:** Positive Phase IIb validated clinical relevance of targeting IFNa
Anifrolumab: Only successful Phase II in SLE meeting primary and all key secondary endpoints

Anifrolumab Phase II lupus/SLE

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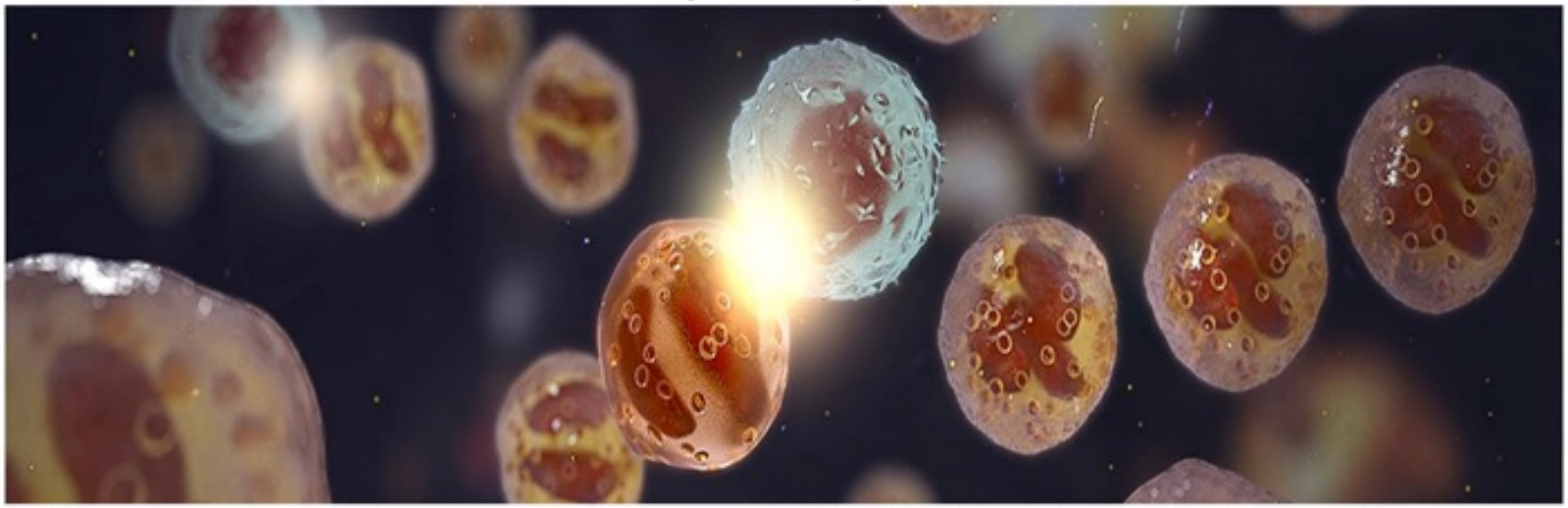
Richard Alan Furie, MD
Chief, Division of Rheumatology, North Shore-LIJ Health System

OP3223

Anifrolumab, an Anti-Interferon-Alpha Receptor Monoclonal Antibody, in Moderate to Severe Systemic Lupus Erythematosus (SLE)

R Furie[1], JT Merrill[2], VP Werth[3,4], M Khamashta[5], K Kalunian[6], P Brohawn[7], G Illei[7], J Drappa[7], L Wang[7], S Yoo[8]

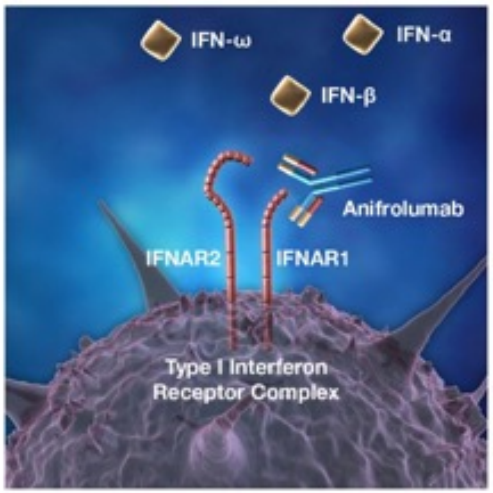
[1]Division of Rheumatology, Hofstra North Shore –LIJ School of Medicine, North Shore – LIJ Health System, Great Neck, NY, USA; [2]Oklahoma Medical Research Foundation, Oklahoma City, OK, USA; [3]Philadelphia VA Medical Center, Philadelphia, PA, USA; [4]University of Pennsylvania Philadelphia, PA, USA; [5]Graham Hughes Lupus Research Laboratory, King's College London, The Rayne Institute, St Thomas' Hospital, London, UK; [6]UCSD School of Medicine, La Jolla, CA, USA; [7]MedImmune, Gaithersburg, MD, USA; [8]Regenxbio, Rockville, MD, USA



MUSE: A Phase II, Randomized Study to Evaluate the Efficacy and Safety of **M**EDI-546 in **S**ubjects with **S**ystemic Lupus **E**rythematosus

The type I interferon system in systemic lupus erythematosus

- Central pathogenic mediator in SLE[1,2]
- Trial results for sifalimumab[3] and rontalizumab[4] have been mixed
- All type I IFN signaling is mediated by the type I IFN-α receptor (IFNAR)[5]
- Inhibiting IFNAR has the potential to block the biological effects of all type I IFNs[6]
- Anifrolumab is a unique, fully human, IgG_1 κ monoclonal antibody that binds to IFNAR[7] and prevents binding of type I IFNs



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IFN, interferon; IFNAR, type I IFN-α receptor; SLE, systemic lupus erythematosus

1. Lauwerys BR et al. *Rheumatology* (Oxford) 2014;53:1369-76; 2. Crow MK. *J Immunol* 2014;192:5459-68; 3. Khamashta M et al. *Arthritis Rheumatol* 2014:3529-40 (Abstract L4); 4. Kalunian KC et al. *Ann Rheum Dis* 2015:doi: 10.1136/annrheumdis-2014-206090; 5. Ivashkiv LB et al. *Nat Rev Immunol* 2014;14:36-49; 6. Lichtman EI et al. *Clin Immunol* 2012;143:210-21; 7. Peng L et al. *mAbs* 2015;7:428-39

Key eligibility and stratification

Inclusion

1. Positive ANA and/or elevated anti-dsDNA and/or anti-Sm antibodies
2. Moderate to severe active SLE, defined as:
   - SLEDAI-2K ≥6 **and**
   - BILAG 2004 organ domain scores of ≥1A or ≥2B **and**
   - PGA ≥1.0 **and**
   - Clinical SLEDAI-2K score ≥4 points (Day 1)
3. Stable treatment with at least one of the following:
   - Oral prednisone ≤40 mg/day or antimalarial or immunosuppressive (AZA, MMF, MTX)

Exclusion

1. Active and severe lupus nephritis or neuropsychiatric SLE

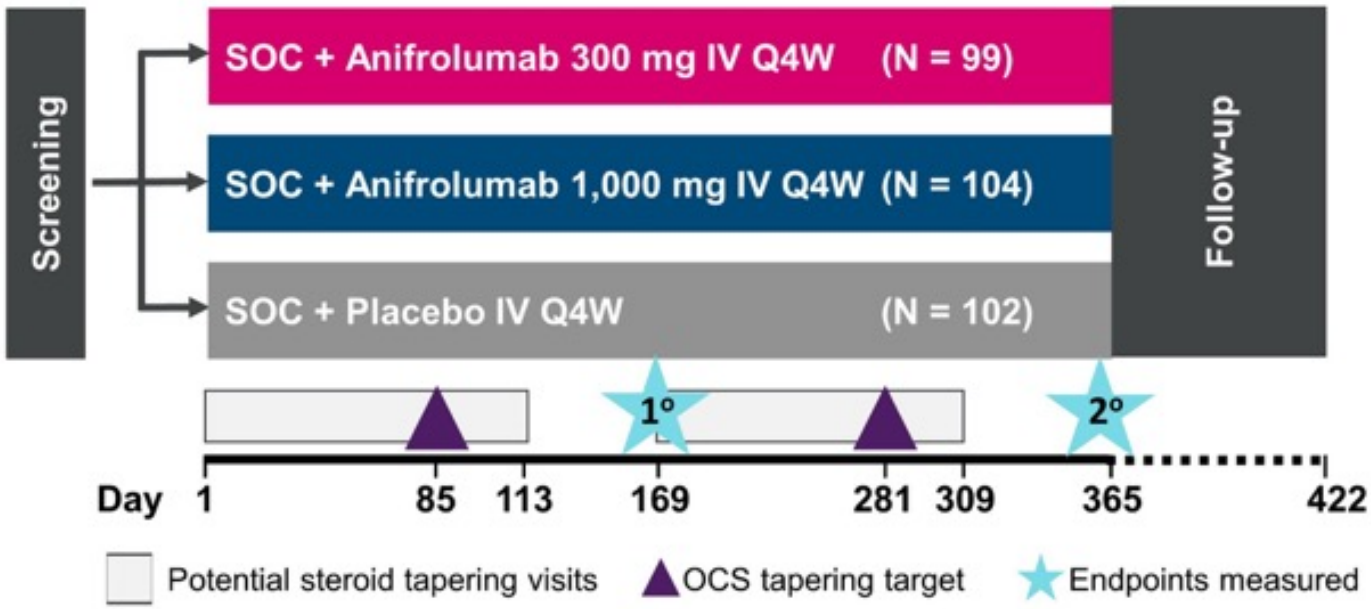
Stratification factors

1. IFN gene signature (IFN high or IFN low)
2. Dosage of oral corticosteroids (OCS) (<10 mg/day or ≥10 mg/day)
3. SLEDAI−2K score (<10 or ≥10)

[4]

ANA, antinuclear antibody; AZA, azathioprine; BILAG, British Isles Lupus Assessment Group; dsDNA, double-stranded DNA; MMF, mycophenolate mofetil; MTX, methotrexate; OCS, oral corticosteroids; PGA, Physician Global Assessment; SLEDAI-2K, SLE Disease Activity Index 2000; Sm, Smith

Study design



Primary efficacy measure

- SLE Responder Index [SRI(4)] at Day 169 with a sustained reduction of oral corticosteroid to <10 mg/day prednisone and ≤Day 1 dose, from Day 85 through Day 169

