ΠΑΝΕΠΙΣΤΗΜΙΟ ΠΑΤΡΩΝ
UNIVERSITY OF PATRAS

BELIMUMAB
Σε ποιόν, πότε & γιατί

ΣΤΑΜΑΤΗΣ-ΝΙΚΟΣ ΛΙΟΣΗΣ

Αναπλ. Καθηγητής
Δ/ντής, Ρευματολογικό Τμήμα
Ιατρική Σχολή Παν/μίου Πατρών & ΠΓΝΠ

Σύγκρουση συμφερόντων

- GSK
- MSD
- BMS
- NOVARTIS
- ROCHE
- JANSSEN
- ABBOTT
- PFIZER
- UCB
- ACTELION
- ΕΝΟΡΑΣΙΣ Α.Ε.

BLyS: Member of the Tumor Necrosis Factor Family and B Lymphocyte Stimulator

Paul A. Moore, Ornella Belvedere, Amy Orr, Krystyna Pieri, David W. LaFleur, Ping Feng, Daniel Soppet, Meghan Charters, Reiner Gentz, David Parmelee, Yuling Li, Olga Galperina, Judith Giri, Viktor Roschke, Bernardetta Nardelli, Jeffrey Carrell, Svetlana Sosnovtseva, Wilbert Greenfield, Steven M. Ruben, Henrik S. Olsen, James Fikes, David M. Hilbert*

9 JULY 1999 VOL 285 SCIENCE www.sciencemag.org

Ονοματολογία

- **BLyS: B Lymphocyte Stimulator** **(1999)**
- **BAFF: B cell Activating Factor belonging to the TNF-Family**
- **TALL-1**
- **zTNF4**
- **THANK**
- **TNFSF13b**

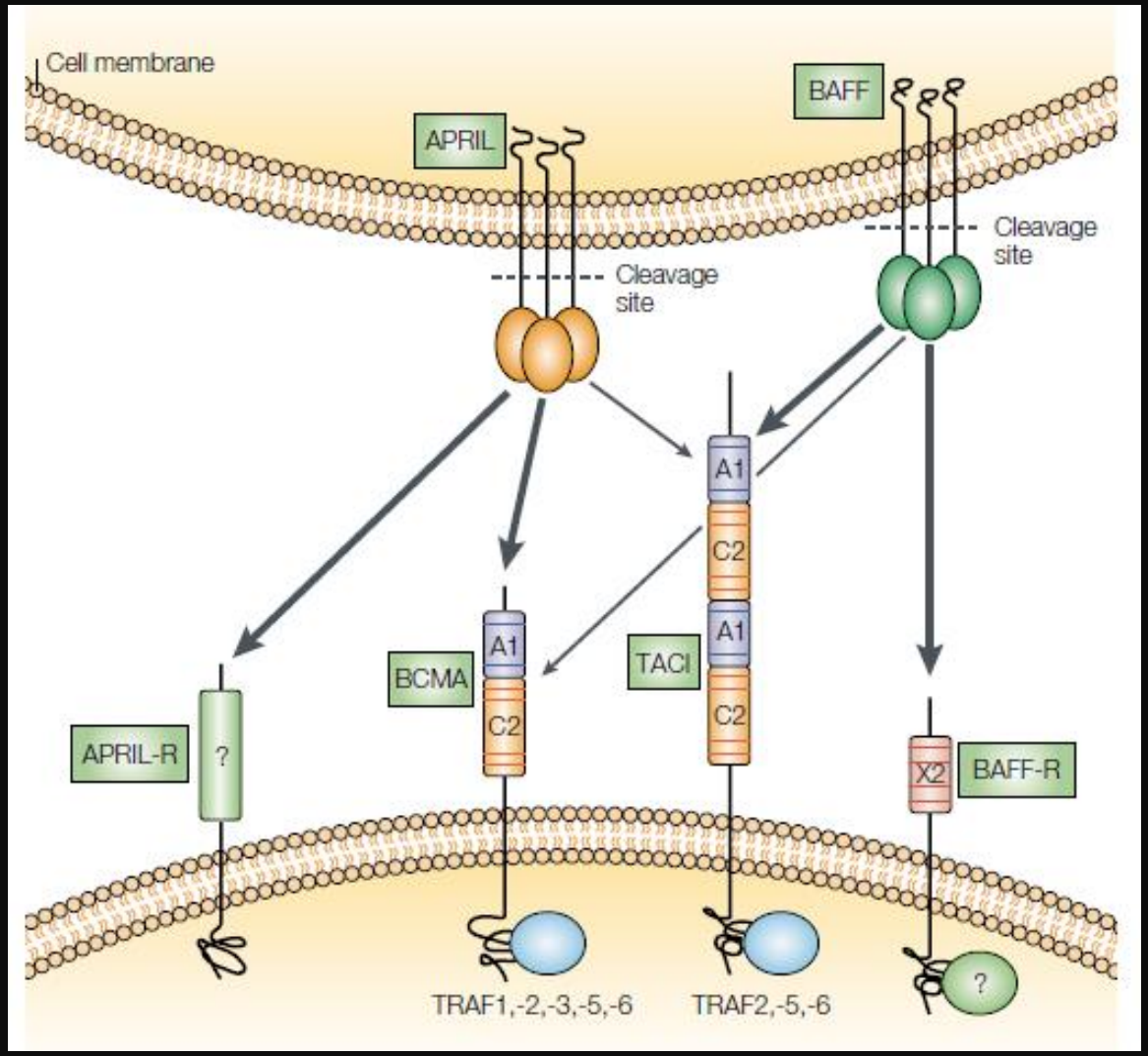
BLyS: Πού παράγεται ?

- Το mRNA του BLyS βρίσκεται σε μονοκύτταρα, μακροφάγα, δενδριτικά κύτταρα (↑↑↑IFN-γ).
- Στα ουδετερόφιλα (↑↑ G-CSF και ↑↑IFN-γ).
- Ελάχιστο BLyS mRNA βρίσκεται στα Τ κύτταρα και **ΚΑΘΟΛΟΥ** στα Β κύτταρα.
- Τα δενδριτικά και τα ουδετερόφιλα παράγουν περισσότερο **διαλυτό BLyS**.
- Το BLyS παράγεται μετά απο ενεργοποίηση της εναλλακτικής οδού του NF-κB.

Φυσιολογικός ρόλος του BLyS

- Τα BAFF -/- ποντίκια **ΔΕΝ έχουν ΚΑΘΟΛΟΥ** ώριμα Β λεμφοκύτταρα (!!!)
- Δεν έχουν **ΚΑΘΟΛΟΥ ΜΖ** Β λεμφοκύτταρα.
- Δεν έχουν **ΚΑΘΟΛΟΥ χυμική ανοσία**.
- **Εχουν** ανώριμα Β λεμφοκύτταρα

Οι 3 υποδοχείς του BLyS
(… και του APRIL)



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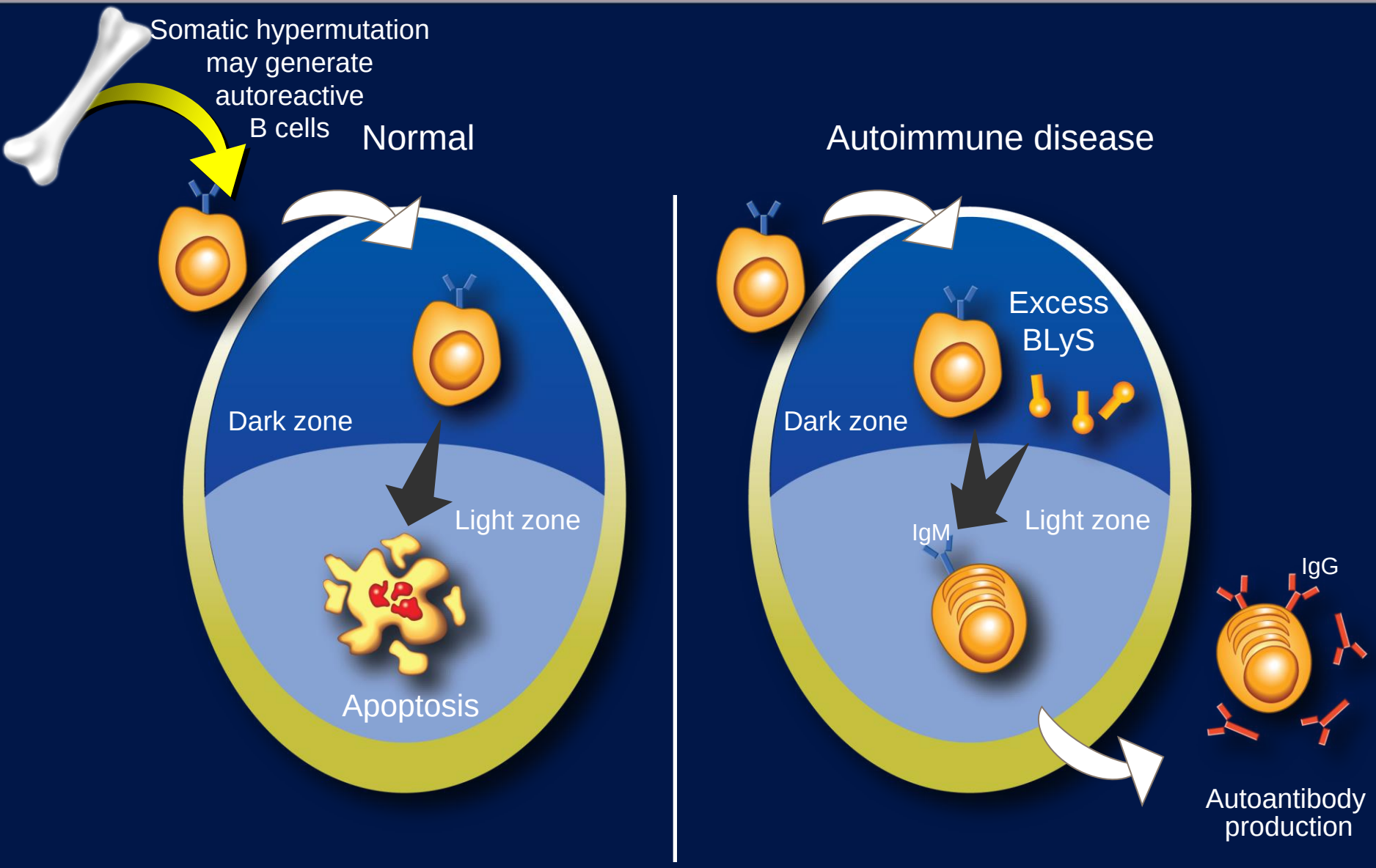
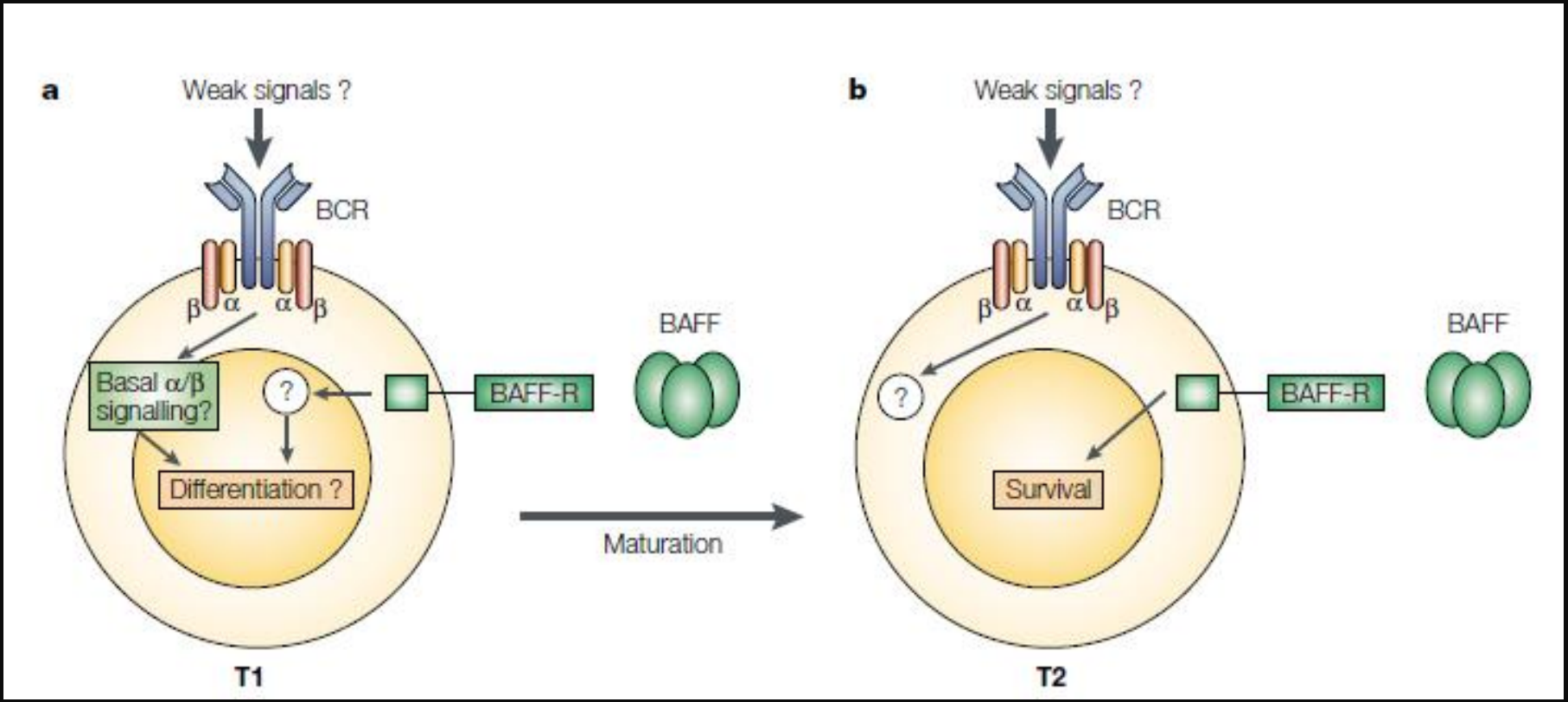
BLyS is a critical survival factor for transitional and mature B cells



BLyS: Ο ρόλος του στην ωρίμανση του Β λεμφοκυττάρου



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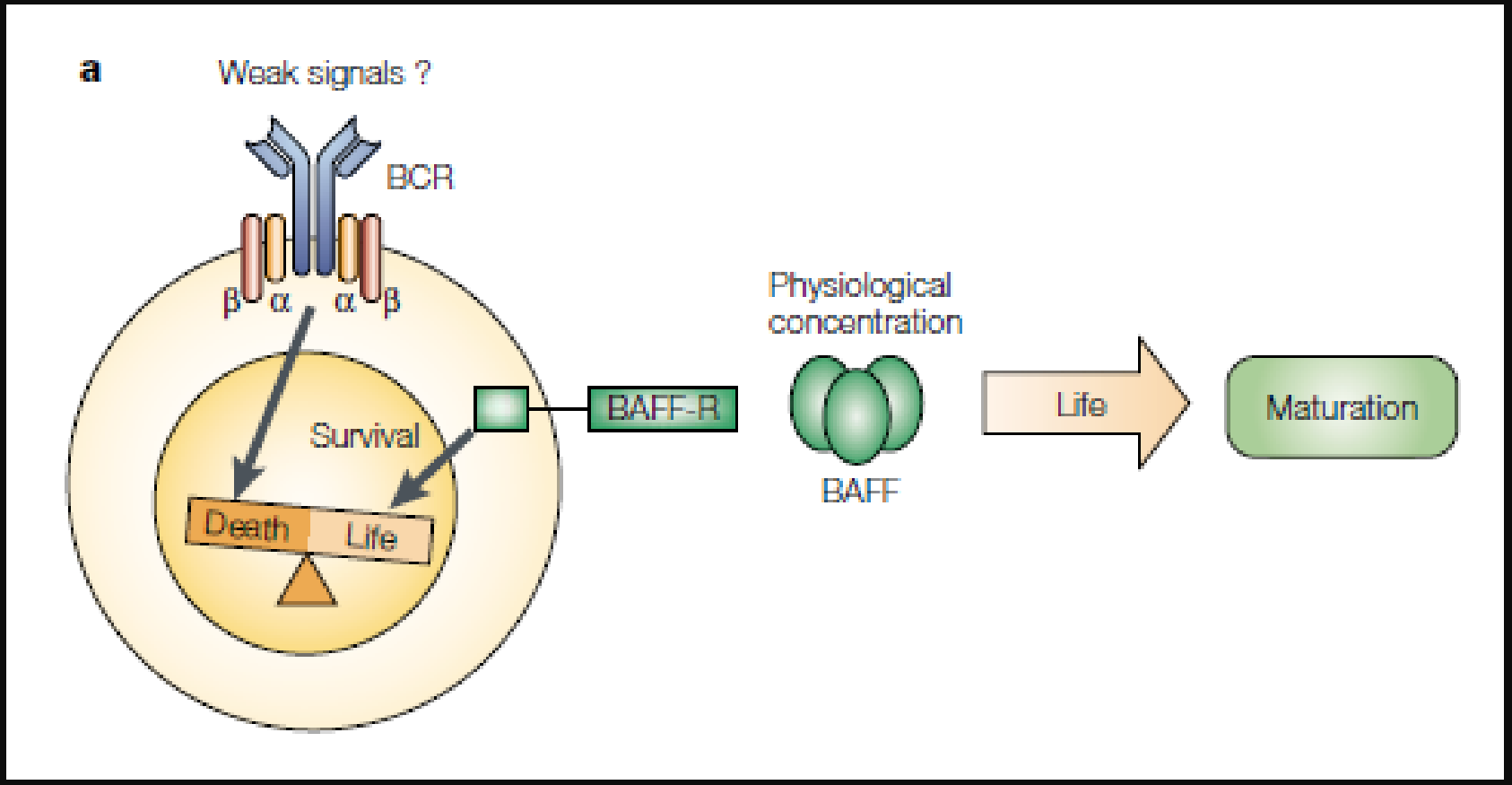
BLyS: Θετική επιλογή



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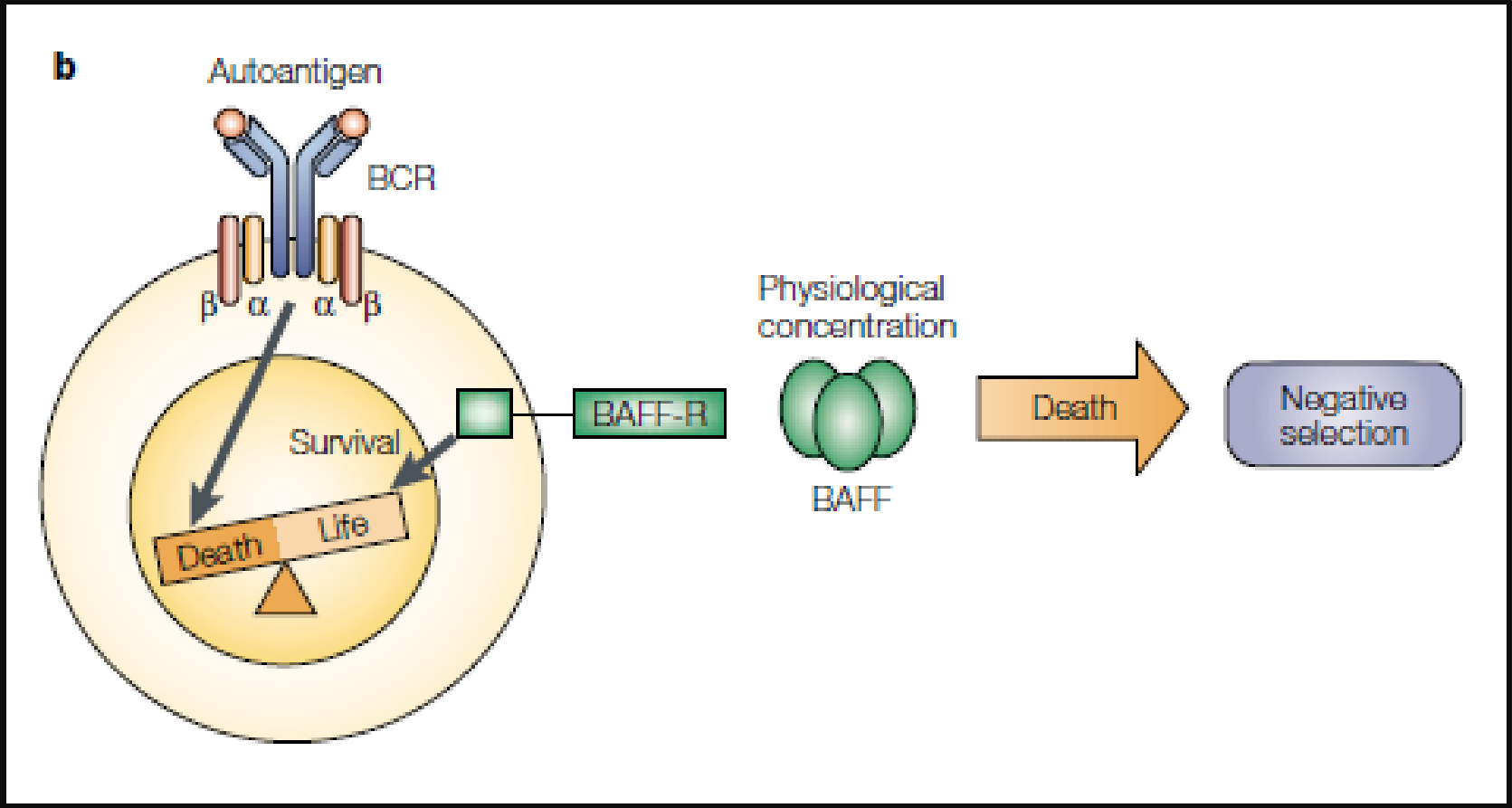
BLyS: Αδυναμία διάσωσης απο αρνητική επιλογή



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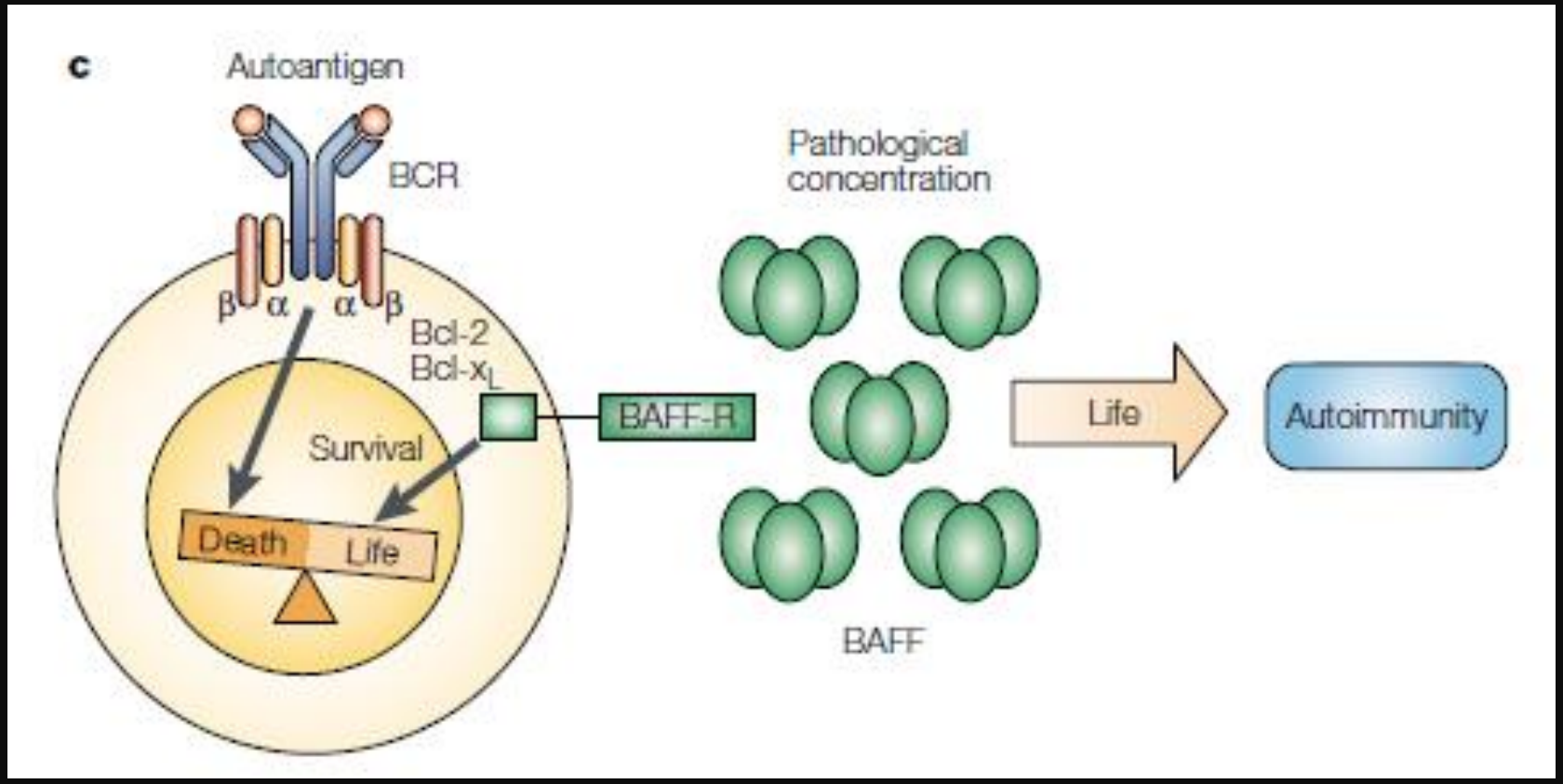
Περίσσεια BLyS: Αυτοανοσία !