16

Q4W, every 4 weeks; SOC, standard of care; SRI, SLE responder index

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NCT01438489

Baseline demographics (mITT population)

		Placebo (N=102)	Anifrolumab 300 mg (N=99)	Anifrolumab 1,000 mg (N=104)
Age (years)	Mean (SD)	39.3 (12.9)	39.1 (11.9)	40.8 (11.6)
Sex, n (%)	Male Female	9 (8.8) 93 (91.2)	6 (6.1) 93 (93.9)	5 (4.8) 99 (95.2)
Ethnicity, n (%)	Hispanic Non-Hispanic	42 (41.2) 60 (58.8)	46 (46.5) 53 (53.5)	40 (38.5) 64 (61.5)
Race, n (%)	White Black Asian American Indian or Alaskan Native Other	41 (40.2) 12 (11.8) 13 (12.7) 0 (0.0) 36 (35.3)	35 (35.4) 19 (19.2) 3 (3.0) 4 (4.0) 38 (38.4)	51 (49.0) 10 (9.6) 6 (5.8) 1 (1.0) 36 (34.6)

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mITT, modified intention-to-treat; SD, standard deviation

Baseline disease characteristics (mITT population)

		Placebo (N=102)	Anifrolumab 300 mg (N=99)	Anifrolumab 1,000 mg (N=104)
SLEDAI-2K score	Mean (SD)	11.1 (4.4)	10.7 (3.7)	10.9 (4.1)
Clinical SLEDAI score	Mean (SD)	9.0 (2.9)	8.9 (2.5)	8.9 (3.0)
BILAG 2004 score	Mean (SD)	19.8 (5.8)	19.6 (5.8)	18.6 (5.7)
PGA score	Mean (SD)	1.77 (0.44)	1.86 (0.39)	1.86 (0.39)
CLASI activity	Mean (SD)	6.7 (5.1)	7.5 (6.3)	7.1 (6.2)
Positive anti-dsDNA	FARR, n (%)	66 (80.5)	56 (72.7)	63 (76.8)
	Multiplex, n (%)	27 (26.5)	24 (24.2)	28 (26.9)
Low C3	n (%)	43 (42.2)	28 (28.3)	48 (46.2)
Low C4	n (%)	25 (24.5)	21 (21.2)	28 (26.9)
IFN high (4-gene signature)	n (%)	76 (74.5)	75 (75.8)	78 (75.0)

CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index

Baseline concomitant therapies (mITT population)

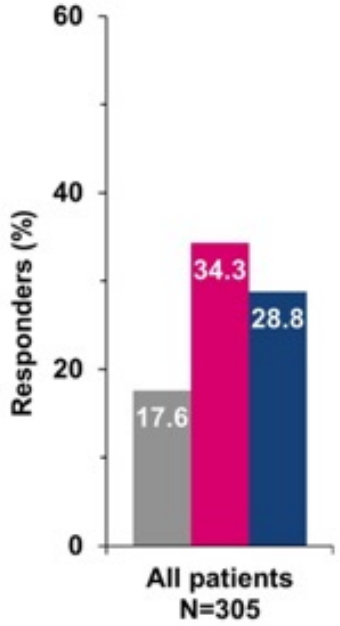
		Placebo (N=102)	Anifrolumab 300 mg (N=99)	Anifrolumab 1,000 mg (N=104)
OCS	n (%)	88 (86.3)	79 (79.8)	91 (87.5)
OCS dosage, n (%)	≥10 mg/day	64 (62.7)	55 (55.6)	63 (60.6)
	<10 mg/day	38 (37.3)	44 (44.4)	41 (39.4)
Anti-malarial	n (%)	75 (73.5)	76 (76.8)	68 (65.4)
Immunosuppressives				
Azathioprine	n (%)	19 (18.6)	23 (23.2)	21 (20.2)
Methotrexate	n (%)	16 (15.7)	19 (19.2)	25 (24.0)
Mycophenolate	n (%)	11 (10.8)	11 (11.1)	11 (10.6)

Patient disposition (mITT population)

	Placebo (N=102)	Anifrolumab 300 mg (N=99)	Anifrolumab 1,000 mg (N=104)
Completed treatment, n (%)	71 (69.6)	87 (87.9)	76 (73.1)
Reasons for not completing treatment			
Withdrawal of consent, n (%)	13 (12.7)	3 (3.0)	5 (4.8)
AE, n (%)	8 (7.8)	2 (2.0)	10 (9.6)
Death, n (%)	0 (0.0)	0 (0.0)	1 (1.0)
Lost to follow-up, n (%)	2 (2.0)	0 (0.0)	1 (1.0)
Other, n (%)	8 (7.8)	7 (7.1)	11 (10.6)

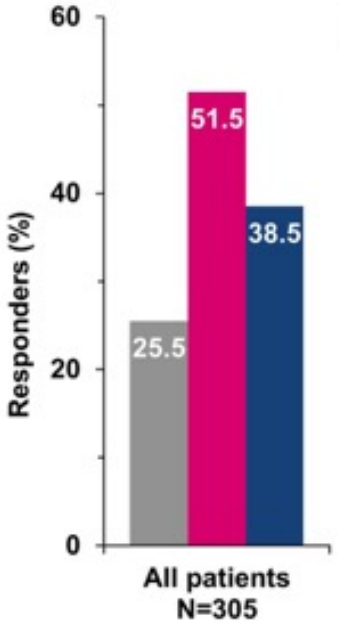
SRI(4) including OCS taper

Primary endpoint Day 169



	300 mg	1,000 mg
Delta:	16.7%	11.2%
OR:	2.38	1.94
90% CI:	(1.33, 4.26)	(1.08, 3.49)
P:	0.014	0.063

Secondary endpoint Day 365



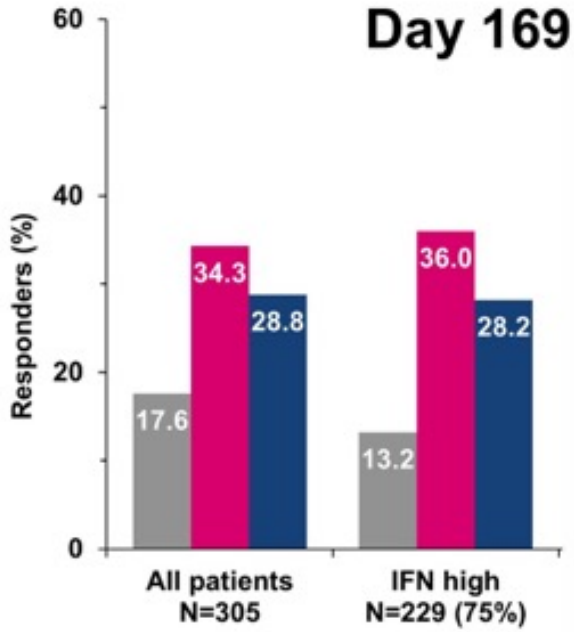
300 mg	1,000 mg
26.0%	13.0%
3.08	1.84
(1.86, 5.09)	(1.11, 3.04)
<0.001	0.048

Placebo Anifrolumab 300 mg Q4W Anifrolumab 1,000 mg Q4W

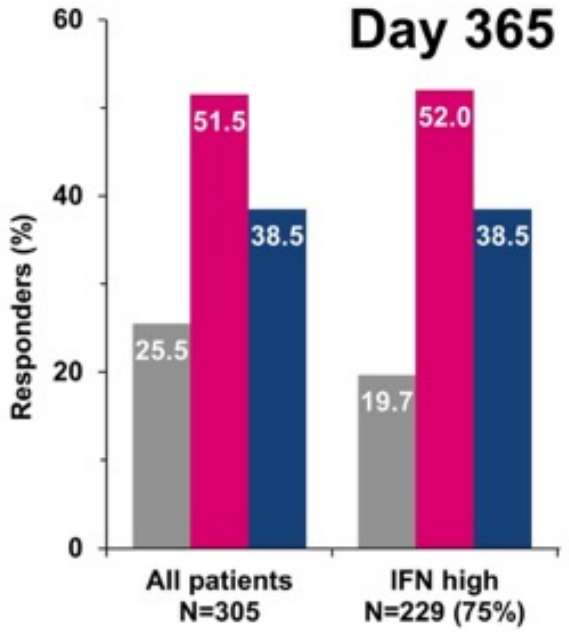
Dropouts and patients whose medication use exceeded protocol threshold were imputed as failures[10]

Delta=dosage vs. placebo

SRI(4) including OCS taper



	300 mg	1,000 mg	300 mg	1,000 mg
Delta:	16.7%	11.2%	22.8%	15.0%
OR:	2.38	1.94	3.55	2.65
90% CI:	(1.33, 4.26)	(1.08, 3.49)	(1.72, 7.32)	(1.27, 5.53)
P:	0.014	0.063	0.004	0.029



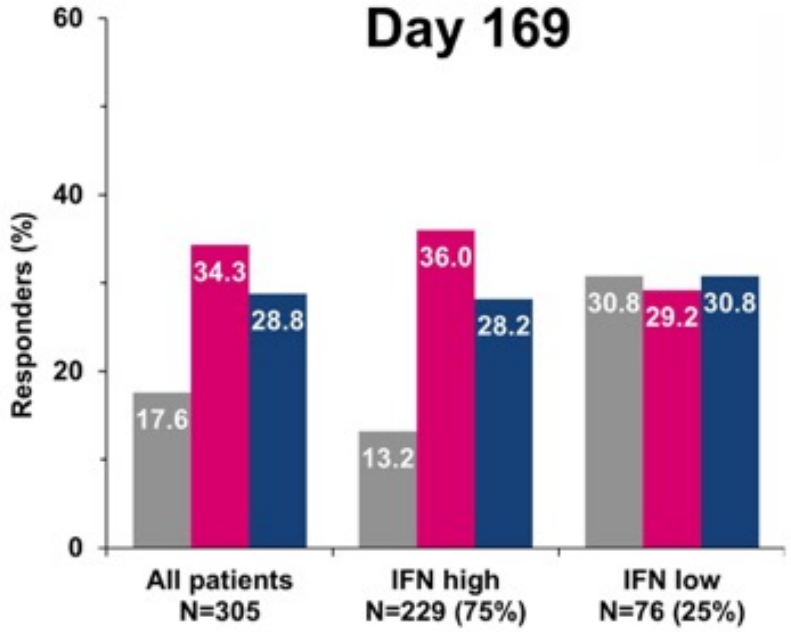
	300 mg	1,000 mg	300 mg	1,000 mg
	26.0%	13.0%	32.3%	18.8%
	3.08	1.84	4.30	2.52
	(1.86, 5.09)	(1.11, 3.04)	(2.34, 7.91)	(1.37, 4.64)
	<0.001	0.048	<0.001	0.013