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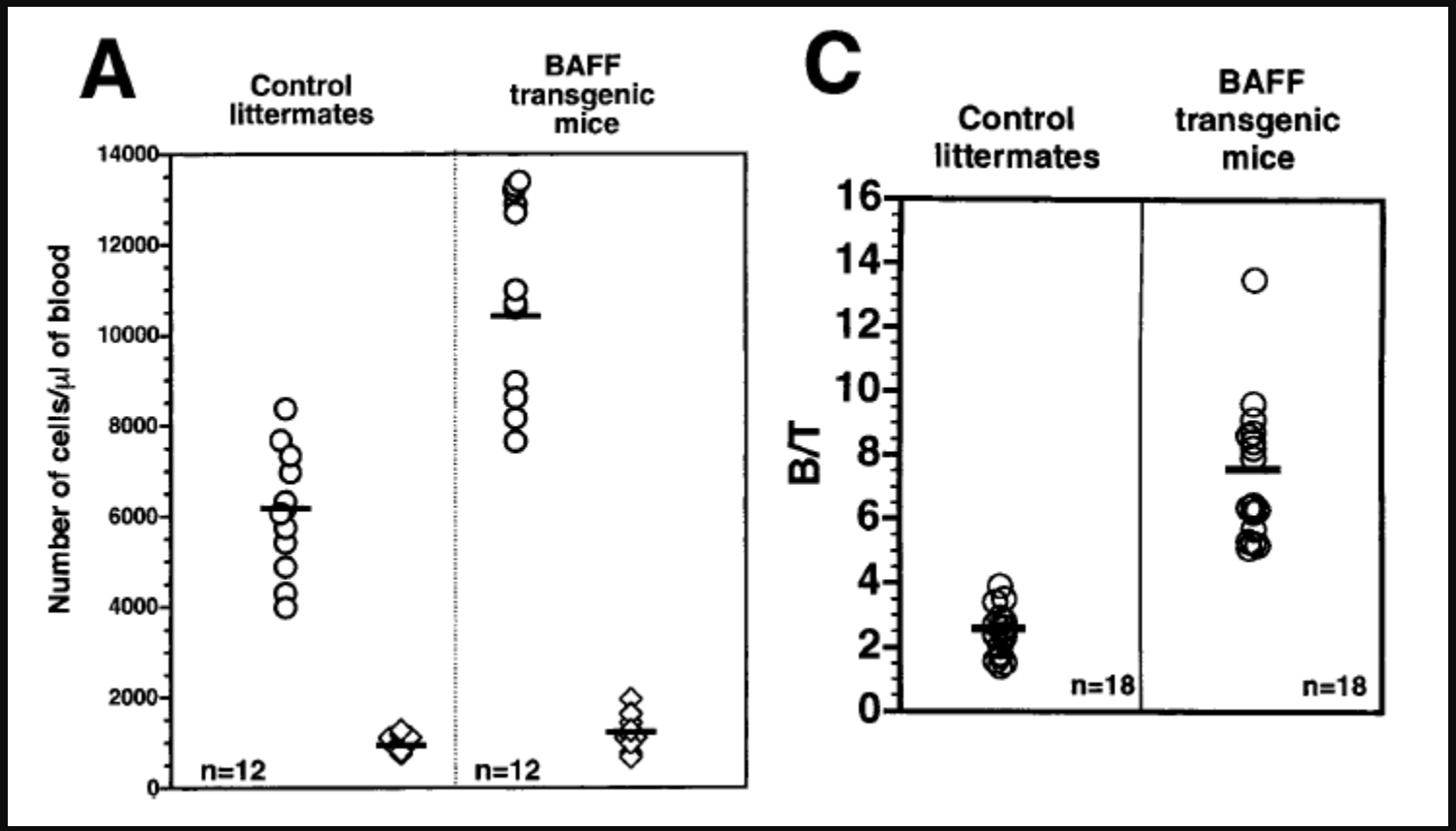
Οι ΔΥΟ ΜΕΙΖΟΝΕΣ ρόλοι του BLyS

1) Είναι ο **ΚΥΡΙΟΣ ρυθμιστής του αριθμού** των άωρων και ώριμων Β λεμφοκυττάρων. Ελέγχει τη διαφοροποίησή τους και το χρόνο ζωής τους.

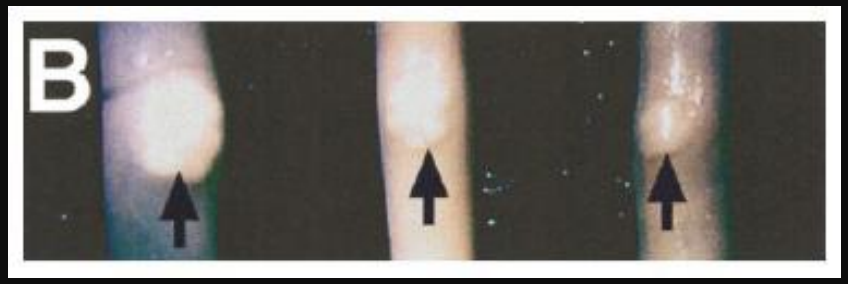
2) Είναι **κεντρικός ρυθμιστής της «αυστηρότητας»** με την οποία γίνεται η εξάλειψη αυτοδραστικών Β λεμφοκυττάρων. Ρυθμίζει την **ανοσολογική ανοχή** τους.

BAFF διαγονιδιακό ποντίκι:
Πάρα πολλά Β λεμφοκύτταρα



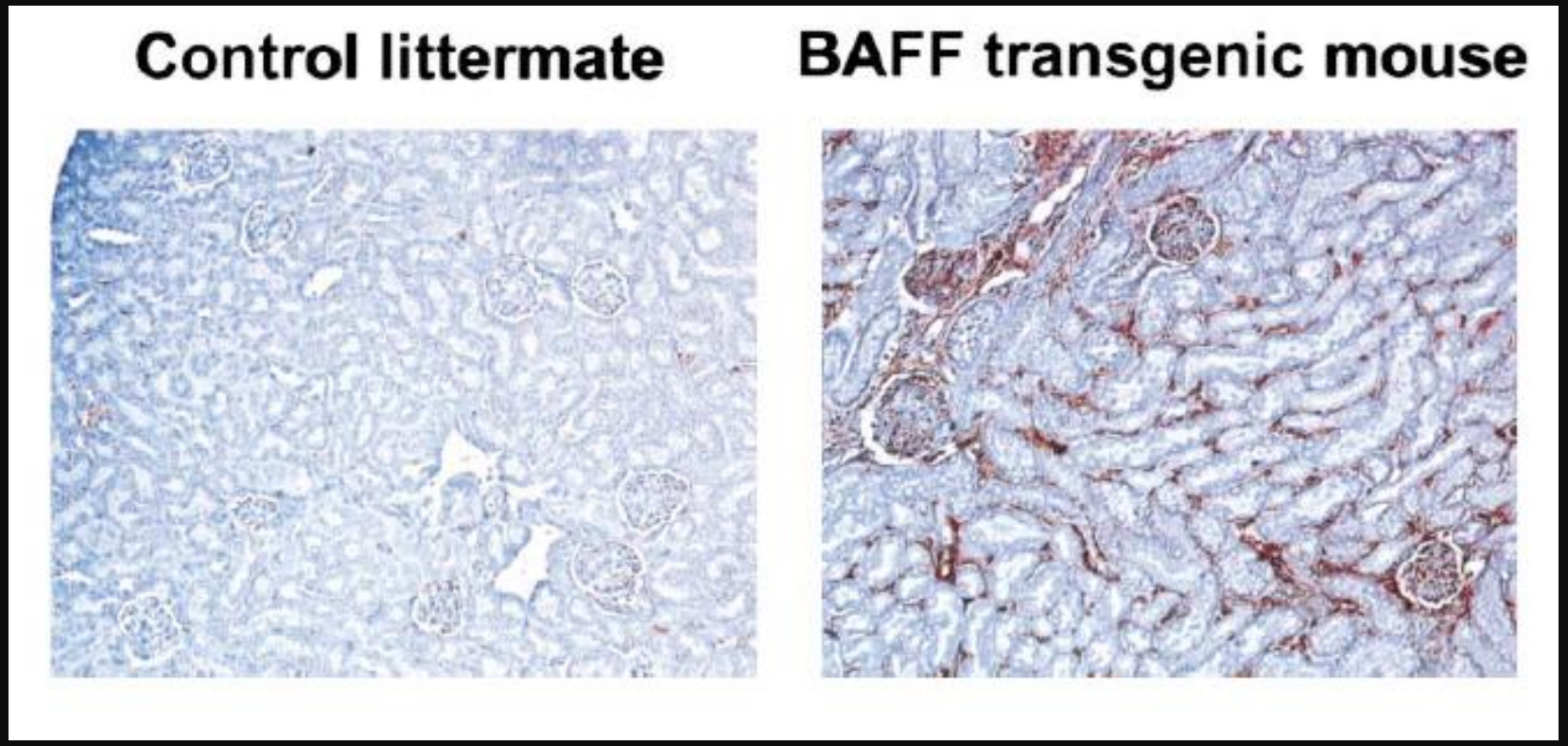
Mackay F et al: J Exp Med 1999; 190:1697.

BAFF διαγονιδιακό ποντίκι:
Υπερπλασία λεμφικών οργάνων



Mackay F et al: J Exp Med 1999; 190:1697.

BAFF διαγονιδιακό ποντίκι: Νεφρίτιδα



Mackay F et al: J Exp Med 1999; 190:1697.

BLyS και ΣΕΛ: Ανθρωποι και ποντίκια

- **Αυξημένα** επίπεδα BLyS στα NZBxNZW F1.
- **Αυξημένα** επίπεδα BLyS στα MRL/lpr.

- Εξουδετέρωση του BLyS στα μοντέλα αυτά «θεραπεύει» το lupus-like νόσημά τους.

- **Αυξημένα επίπεδα BLyS στον ορό ασθενών με ΣΕΛ** (αλλά και σε άλλα αυτοάνοσα νοσήματα).

B cells in SLE: Dysfunctional tolerance checkpoints

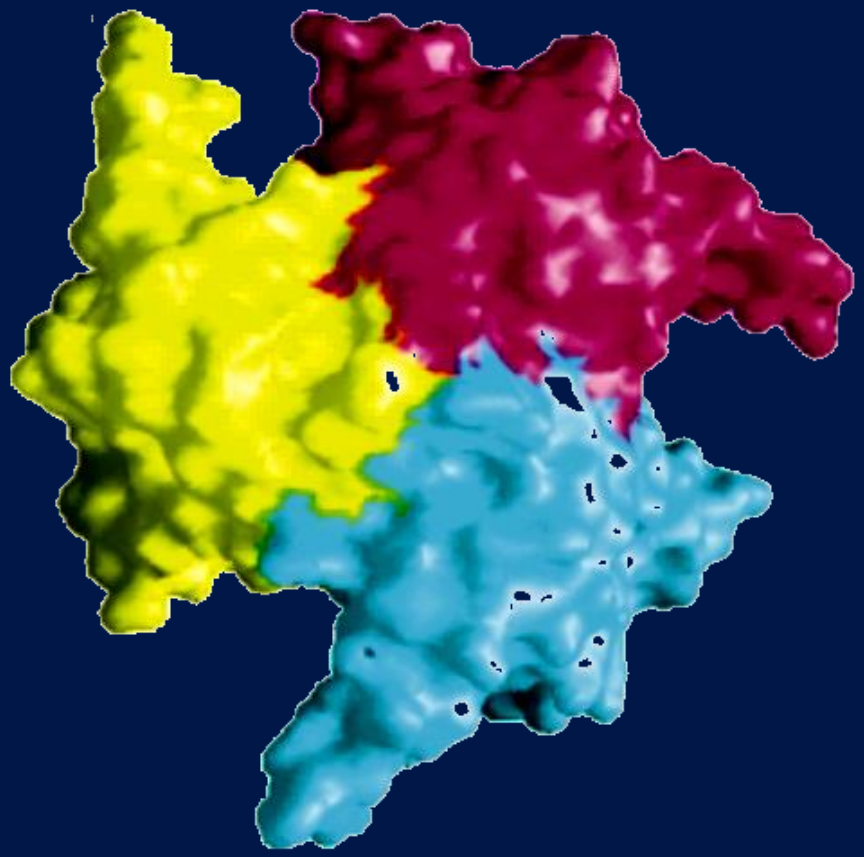
- **1ο checkpoint**: Μέσα στον Μυελό. Newly emigrant B cells ($CD19^+CD10^+IgM^+CD27^-$).
- Normals: 40.7% autoreactive.

- **2ο checkpoint**: Στα δευτερογενή λεμφικά όργανα. Mature naïve B cells ($CD19^+CD10^-IgM^+CD27^-$).

- Τελικά: **5-20%** των normal mature naïve = αυτοδραστικά
- **25-50%** των lupus mature naïve = αυτοδραστικά

Yurasov S et al. J Exp Med 2005; 201:703.

BLyS (B-lymphocyte stimulator)

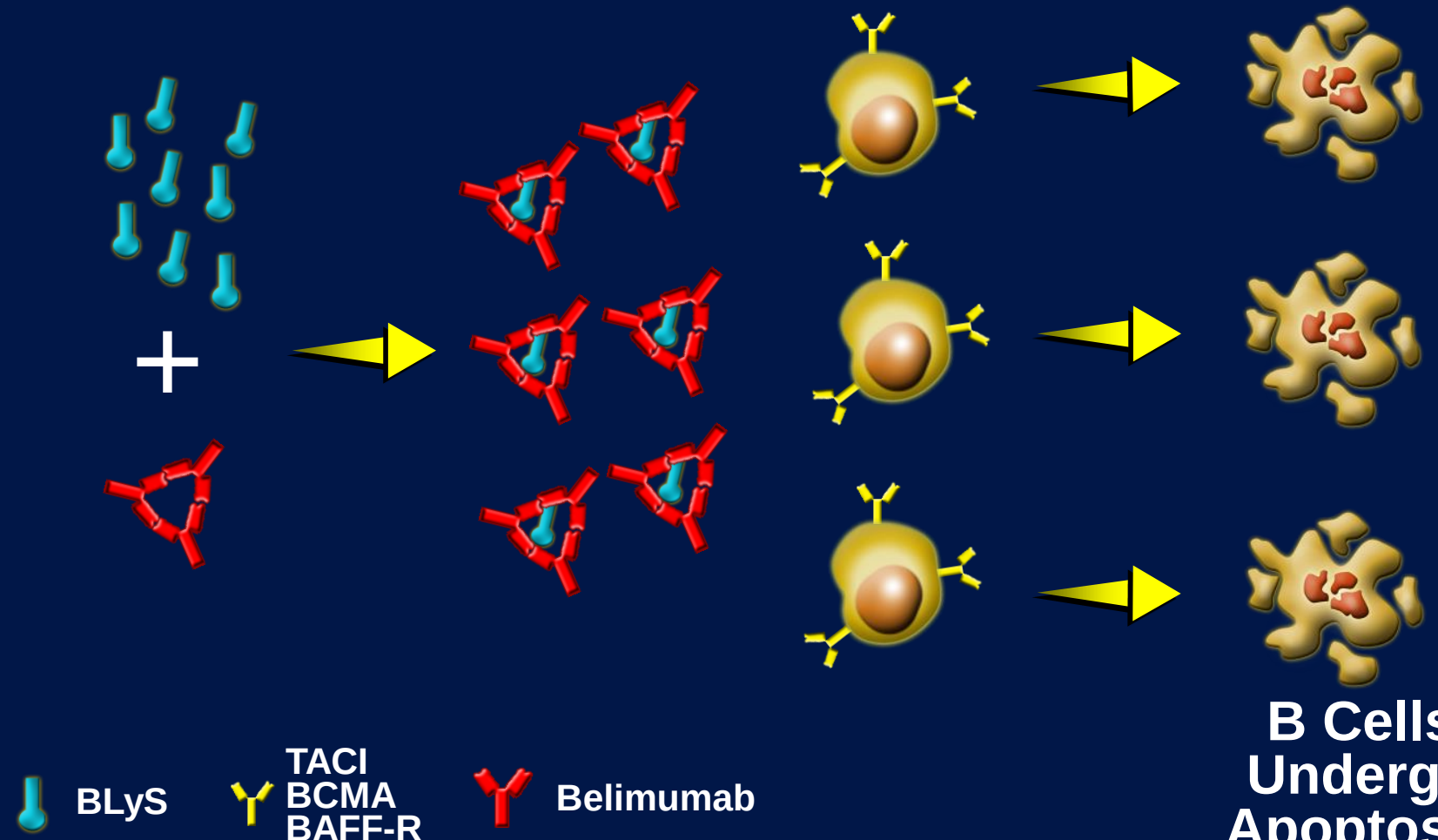


- A soluble ligand of the TNF family
- BLyS plays a critical role in promoting the auto-reactive B cell survival and differentiation

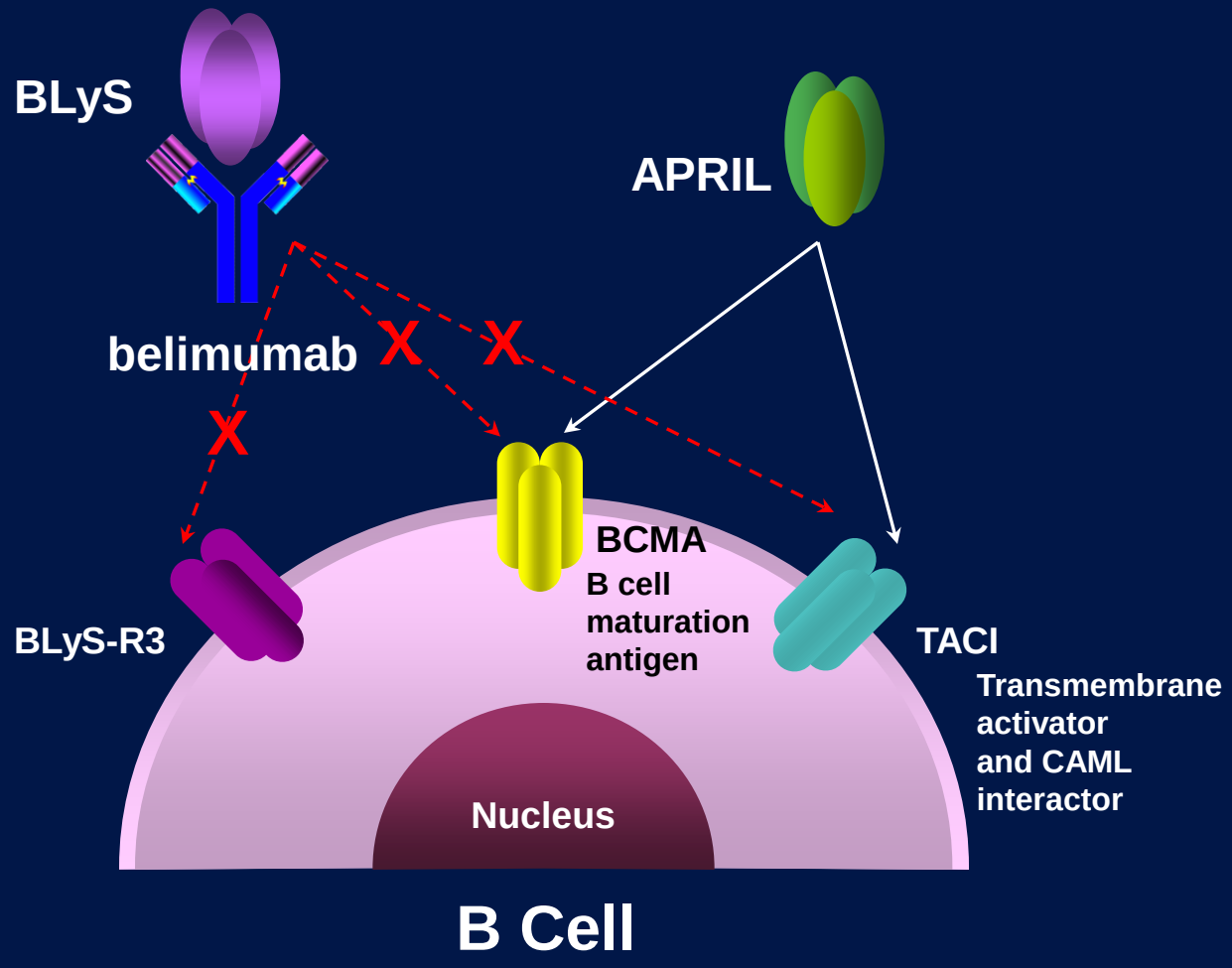
BLyS = B-lymphocyte Stimulator

1. Oren DA, et al. Nat Struct Biol 2002;9:288–92
2. Cancro MP, et al. J Clin Invest 2009;119(5):1066–73
3. Miller JP, et al. J Immunol 2006;176:6405–10

Belimumab: fully human monoclonal antibody that selectively inhibits the biological activity of BLyS

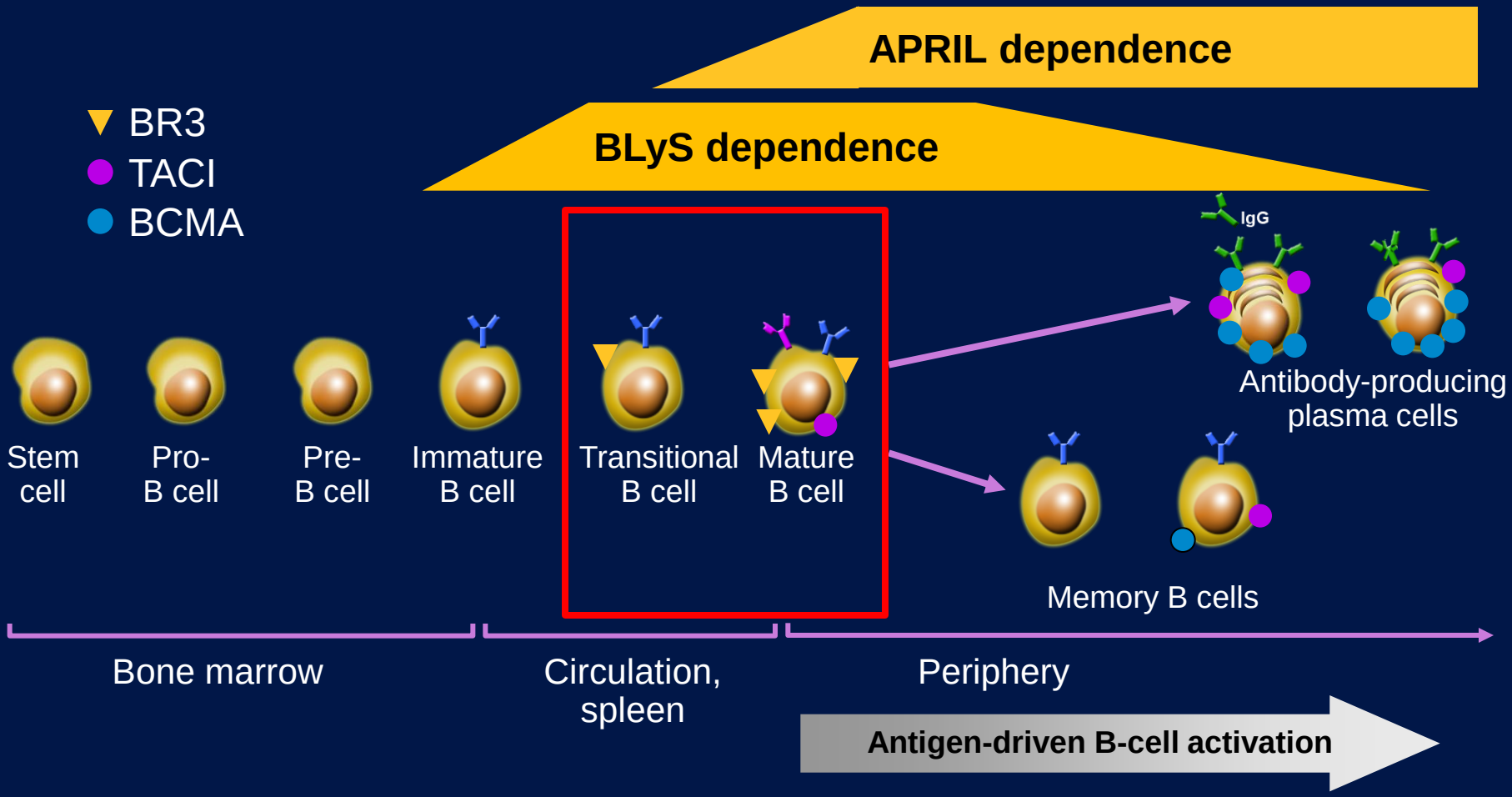


Belimumab Inhibits Binding of BLyS to Three Receptors



BLyS-targeted therapy is restricted to early-stage B cells in the periphery

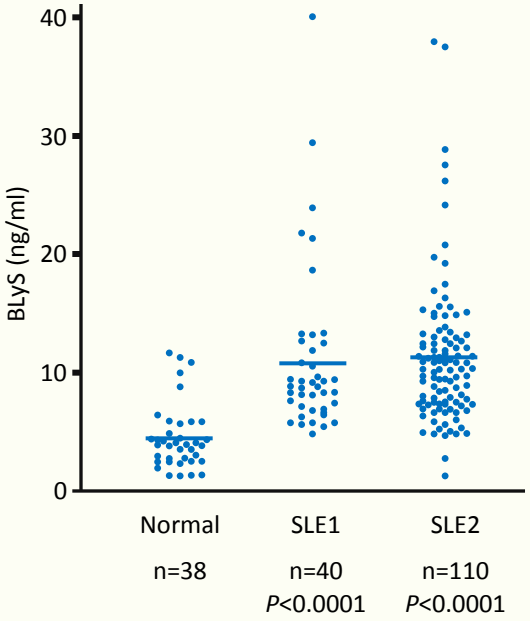
BLyS primarily binds to BR3, which is expressed in early B-cell development