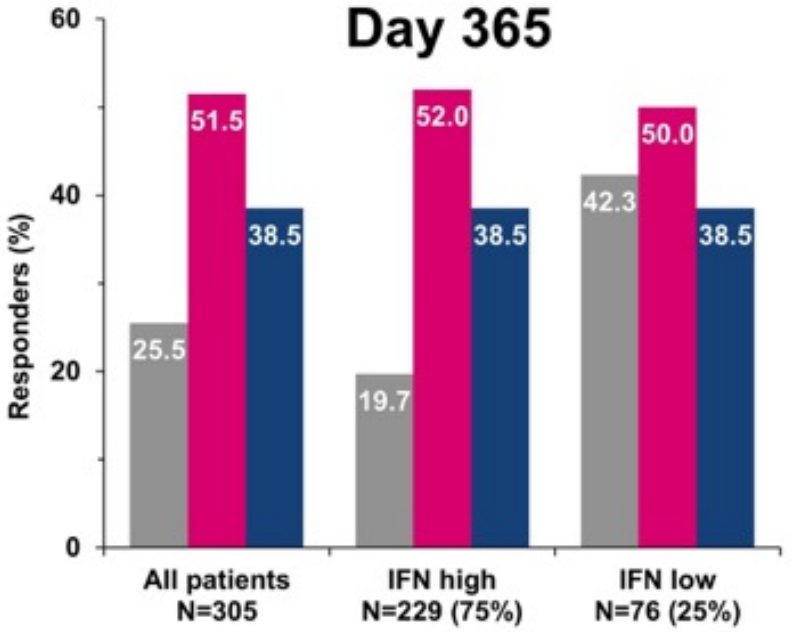
Placebo Anifrolumab 300 mg Q4W Anifrolumab 1,000 mg Q4W

Dropouts and patients whose medication use exceeded protocol threshold were imputed as failures

Delta=dosage vs. placebo

SRI(4) including OCS taper





	300 mg	1,000 mg	300 mg	1,000 mg	300 mg	1,000 mg
Delta:	16.7%	11.2%	22.8%	15.0%	-1.6%	0.0%
OR:	2.38	1.94	3.55	2.65	0.96	1.04
90% CI:	(1.33, 4.26)	(1.08, 3.49)	(1.72, 7.32)	(1.27, 5.53)	(0.34, 2.74)	(0.37, 2.88)
P:	0.014	0.063	0.004	0.029	0.946	0.953

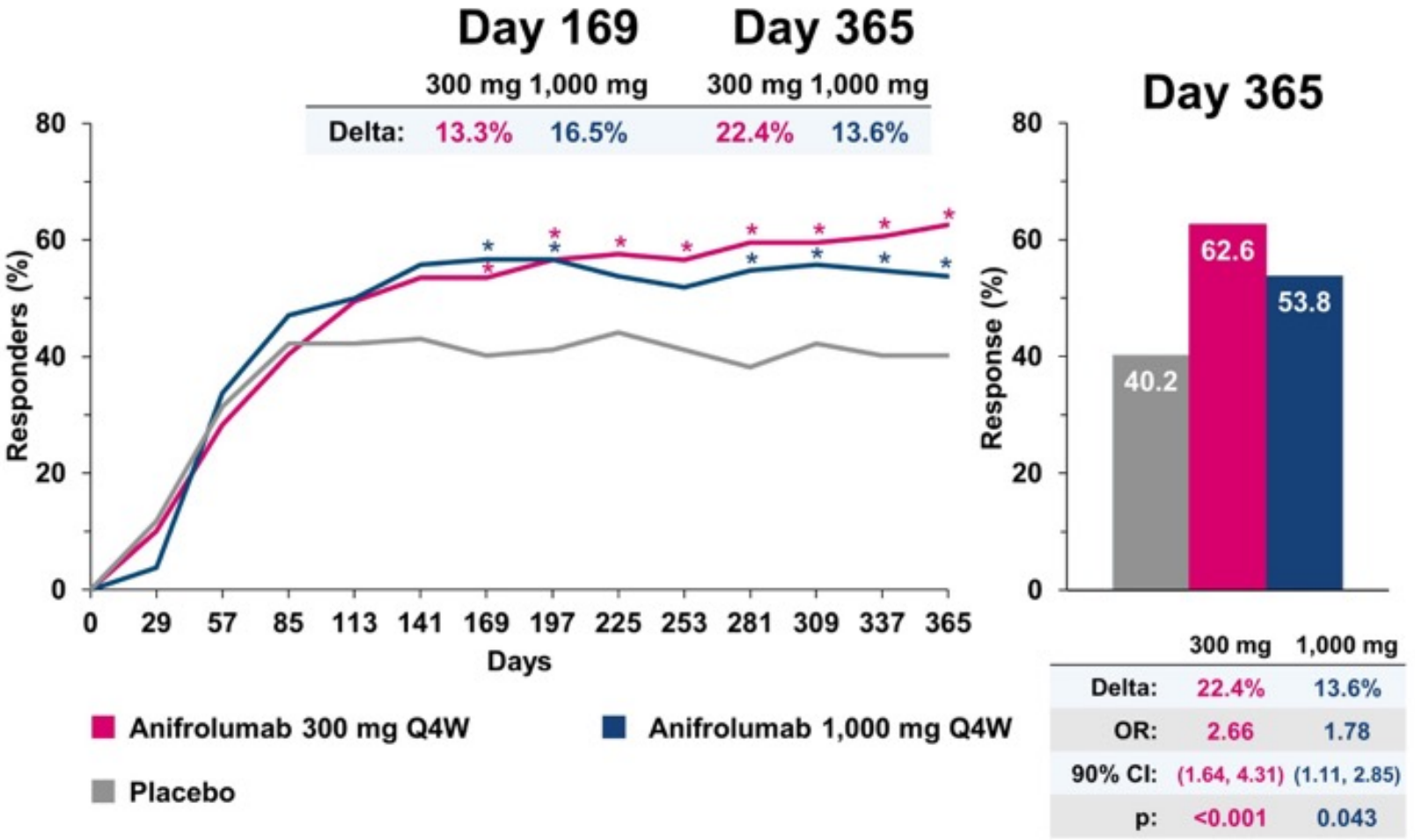
300 mg	1,000 mg	300 mg	1,000 mg	300 mg	1,000 mg
26.0%	13.0%	32.3%	18.8%	7.7%	-3.8%
3.08	1.84	4.30	2.52	1.47	0.89
(1.86, 5.09)	(1.11, 3.04)	(2.34, 7.91)	(1.37, 4.64)	(0.55, 3.93)	(0.34, 2.35)
<0.001	0.048	<0.001	0.013	0.514	0.849

Placebo Anifrolumab 300 mg Q4W Anifrolumab 1,000 mg Q4W

Dropouts and patients whose medication use exceeded protocol threshold were imputed as failures

Delta=dosage vs. placebo

SRI(4) excluding OCS taper



	300 mg	1,000 mg
Delta:	22.4%	13.6%
OR:	2.66	1.78
90% CI:	(1.64, 4.31)	(1.11, 2.85)
p:	<0.001	0.043

24

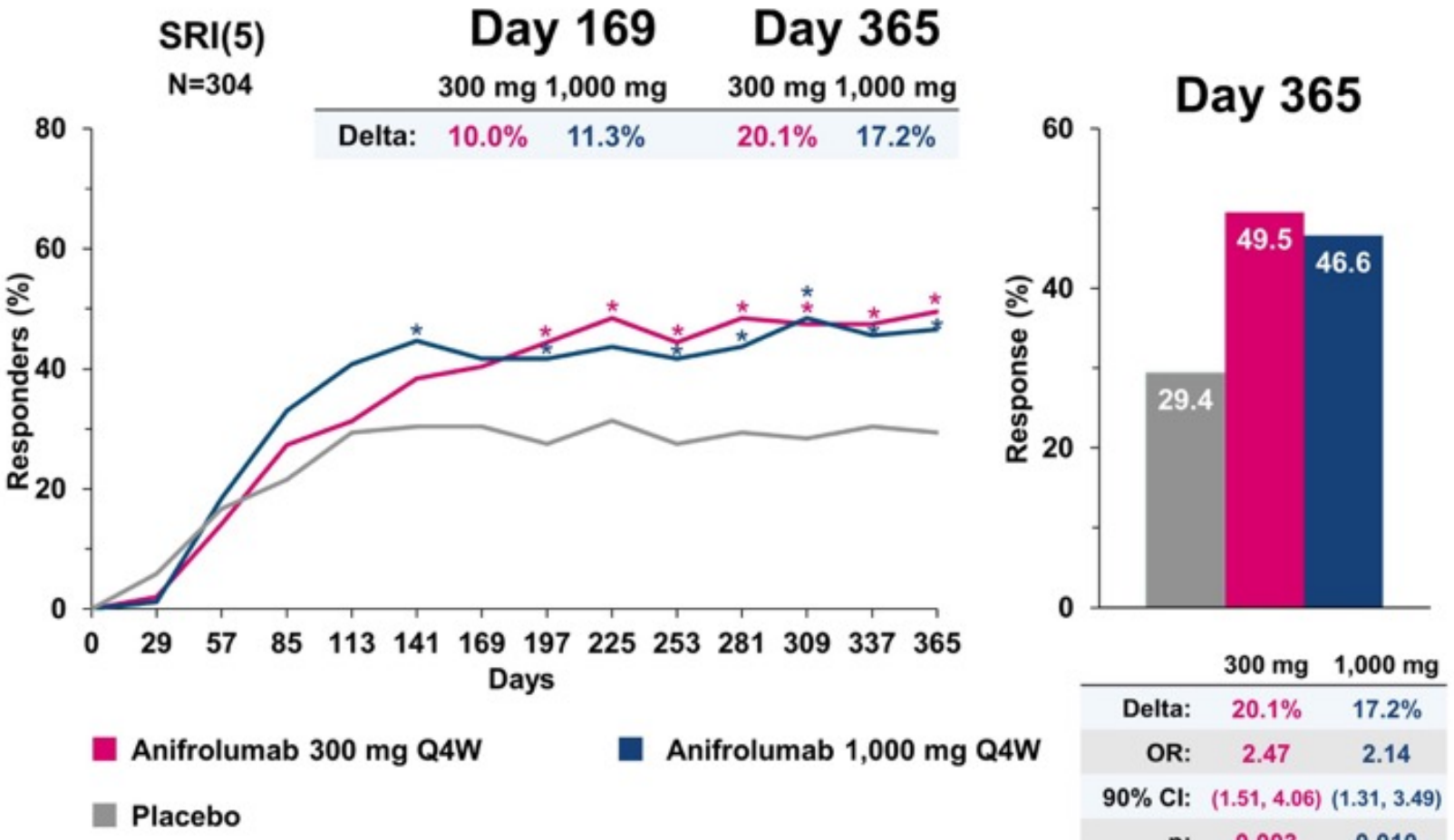
11

*p≤0.05 compared with placebo

Delta=dosage vs. placebo

mITT population

SRI(5) in patients with a baseline SLEDAI score of ≥5



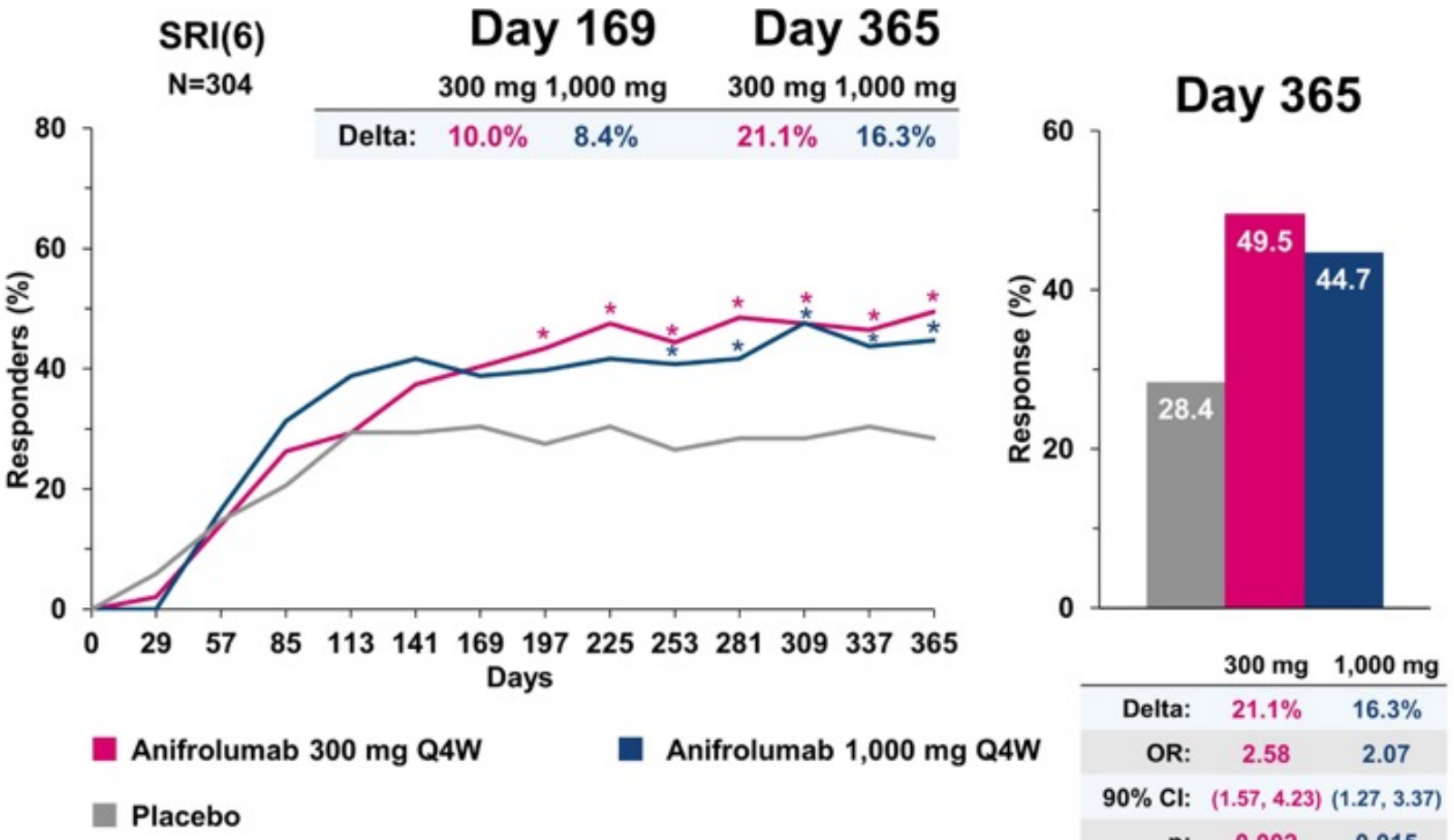
	300 mg	1,000 mg
Delta:	20.1%	17.2%
OR:	2.47	2.14
90% CI:	(1.51, 4.06)	(1.31, 3.49)
p:	0.003	0.010

25

*p≤0.05 compared with placebo

Delta=dosage vs. placebo

SRI(6) in patients with a baseline SLEDAI score of ≥6

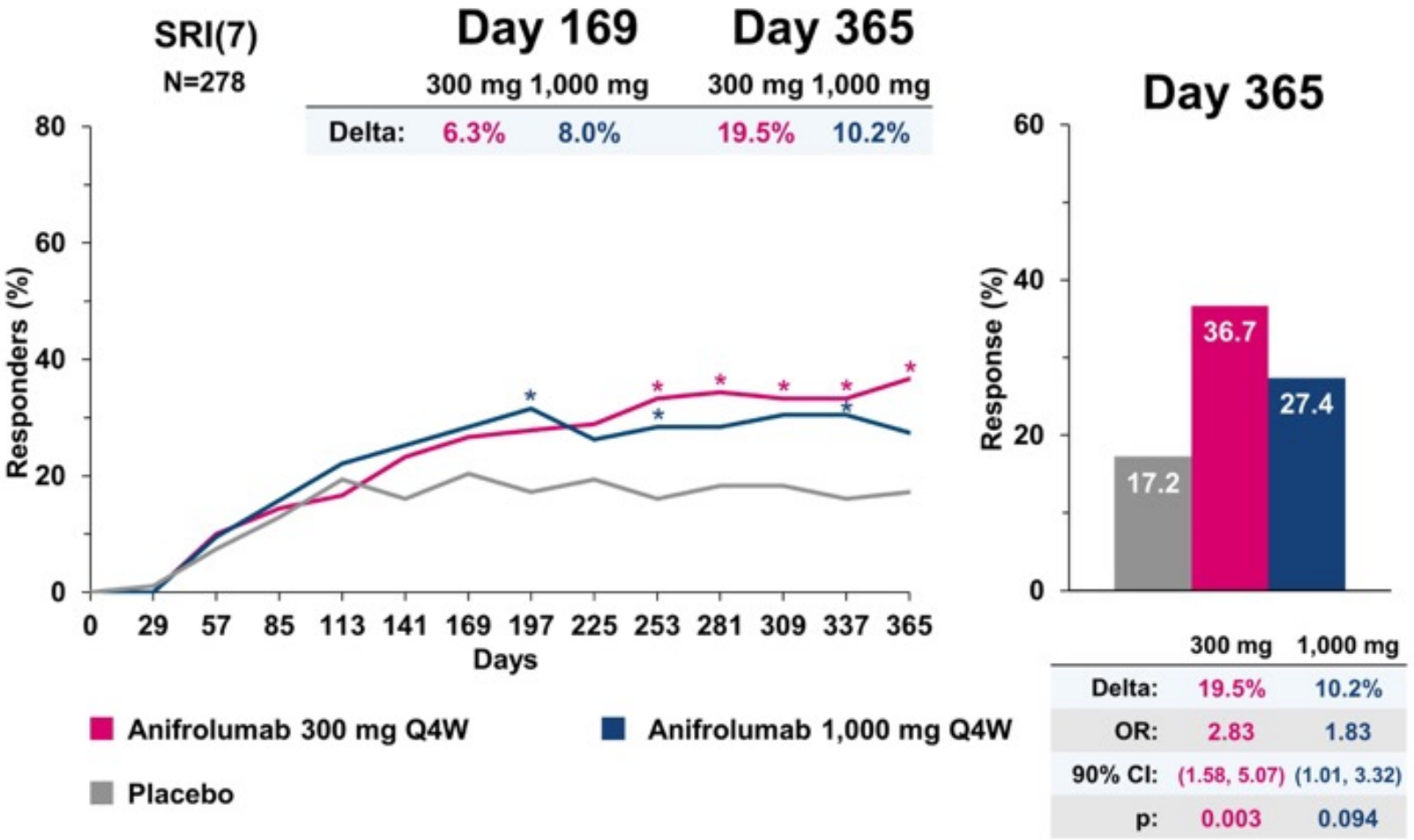


	300 mg	1,000 mg
Delta:	21.1%	16.3%
OR:	2.58	2.07
90% CI:	(1.57, 4.23)	(1.27, 3.37)
p:	0.002	0.015