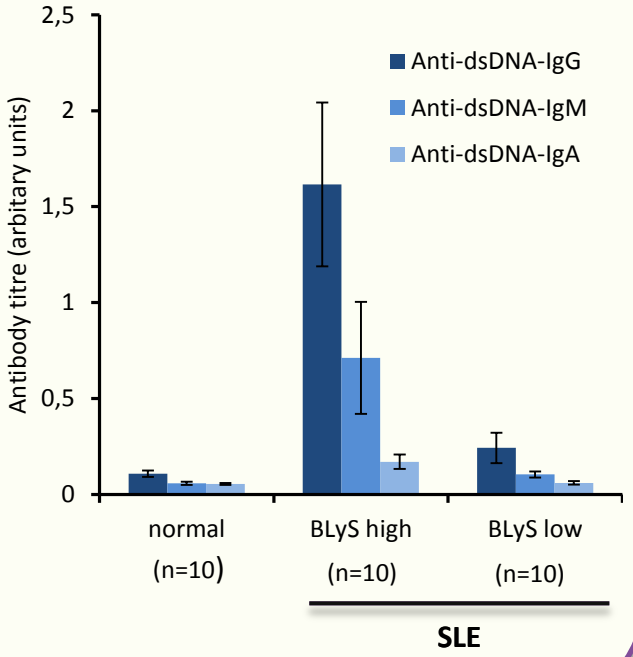
Adapted from Cancro MP, et al. J Clin Invest 2009;119:1066–73

Elevated BLyS levels in SLE patients correlated with high anti-dsDNA titres and changes in SELENA-SLEDAI score

BLyS levels found to be elevated in patients with SLE[1]



Elevated BLyS levels correlated with elevated anti-dsDNA[1]



Increased BLyS levels associated with worsening of SLE[2]*

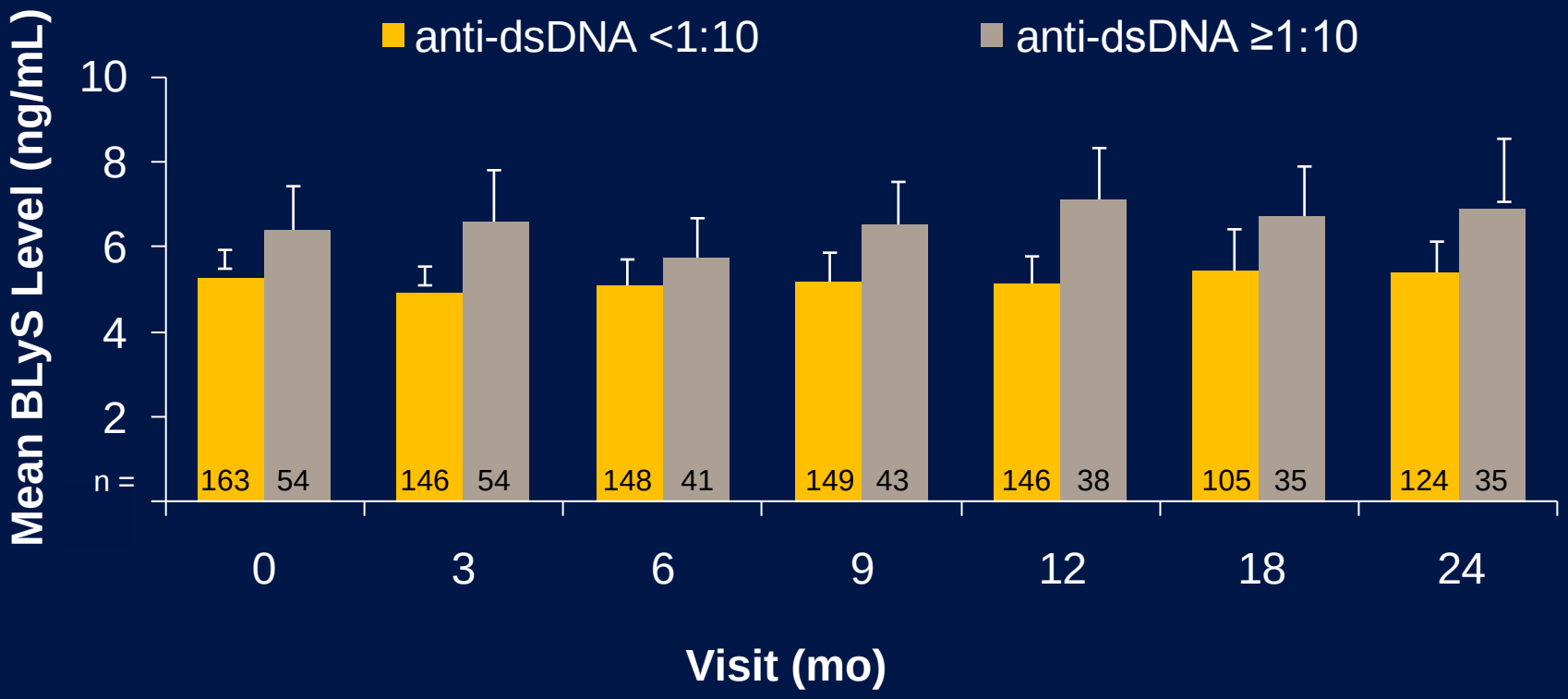
Independent variable	Relationship to increase in SS
BLyS level at previous visit	Positive *P*=0.0042
Change in BLyS level from previous visit	Positive *P*=0.0007

* Multivariate analysis of the association of BLyS level with a change in SELENA-SLEDAI (SS) score from previous visit. SELENA-SLEDAI was administered and plasma BLyS autoantibodies were measured at baseline, 3, 6, 9, 12, 18 and 24 months and at any unscheduled visits.

1. Zhang J, *et al. J Immunol* 2001; **166:**6–10;
2. Petri M, *et al. Arthritis Rheum* 2008; **58:**2453–2459.

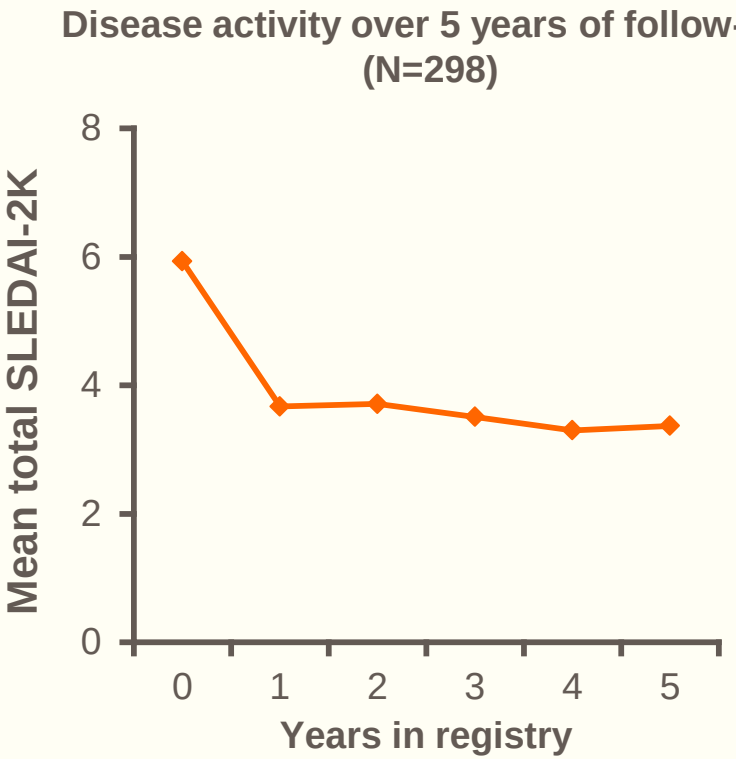
BLyS Levels Predict Increased SLE Disease Activity

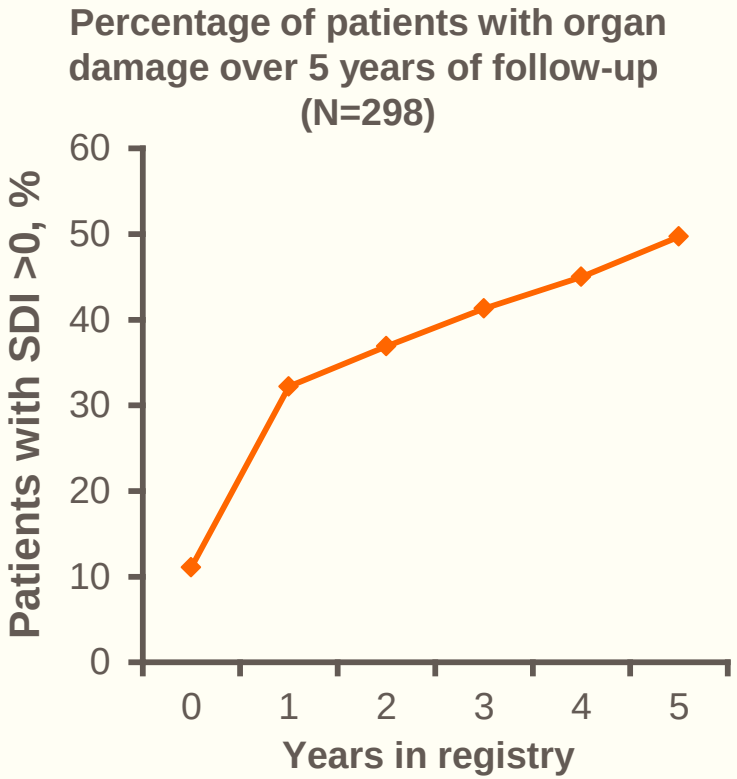
Higher BLyS Levels in SLE Patients Directly Correlated With Higher Anti-dsDNA Titers



Petri M et al. Arthritis Rheum. 2008;58:2453-9.

Even with low disease activity, patients still accrue organ damage



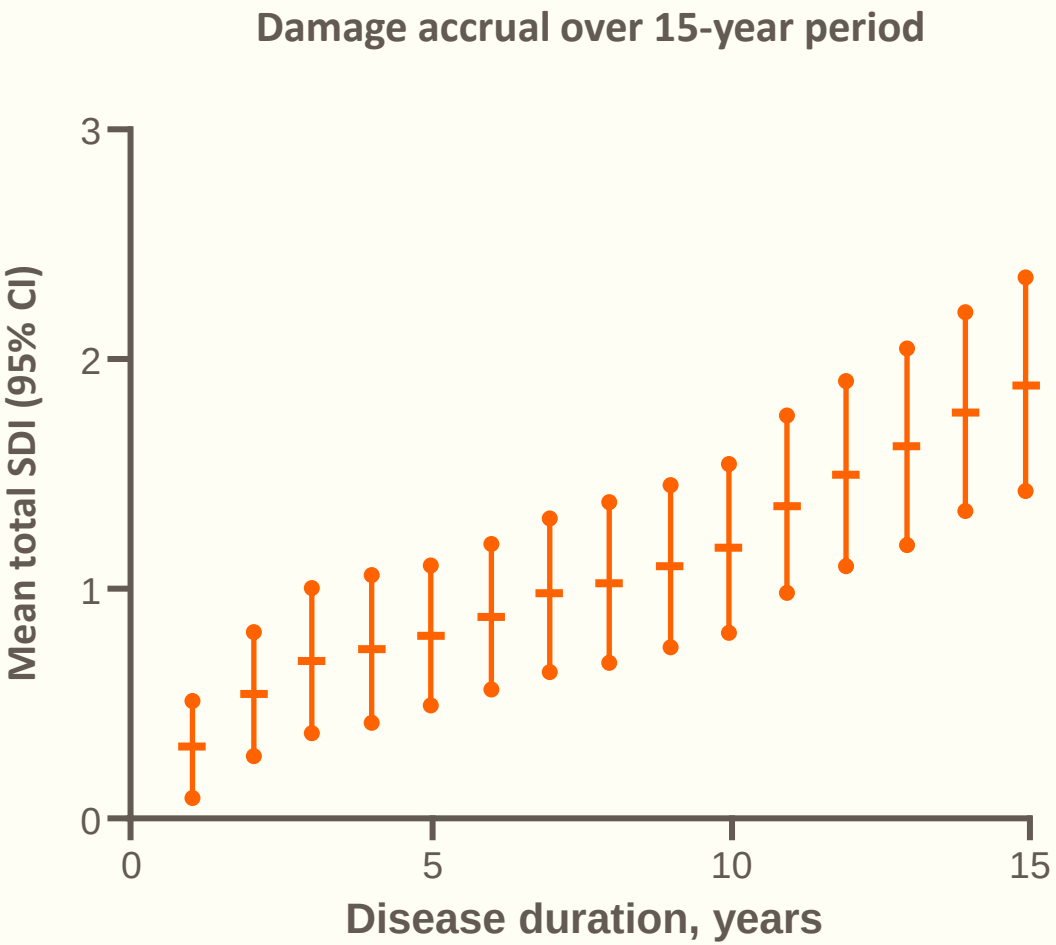


Prospective analysis of patients in the SLICC cohort recruited within 15 months of diagnosis and followed annually for ≥5 years.