*p≤0.05 compared with placebo

Delta=dosage vs. placebo

SRI(7) in patients with a baseline SLEDAI score of ≥7

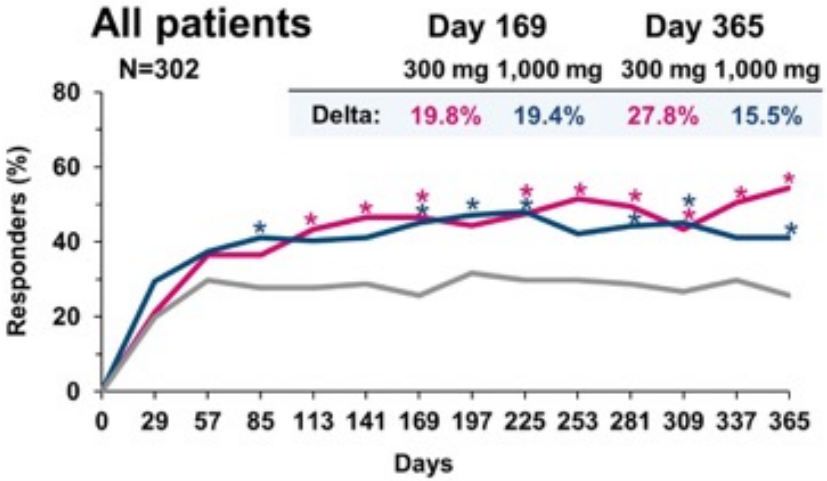


27

*p≤0.05 compared with placebo

Delta=dosage vs. placebo

BICLA response



Placebo

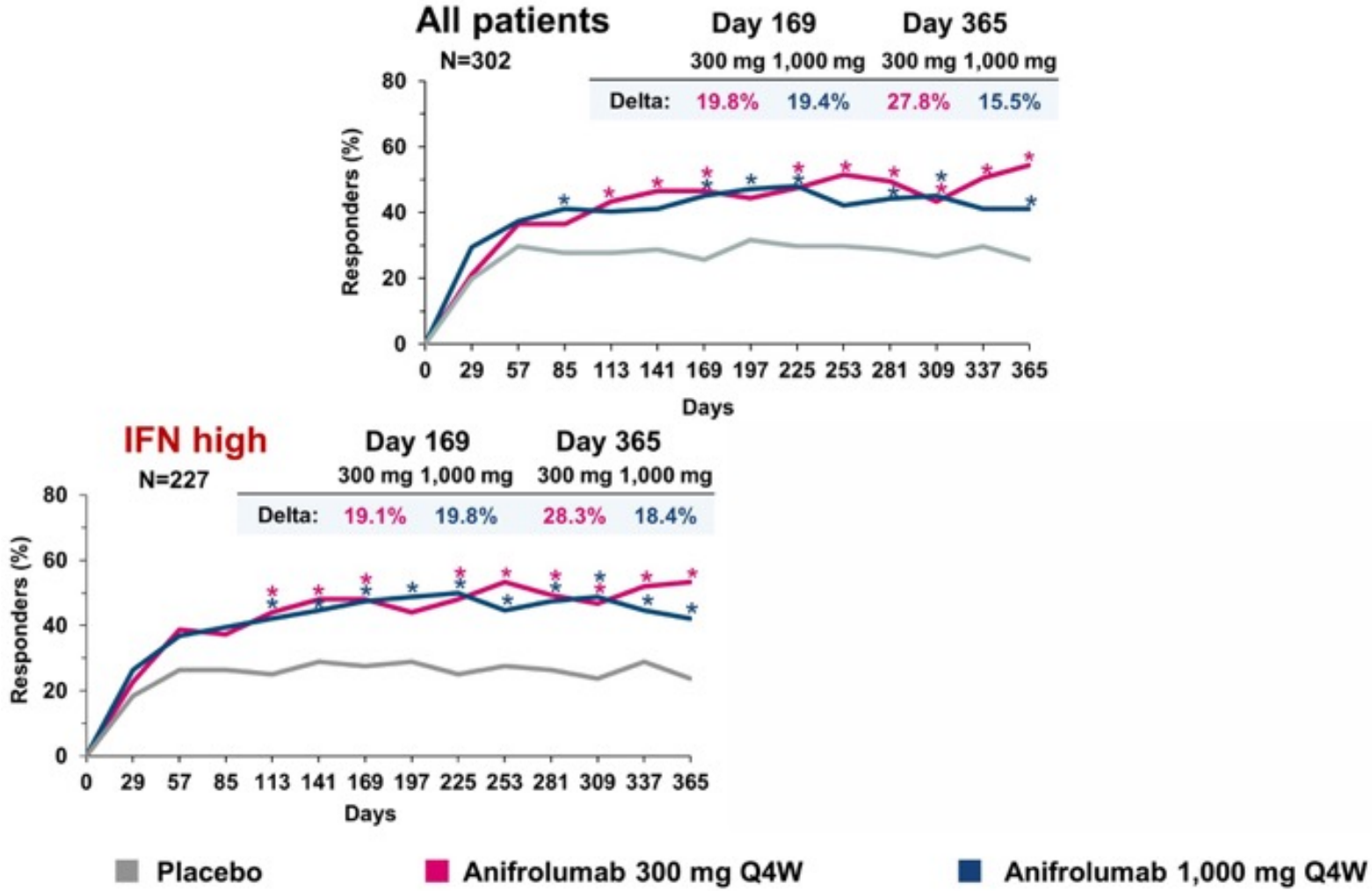
Anifrolumab 300 mg Q4W

Anifrolumab 1,000 mg Q4W

*p≤0.05 compared with placebo

Delta=dosage vs. placebo

BICLA response

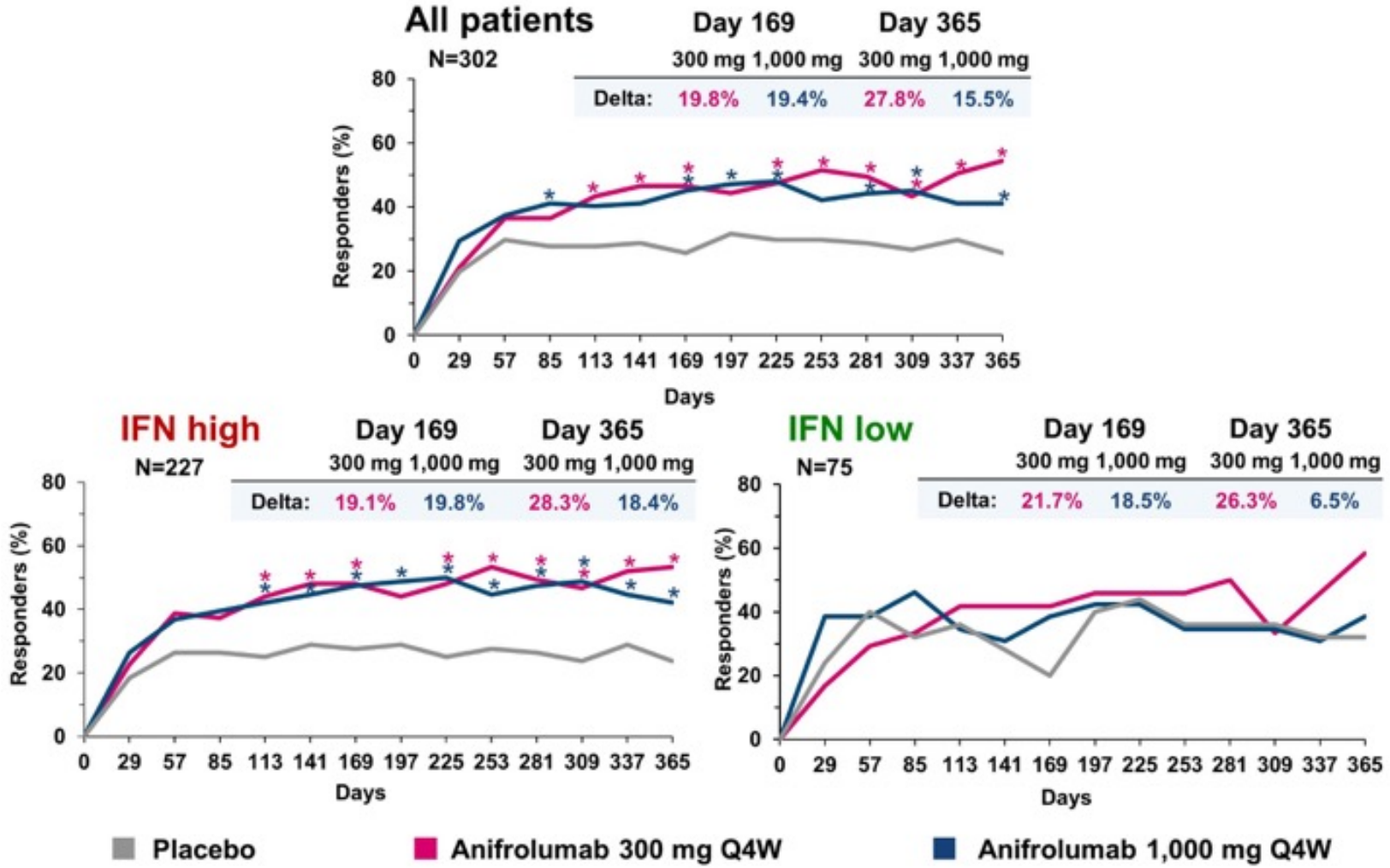


*p≤0.05 compared with placebo

15

Delta=dosage vs. placebo

BICLA response



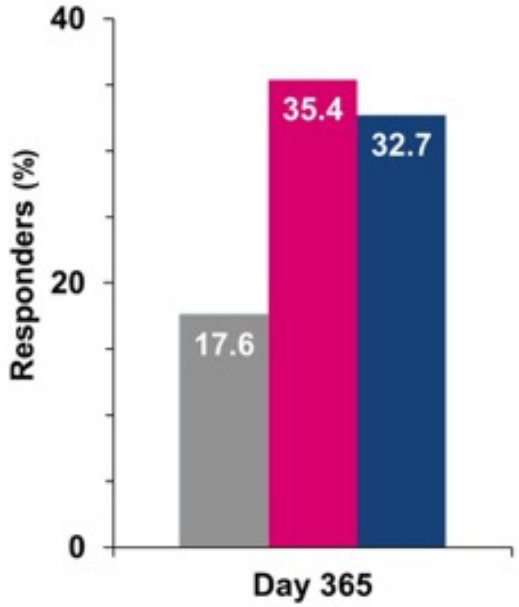
*p≤0.05 compared with placebo

15

Delta=dosage vs. placebo

Low disease activity at Day 365

Percentage of patients with SLEDAI 2K ≤2



	300 mg	1,000 mg
Delta:	17.8%	15.1%
OR:	2.68	2.35
90% CI:	(1.53, 4.70)	(1.34, 4.11)
p:	0.004	0.012

Placebo Anifrolumab 300 mg Q4W Anifrolumab 1,000 mg Q4W

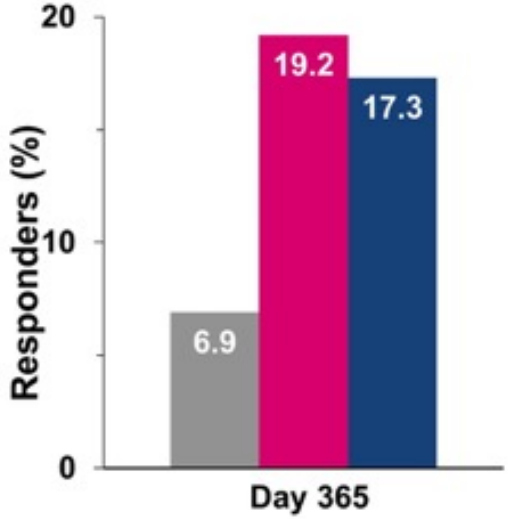
16

Delta=dosage vs. placebo mITT population

Major clinical response at Day 365

Major clinical response:

- BILAG 2004 Index C score or better at Day 169
- Maintenance of response through Day 365



	300 mg	1,000 mg
Delta:	12.3%	10.4%
OR:	3.24	2.88
90% CI:	(1.49, 7.04)	(1.32, 6.26)
p:	0.012	0.025

Placebo Anifrolumab 300 mg Q4W Anifrolumab 1,000 mg Q4W

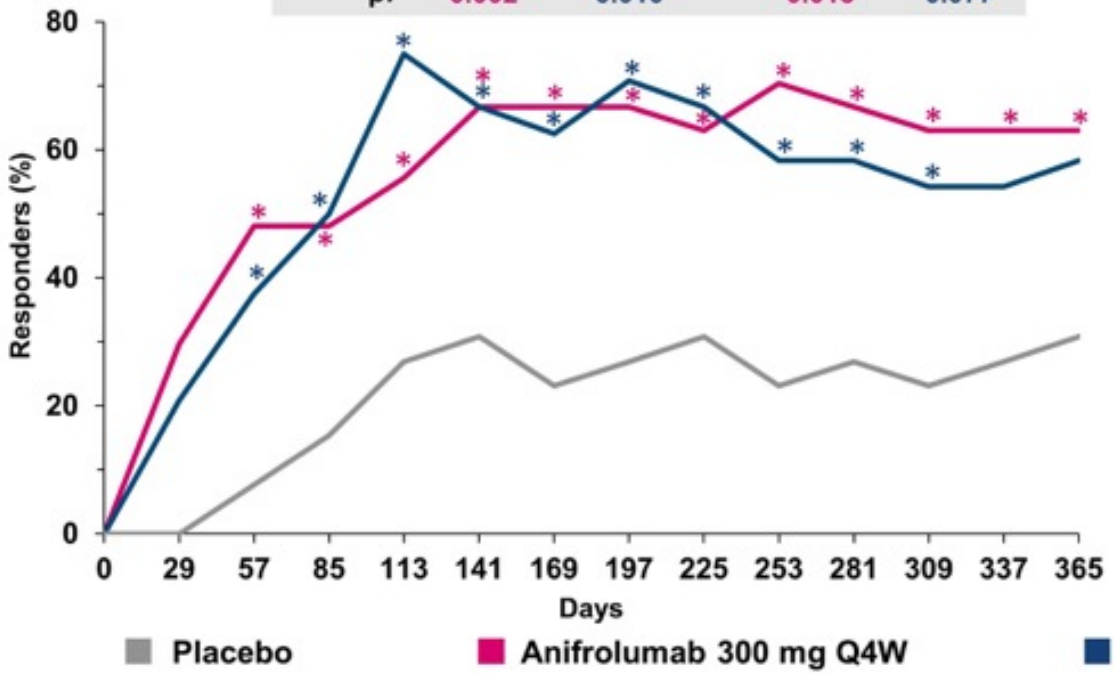
17

Delta=dosage vs. placebo mITT population

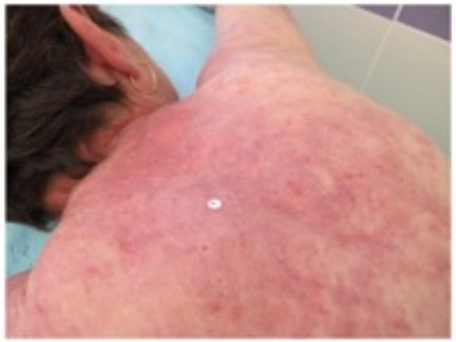
Reduction in CLASI activity

≥50% improvement in patients with CLASI activity score ≥10 at baseline (N=77)

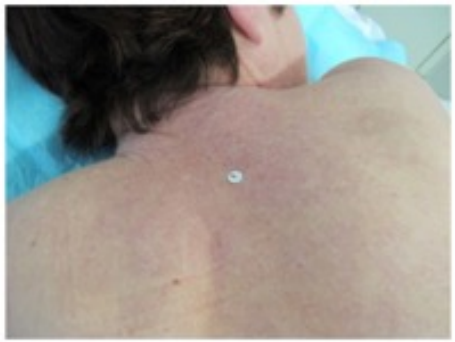
	Day 169		Day 365	
	300 mg	1,000 mg	300 mg	1,000 mg
Delta:	43.6%	39.4%	32.2%	27.5%
OR:	7.31	5.16	4.49	2.97
90% CI:	(2.56, 20.86)	(1.81, 14.73)	(1.67, 12.12)	(1.08, 8.19)
p:	0.002	0.010	0.013	0.077



Day 1



Day 281



Patient was receiving anifrolumab 300 mg Q4W

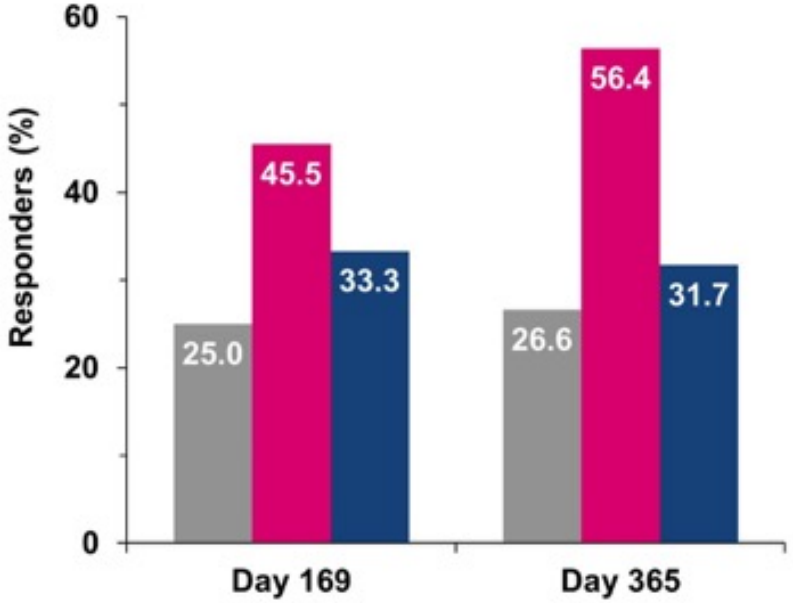
*p≤0.05 compared with placebo

18

Delta=dosage vs. placebo

Corticosteroid reduction

OCS ≤7.5 mg/day in patients with ≥10 mg/day at baseline (N=182)



	Day 169		Day 365	
	300 mg	1,000 mg	300 mg	1,000 mg
Delta:	20.5%	8.3%	29.8%	5.1%
OR:	2.48	1.44	3.59	1.23
90% CI:	(1.28, 4.80)	(0.75, 2.78)	(1.87, 6.89)	(0.64, 2.37)
p:	0.023	0.358	0.001	0.595