Urowitz MB, *et al. Arthritis Care Res* 2012; **64:**132-137

SDI = Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index; SLICC/ACR = Systemic Lupus International Collaborating Clinics.

Damage leads to more damage



- Despite receiving a cocktail of active therapies, all patients (n=73) accrued damage (from 0.33±0.9 to 1.90±2.0)

SoC = standard of care; SDI = Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index.

Gladman DD, *et al. J Rheumatol* 2003; **30:**1955–1959

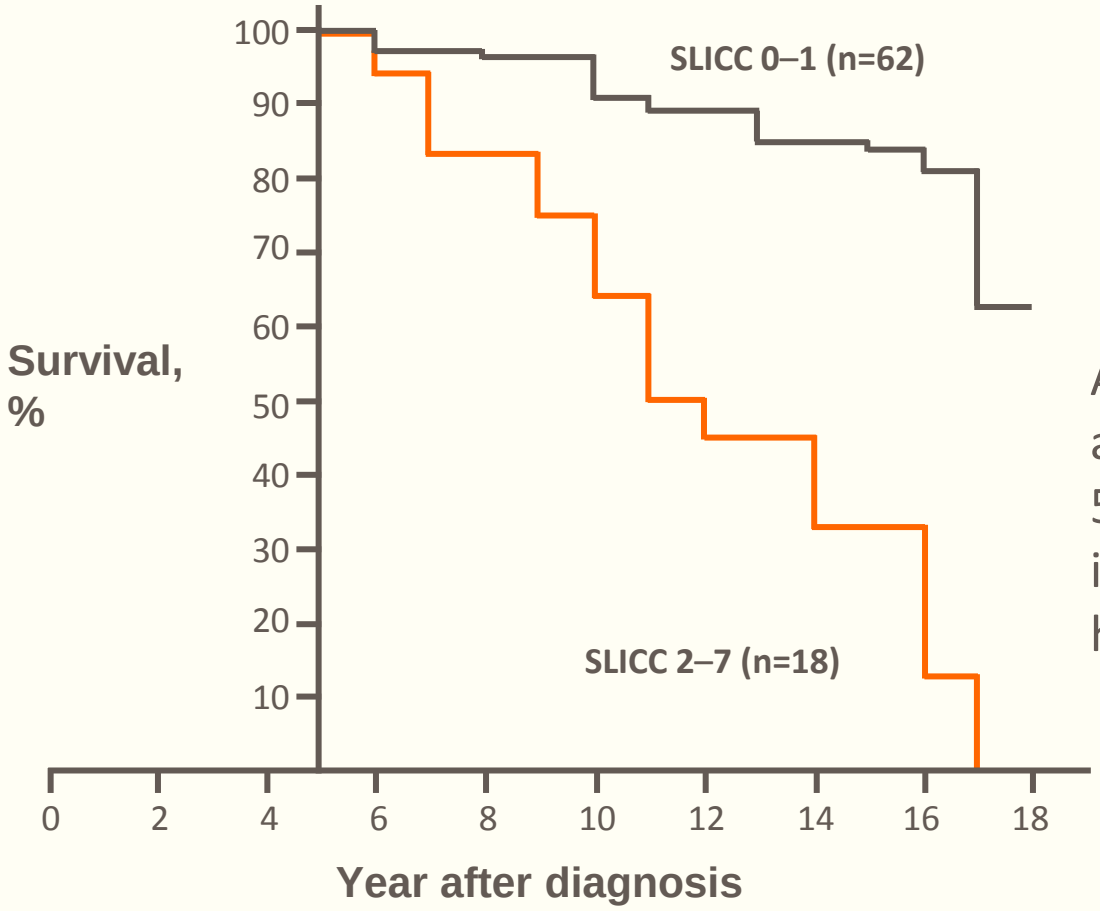
Glucocorticoid therapy is associated with specific morbidities

Damage item	Number of events	Adjusted RR* (95% CI)	P-value
Osteoporotic fracture	24	1.9 (1.5–2.4)	0.0001
Coronary artery disease	21	1.7 (1.2–2.3)	0.0009
Cataracts	47	1.7 (1.3–2.1)	0.0001
Avascular necrosis	47	1.6 (1.3–2.0)	0.0001
Stroke	25	1.3 (0.9–1.8)	0.1
Diabetes mellitus	26	1.5 (1.0–2.3)	0.04
Hypertension	115	1.0 (0.8–1.3)	0.7
Pulmonary fibrosis	15	1.7 (1.2–2.5)	0.006
Venous insufficiency	13	1.2 (0.7–2.1)	0.4
Cognitive impairment/psychosis	30	2.0 (1.2–3.2)	0.007
Renal failure	15	1.3 (0.9–1.9)	0.2
Deforming/erosive arthritis	27	1.1 (0.8–1.6)	0.4
Scarring alopecia	28	1.1 (0.7–1.7)	0.7
Pulmonary hypertension	18	0.9 (0.5–1.5)	0.6
Malignancy	11	0.8 (0.5–1.5)	0.6

* Risk ratio associated with cumulative corticosteroid dose of 36.5 g, adjusted for age, sex and race.

Zonana-Nacach A, *et al. Arthritis Rheum* 2000; **43:**1801–1808

Damage leads to death

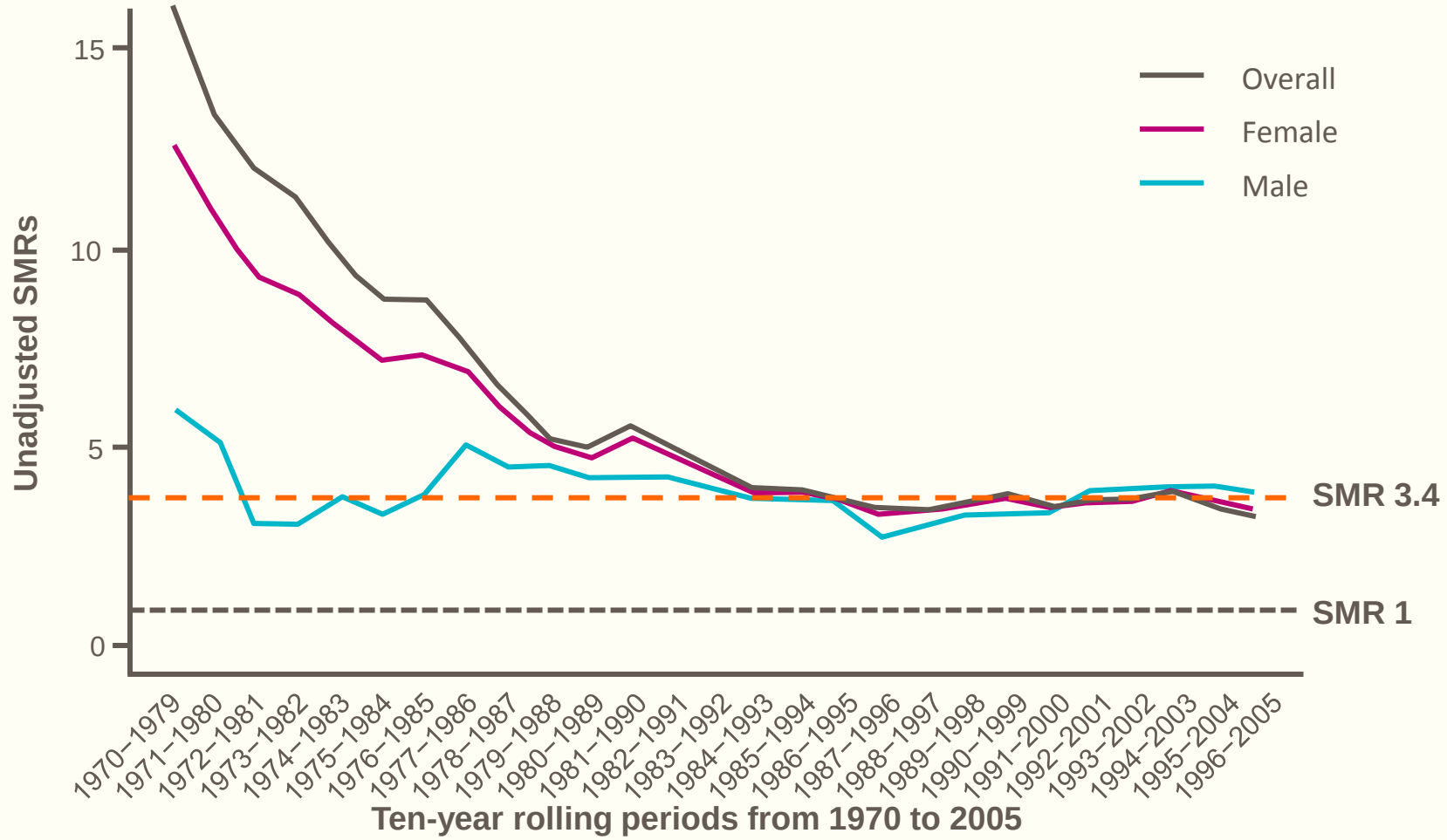


An SDI >1, approximately 5-years after diagnosis, is associated with a higher rate of mortality

SLICC = Systemic Lupus International Collaborating Clinics

Nived O, *et al. J Rheum* 2002; **29**:1398–1400

Mortality rates for patients with SLE remain unacceptably high

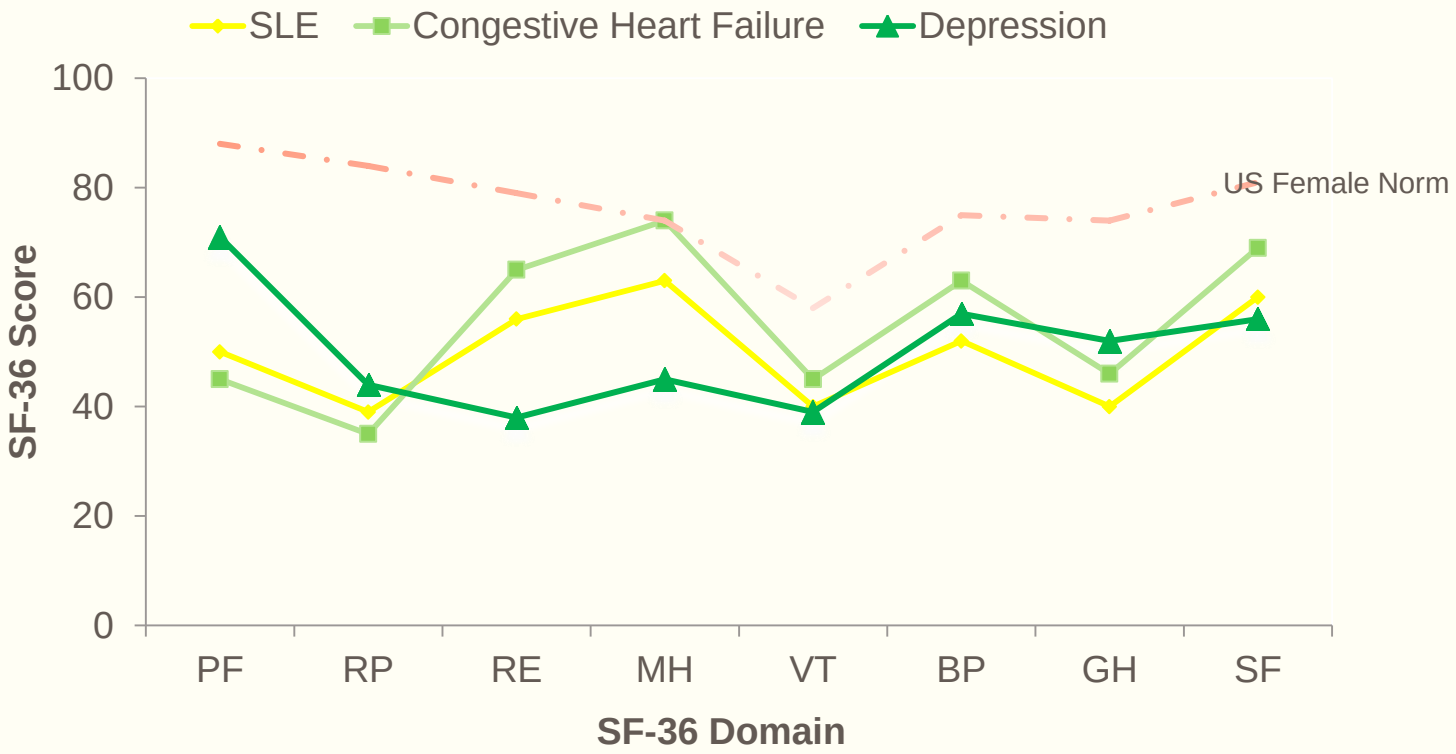


SMR = standardised mortality ratio.