Placebo Anifrolumab 300 mg Q4W Anifrolumab 1,000 mg Q4W

19

Delta=dosage vs. placebo

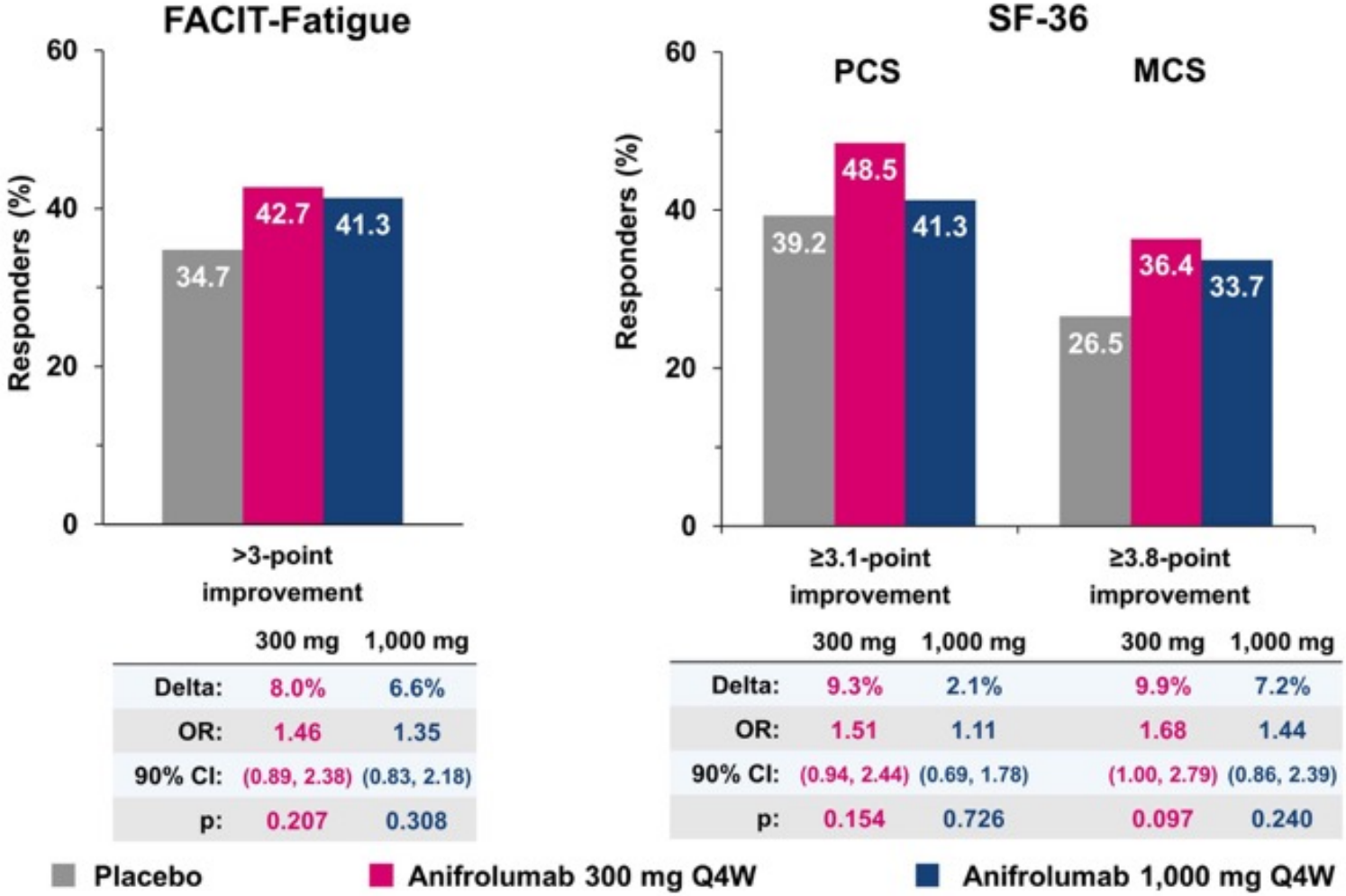
BILAG 1A/2B flares

	Placebo (N=102)	Anifrolumab 300 mg (N=99)	Anifrolumab 1,000 mg (N=104)
Patients with flares, n (%)	17 (16.7)	12 (12.1)	12 (11.5)
Total number of flares	53	25	36
Total duration of follow-up, years	85.1	93.8	92.2

20

mITT population

FACIT-Fatigue and SF-36 at Day 365



	300 mg	1,000 mg
Delta:	8.0%	6.6%
OR:	1.46	1.35
90% CI:	(0.89, 2.38)	(0.83, 2.18)
p:	0.207	0.308

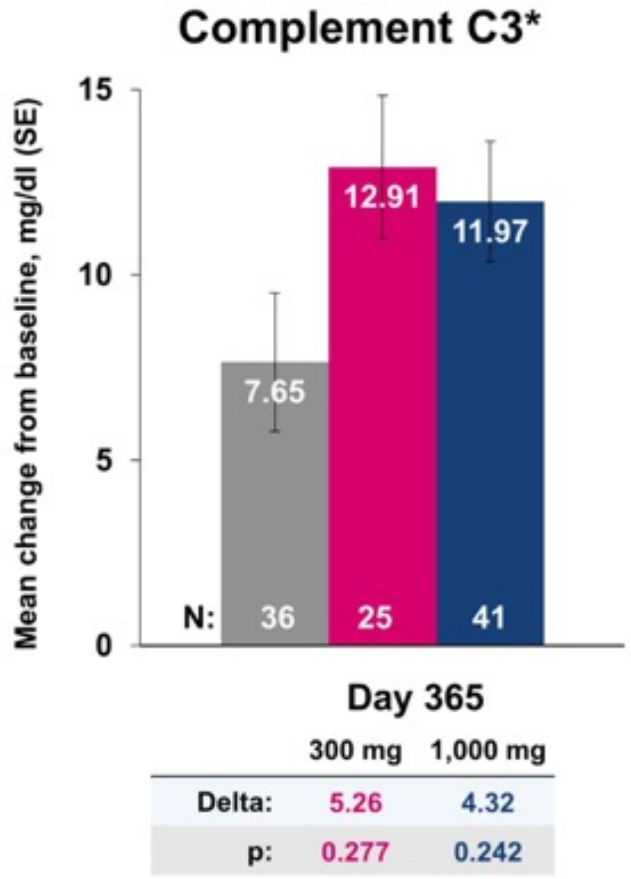
	300 mg	1,000 mg	300 mg	1,000 mg
Delta:	9.3%	2.1%	9.9%	7.2%
OR:	1.51	1.11	1.68	1.44
90% CI:	(0.94, 2.44)	(0.69, 1.78)	(1.00, 2.79)	(0.86, 2.39)
p:	0.154	0.726	0.097	0.240

Placebo Anifrolumab 300 mg Q4W Anifrolumab 1,000 mg Q4W

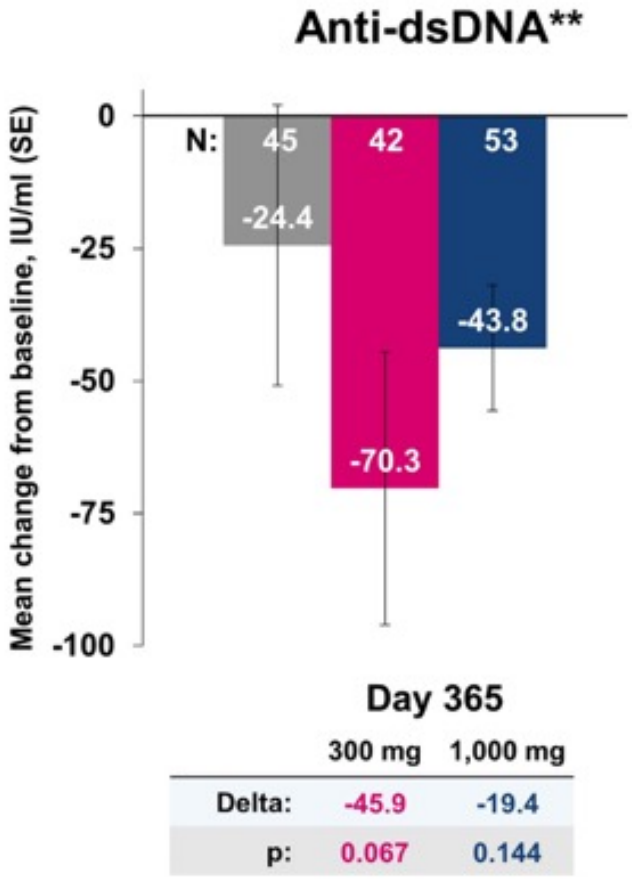
FACIT, Functional Assessment of Chronic Illness Therapy; MCS, Mental Component Summary; PCS, Physical Component Summary; SF-36, Short Form 36 Health Survey

Delta=dosage vs. placebo mITT population

Changes in C3 and anti-dsDNA at Day 365



	300 mg	1,000 mg
Delta:	5.26	4.32
p:	0.277	0.242



	300 mg	1,000 mg
Delta:	-45.9	-19.4
p:	0.067	0.144

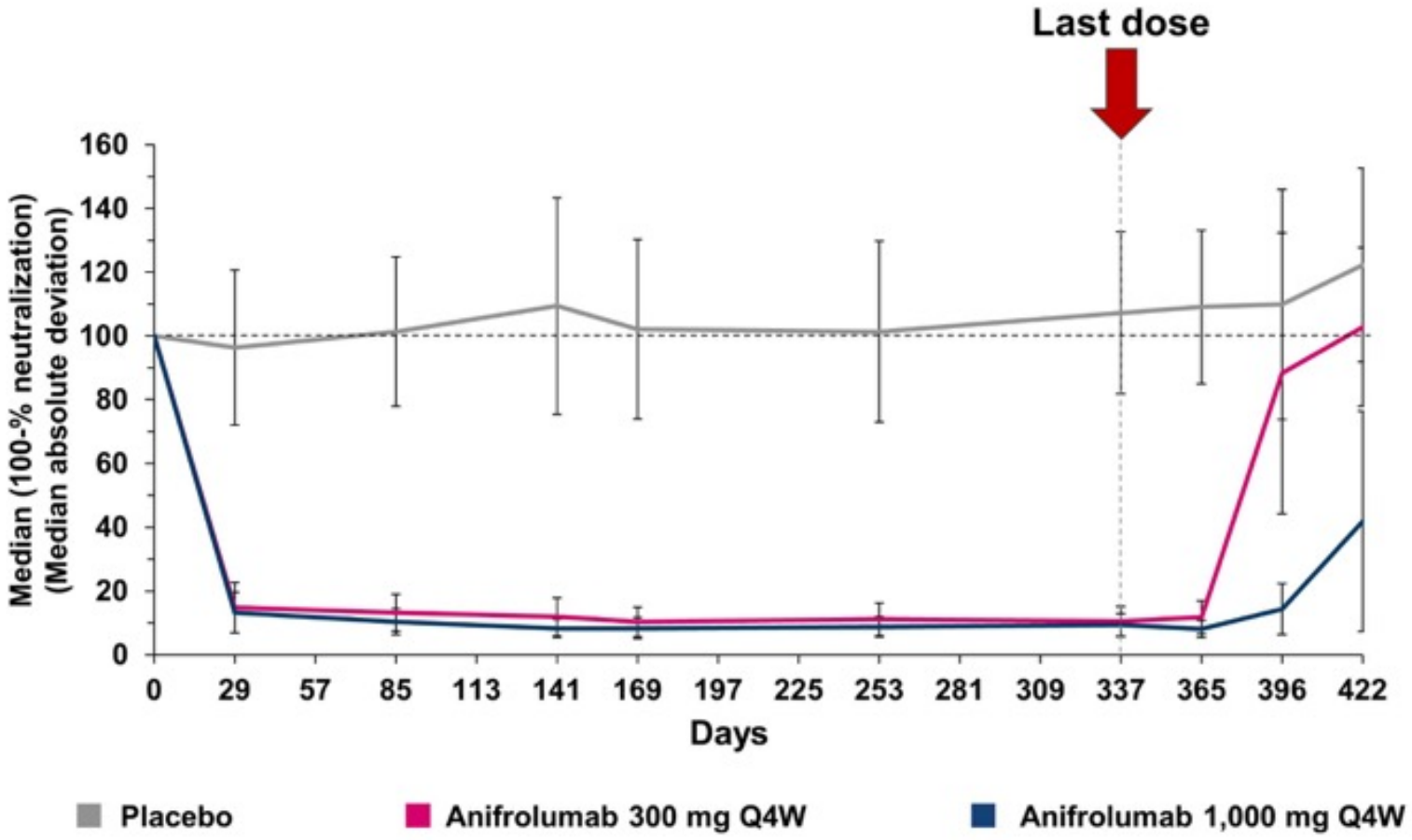
Anifrolumab 300 mg Q4W Anifrolumab 1,000 mg Q4W
Placebo