Urowitz M, et al. J Rheum 2008; 35:2152–2158

Uncontrolled disease also leads in low values of quality of life

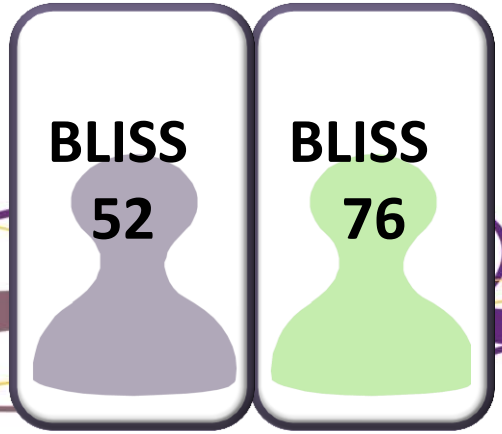
Quality of life values of SLE patients are matching those of Depression and Congestive Heart Failure, which represent patients groups with very high humanistic burden



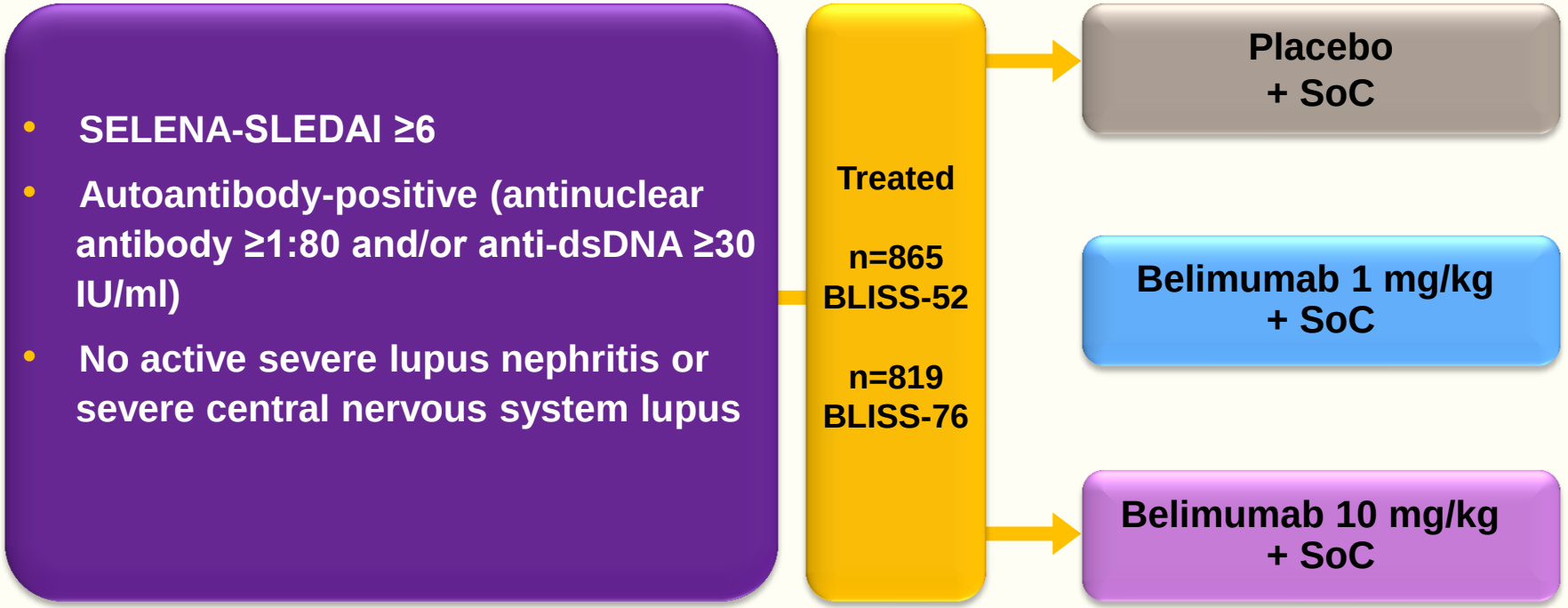
BP, bodily pain; GH, general health; MH, mental health; PF, physical functioning; RE, role emotional; RP, role physical; SF, social functioning; VT, vitality

Jolly M. *J Rheumatol*. 2005;32:1706-8

BLISS-52 and BLISS-76 clinical trials

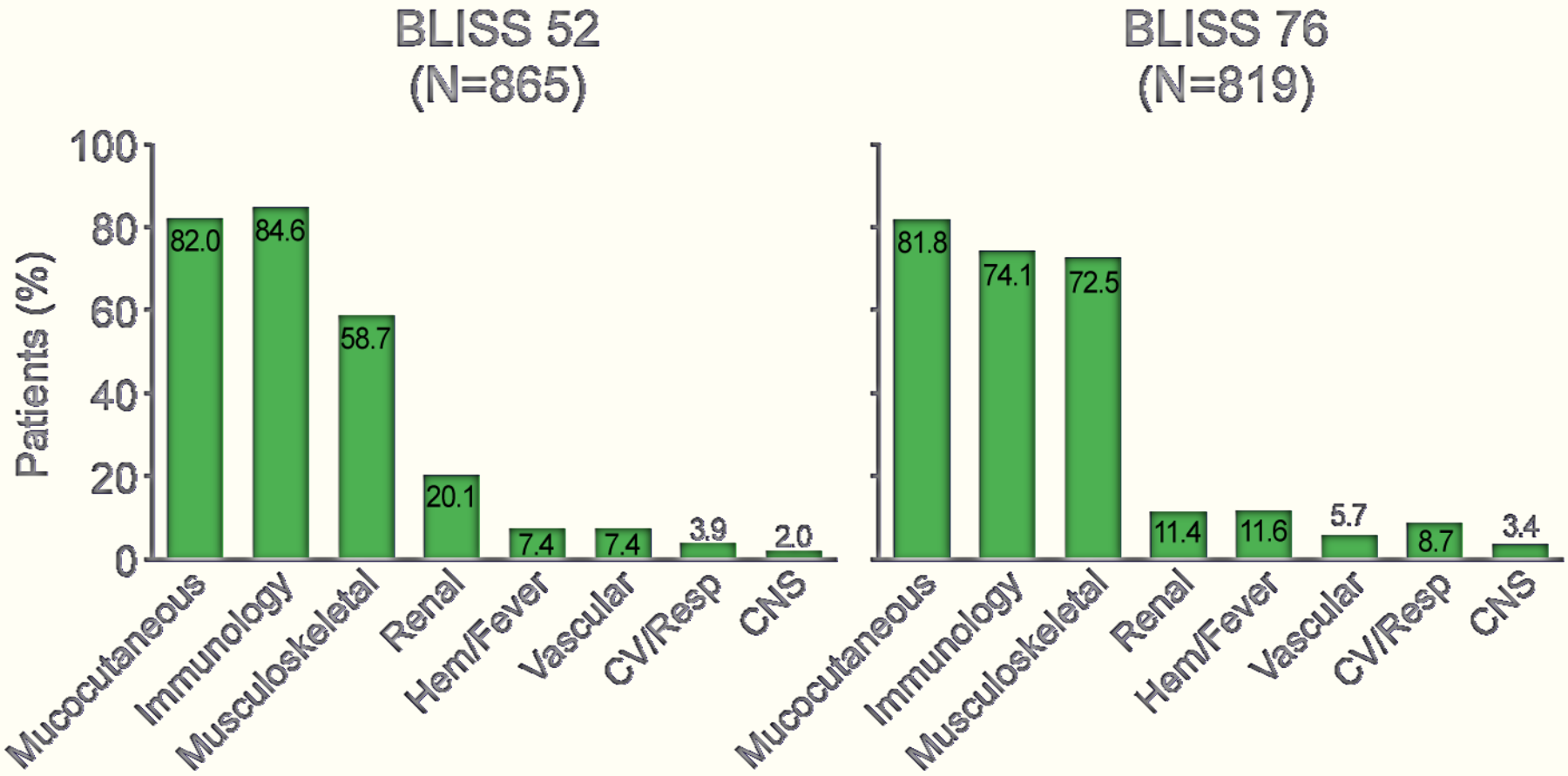


Trial design in BLISS studies



1. Navarra SV, *et al. Lancet* 2011; 377:721–731;
2. Furie RA, *et al. Arthritis Rheum* 2011; 63:3918–3930.

Organ Involvement at Baseline



1. Navarra SV, *et al. Lancet* 2011; 377:721–731;
2. Furie RA, *et al. Arthritis Rheum* 2011; 63:3918–3930.

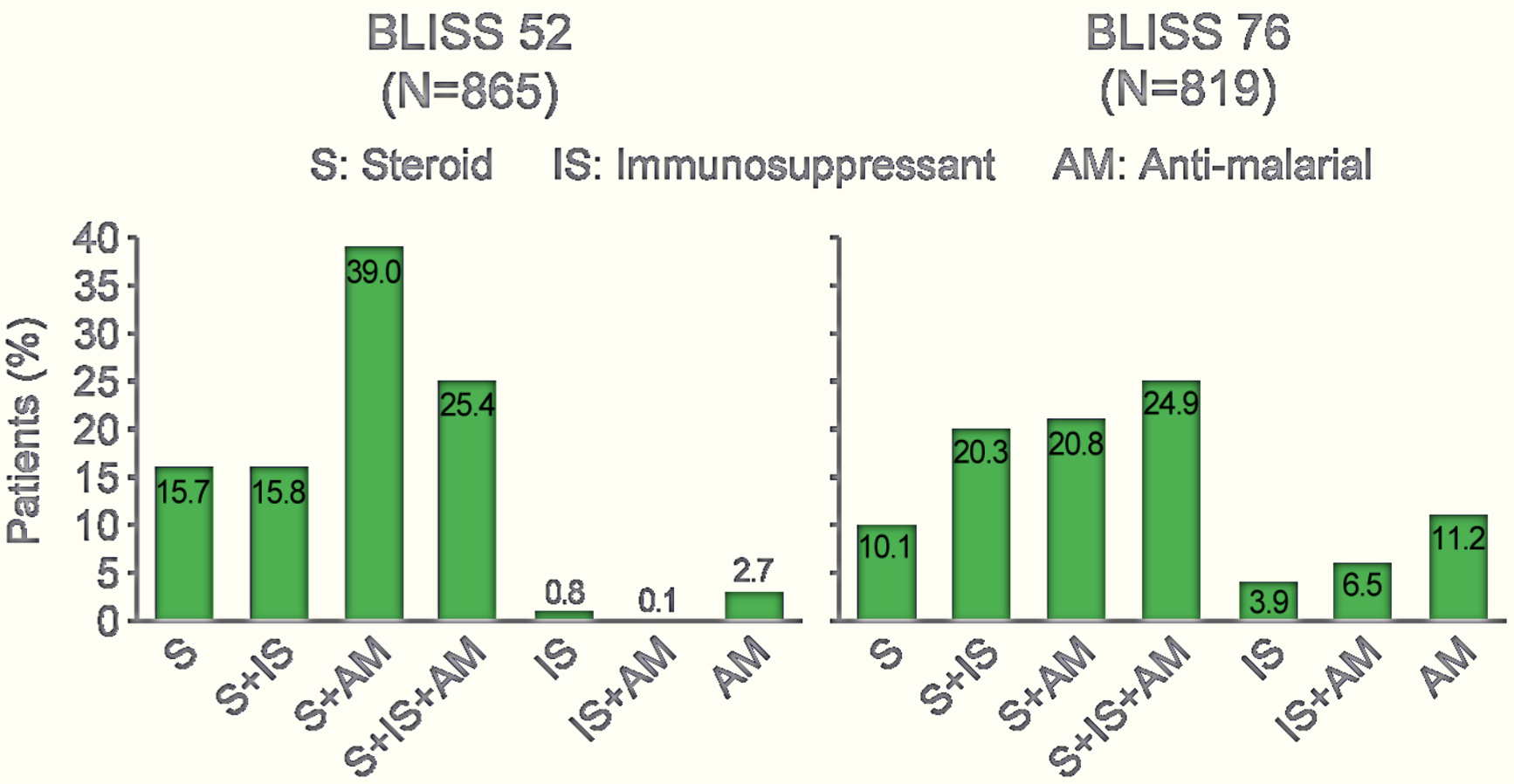
Baseline characteristics of the BLISS 52 and 76 study populations