SE, standard error

*mITT population with low complement level at baseline
**mITT population with detectable anti-dsDNA at baseline

Delta=dosage vs. placebo

Neutralization of 21-gene type I IFN signature*



*Based on patients with positive gene signature at baseline.
Positive is defined as baseline 21-gene signature ≥2

Adverse events: safety population

AE, n (%)	Placebo (N=101)	Anifrolumab 300 mg (N=99)	Anifrolumab 1,000 mg (N=105)	Anifrolumab Total (N=204)
At least 1 event	78 (77.2)	84 (84.8)	90 (85.7)	174 (85.3)
At least 1 event of special interest	12 (11.9)	10 (10.1)	15 (14.3)	25 (12.3)
At least 1 serious event	19 (18.8)	16 (16.2)	18 (17.1)	34 (16.7)
At least 1 treatment-related serious event	6 (5.9)	3 (3.0)	1 (1.0)	4 (2.0)
At least 1 event leading to discontinuation of study drug	8 (7.9)	3 (3.0)	10 (9.5)	13 (6.4)
Death	0 (0.0)	0 (0.0)	1 (1.0)	1 (0.5)

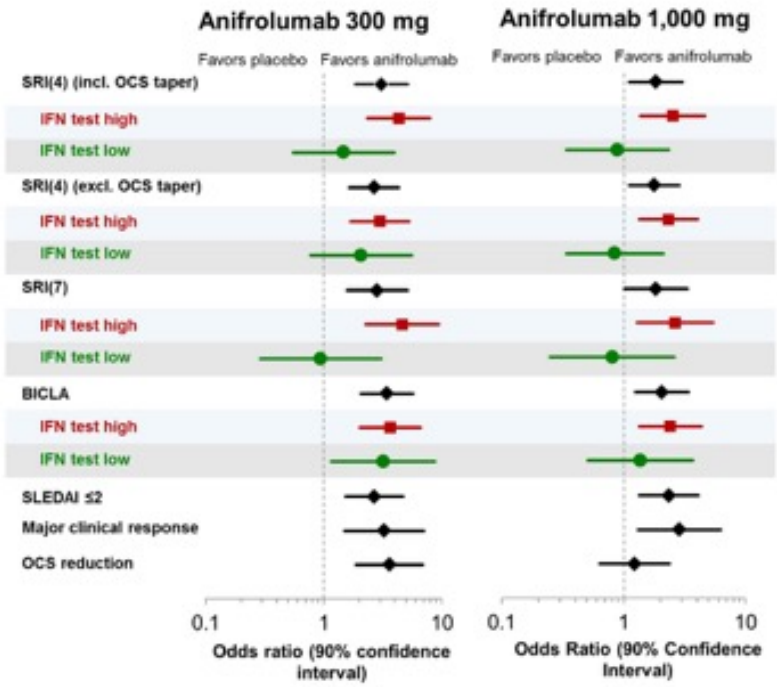
Adverse events of special interest: safety population

Preferred Term, n (%)	Placebo (N=101)	Anifrolumab 300 mg (N=99)	Anifrolumab 1,000 mg (N=105)	Anifrolumab Total (N=204)
Herpes zoster	2 (2.0)	5 (5.1)[a]	10 (9.5)	15 (7.4)
Influenza	2 (2.0)	6 (6.1)	8 (7.6)	14 (6.9)
Varicella	0 (0.0)	1 (1.0)	0 (0.0)	1 (0.5)
Latent tuberculosis	1 (1.0)	1 (1.0)	1 (1.0)	2 (1.0)
Mycobacterium tuberculosis complex test positive	0 (0.0)	1 (1.0)	0 (0.0)	1 (0.5)
Invasive ductal breast carcinoma	0 (0.0)	1 (1.0)	0 (0.0)	1 (0.5)
Lung neoplasm (malignant)	0 (0.0)	0 (0.0)	1 (1.0)	1 (0.5)
Infusion-related reaction	6 (5.9)	2 (2.0)	4 (3.8)	6 (2.9)
Hypersensitivity vasculitis	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
Vasculitis	2 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)

[a]One patient also had transverse myelitis with a qualitatively positive varicella-zoster virus PCR in the CSF

Conclusions

- Substantial benefit was achieved across multiple global and organ-specific disease activity measures
- The greater efficacy seen in patients with a high IFN gene signature supports the pathobiology of this treatment strategy
- Safety and tolerability were acceptable
- Phase III study underway with 300 mg as maximum dosage



Targeting the IFNAR is a promising therapeutic approach for patients with SLE who do not respond to currently available therapies

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Anifrolumab current & future plans

AstraZeneca
What science can do

David J. Chang, MD
VP and Head, Inflammation, Autoimmunity & Neuroscience, Global Medicines Development

Potential differentiators of anifrolumab in SLE

First-in-class mechanism of action

- Most advanced molecule targeting IFNAR[1]
- Blocks all Type 1 interferons (not just IFN-α)

Potential best-in-disease efficacy

- **26.0%** treatment difference vs. placebo on SRI(4) response at day 365 with a sustained reduction of OCS
- **29.8%** treatment difference vs. placebo on reduction of OCS dosage at day 365 to <= 7.5 mg/day[2]

Personalised healthcare approach

- Complementary IFN test

1. Type 1 Interferon receptor
2. In patients receiving >=10 mg/day of OCS at baseline

TULIP (Treatment of Uncontrolled Lupus via the Interferon Pathway)
Trial objectives

Primary objective	• Evaluate the effect of anifrolumab compared to placebo on disease activity as measured by **SLE Responder Index of ≥4 [SRI(4)] at week 52**
Key secondary objectives	**Evaluate the effect of anifrolumab compared to placebo on:** • SRI(4) at week 52 in the IFN test-high sub-group • % subjects achieving OCS dose ≤7.5 mg/day at week 40 - 52 • ≥50% reduction in CLASI[1] activity score at week 12 • SRI(4) at week 24 • Annualised flare rate through 52 weeks

1. CLASI = Cutaneous Lupus Erythematosus Disease Area and Severity Index

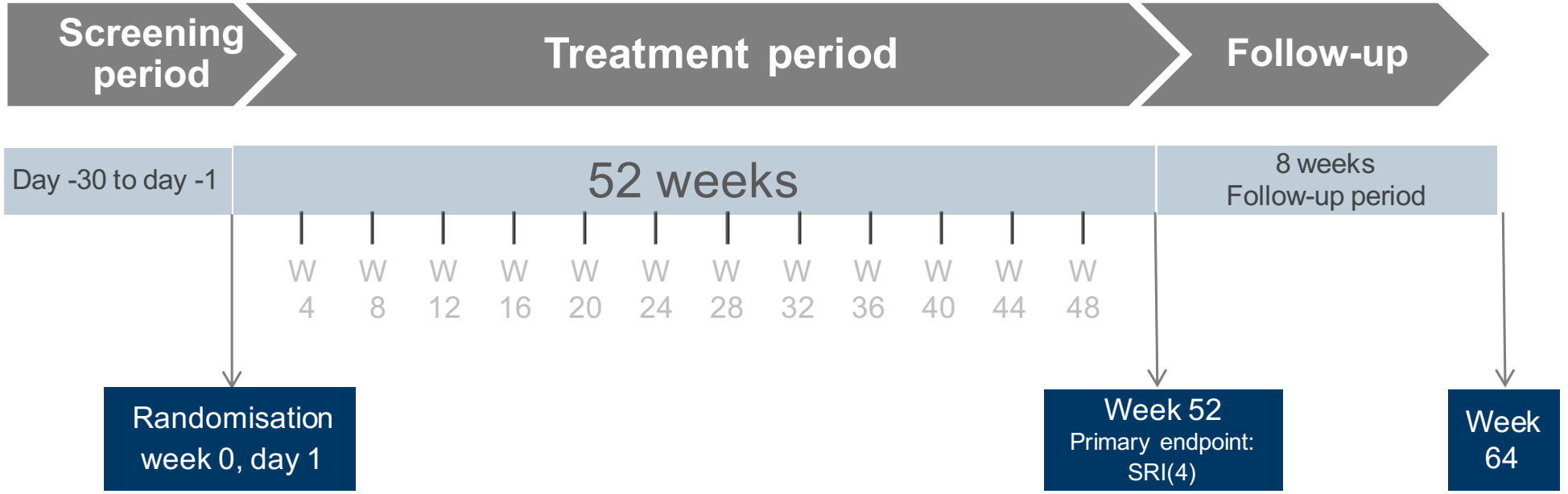
Trial design

Design	Phase III multi-center, randomised, double-blind, placebo controlled trial	
Protocol number	D3461C00005 **TULIP SLE 1**	D3461C00004 **TULIP SLE 2**
Sample size	~170 sites 450 patients	~140 sites 360 patients
Trial population	Adults with active moderate-to-severe SLE, ANA[1] (+) and/or elevated anti-dsDNA[2] or anti-Smith antibodies and receiving standard of care	

Dosing (IV, Q4W)	• 1:2:2 randomisation ratio
	  • anifrolumab 150mg
	  • anifrolumab 300mg
	  • placebo
		• 1:1 randomisation ratio
		  • anifrolumab 300mg
		  • placebo

1: ANA = Anti-Nuclear Antibody
2: anti-double-stranded DNA

Trial schema



Patients completing the trial are eligible for long-term extension trial

Anifrolumab development status

Phase III SLE programme initiated

- Final data available: 2018
- Regulatory submission: 2019

Life-cycle management programme

- Phase II **lupus nephritis** trial expected to start before year-end
- Phase I **subcutaneous administration** trial also expected to start before year-end

Questions & Answers

Participants

- Richard Alan Furie, MD, Chief, Division of Rheumatology, North Shore-LIJ Health System
- Bing Yao, Head of Respiratory, Inflammation & Autoimmunity iMED, MedImmune
- David J. Chang, MD, VP and Head, Inflammation, Autoimmunity & Neuroscience, Global Medicines Development

Please press *1 on your phone to indicate that you wish to ask a question

Confidentiality Notice