	BLISS-52[1] (Week 52)			BLISS-76[2] (Week 76)		
Event	Placebo + SoC (n=287)	Belimumab 1 mg/kg + SoC (n=288)	Belimumab 10 mg/kg + SoC (n=290)	Placebo + SoC (n=275)	Belimumab 1 mg/kg + SoC (n=271)	Belimumab 10 mg/kg + SoC (n=273)
Age*	36.2 ± 11.8	35.0 ± 10.6	35.4 ± 10.8	40.0 ± 11.9	40.0 ± 11.4	40.5 ± 11.1
Female, %	94	94	97	92	93	95
Asian, %	37	37	40	4	2	4
Indigenous American, %	31	34	32	13	12	13
White/Caucasian, %	29	26	24	68	71	69
Black/African-American, %	4	3	4	14	15	14
SLE duration, years*	5.9 ± 6.2	5.0 ± 4.6	5.0 ± 5.1	7.4 ± 6.7	7.9 ± 7.1	7.2 ± 7.5
SELENA-SLEDAI score*	9.7 ± 3.6	9.6 ± 3.8	10.0 ± 3.9	9.8 ± 4.0	9.7 ± 3.7	9.5 ± 3.6
ANA ≥1:80, %	92	94	95	92	95	90
Anti-dsDNA ≥30 IU/mL, %	71	77	75	63	63	66
Prednisone, mg/day*†	11.9 ± 7.9	12.9 ± 8.6	13.2 ± 9.5	9.4 ± 8.9	8.7 ± 7.6	8.4 ± 7.9
Prednisone >7.5 mg/day,%†	67	71	70	46	48	44
Immunosuppressives, %	43	42	42	56	57	54

* Mean ± SD. † Prednisone or prednisone equivalent.
ANA = antinuclear antibodies; dsDNA = double-stranded DNA;
SELENA-SLEDAI = Safety of Estrogens in Lupus Erythematosus National Assessment–Systemic Lupus Erythematosus Disease Activity Index; SoC = standard of care.

1. Navarra SV, *et al. Lancet* 2011; 377:721–731;
2. Furie RA, *et al. Arthritis Rheum* 2011; 63:3918–3930.

Medication Use at Baseline



1. Navarra SV, *et al. Lancet* 2011; 377:721–731;
2. Furie RA, *et al. Arthritis Rheum* 2011; 63:3918–3930.

Primary Endpoint:
SLE Responder Index (SRI) Response Rate at Week 52

SELENA-SLEDAI	BILAG	PGA
Primary measure of clinical improvement	No significant worsening in any specific organ system	No worsening of overall patient condition as assessed by physician

SRI

SRI responders had to meet all 3 criteria

1. Petri M, et al. *N Engl J Med.* 2005;353:2550-2558.
2. Hay EM, et al. *Q J Med.* 1993;86:447-458. 4. Navarra SV, et al. *Lancet*. 2011;377:721-731.
3. Furie R, et al. *Arthritis Rheum.* 2011;63:3918-3930.

Primary Endpoint for Phase III Trials: SLE Responder Index (SRI) Response Rate at Week 52

SELENA-SLEDAI[1]

≥4-point reduction in SELENA-SLEDAI score[2]

BILAG[3]

No new BILAG A
or
2 new BILAG B organ domain scores[2,3]

PGA

No worsening in PGA (<0.3-point increase)[2,4,5]

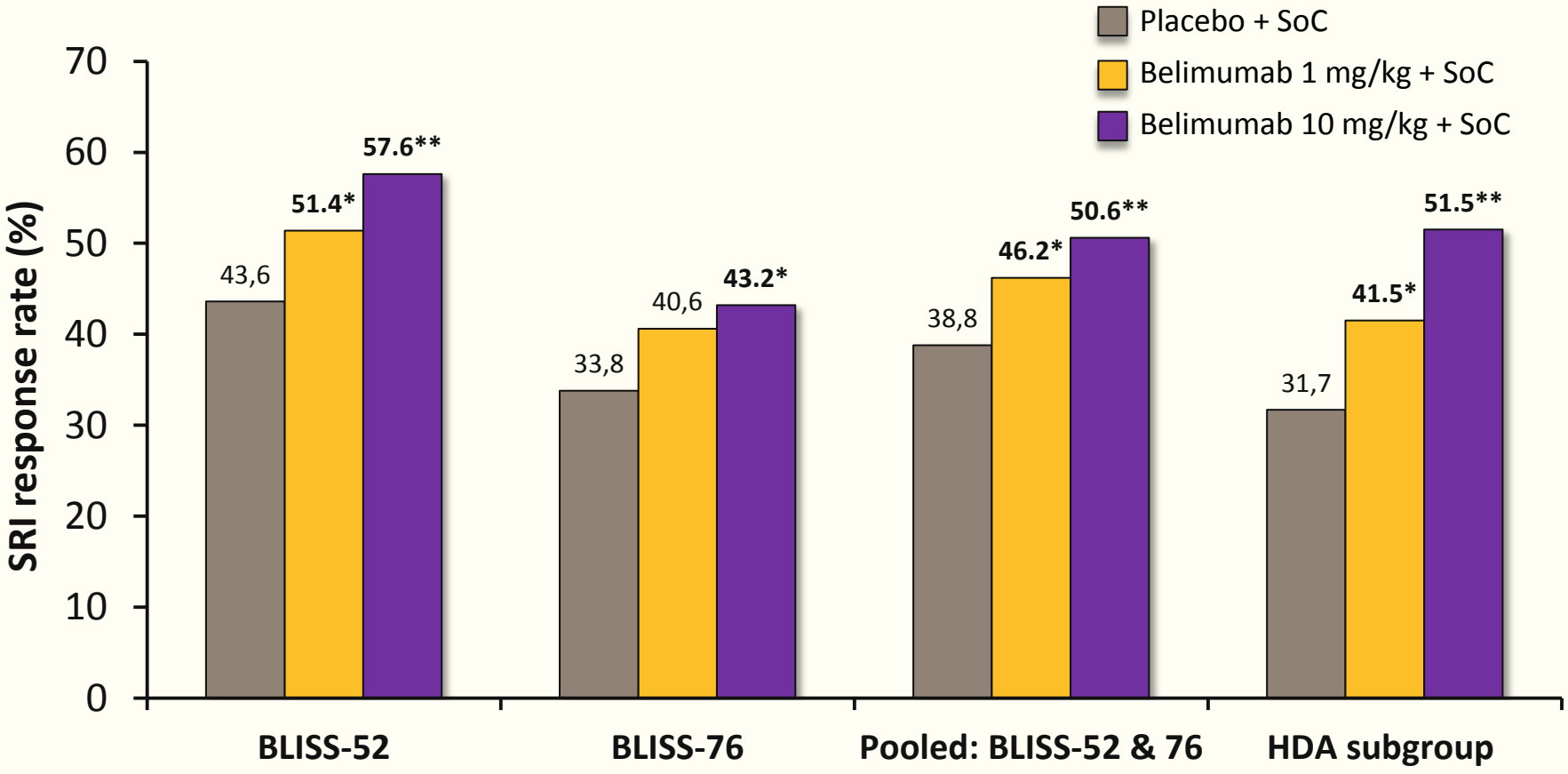
SRI

SRI responders had to meet all 3 criteria

SELENA-SLEDAI=Safety of Estrogens in Lupus Erythematosus: National Assessment Version of the Systemic Lupus Erythematosus Disease Activity Index; BILAG=British Isles Lupus Assessment Group; PGA=Physician's Global Assessment

1. Petri M, et al. *N Engl J Med.* 2005;353:2550-2558.
2. Hay EM, et al. *Q J Med.* 1993;86:447-458. 4. Navarra SV, et al. *Lancet*. 2011;377:721-731.
3. Furie R, et al. *Arthritis Rheum.* 2011;63:3918-3930.

Υπεροχή του belimumab στην επίτευξη κλινικής ανταπόκρισης (SRI) σε σχέση με το SoC



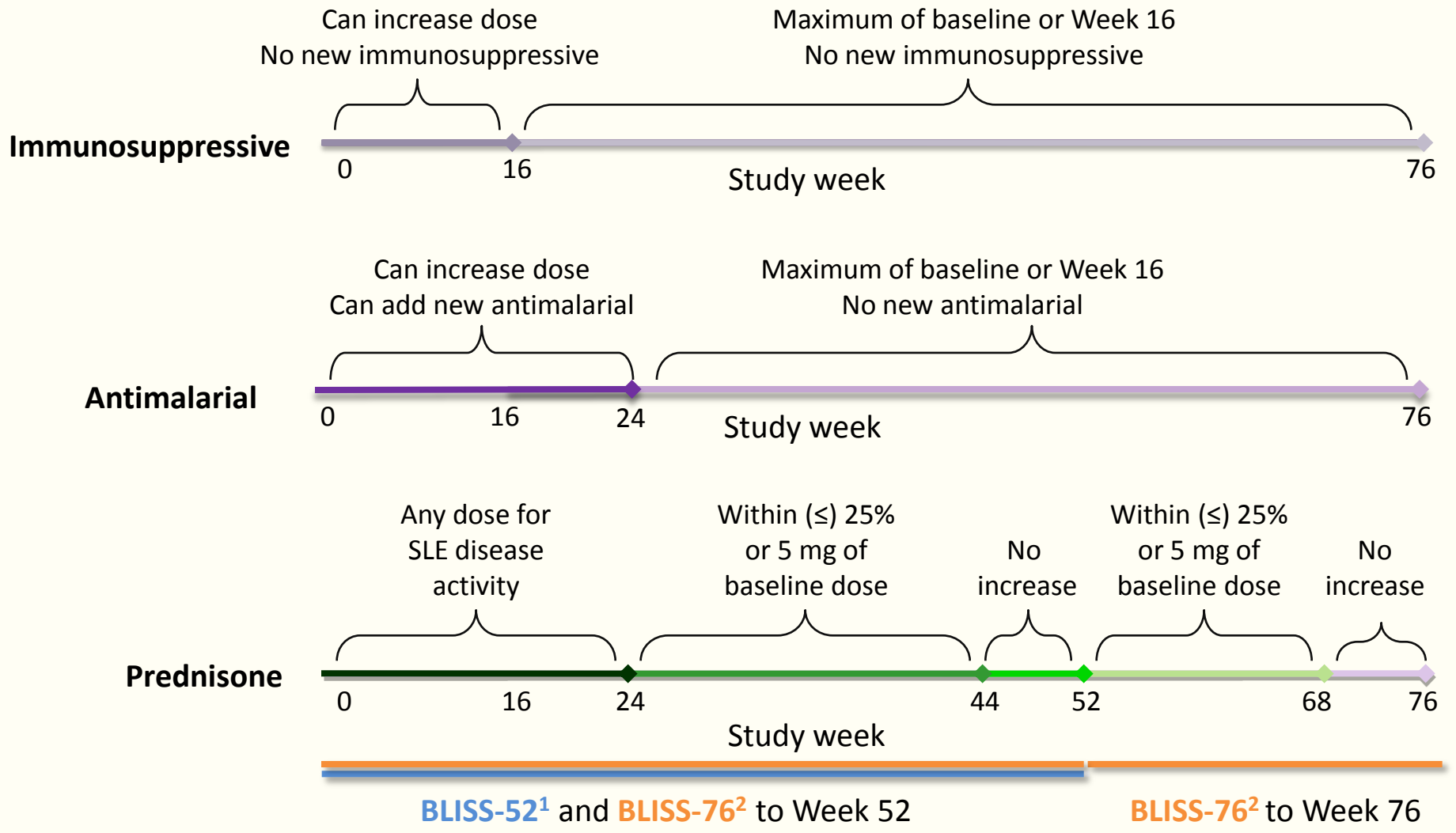
- Significantly higher response rates were observed in patients treated with belimumab 10 mg/kg + SoC compared with those who received placebo + SoC (P<0.05)[1–3]

* P<0.05; ** P<0.001

HDA = high disease activity, SoC = standard of care,
SRI = Systemic Lupus Erythematosus Responder Index.

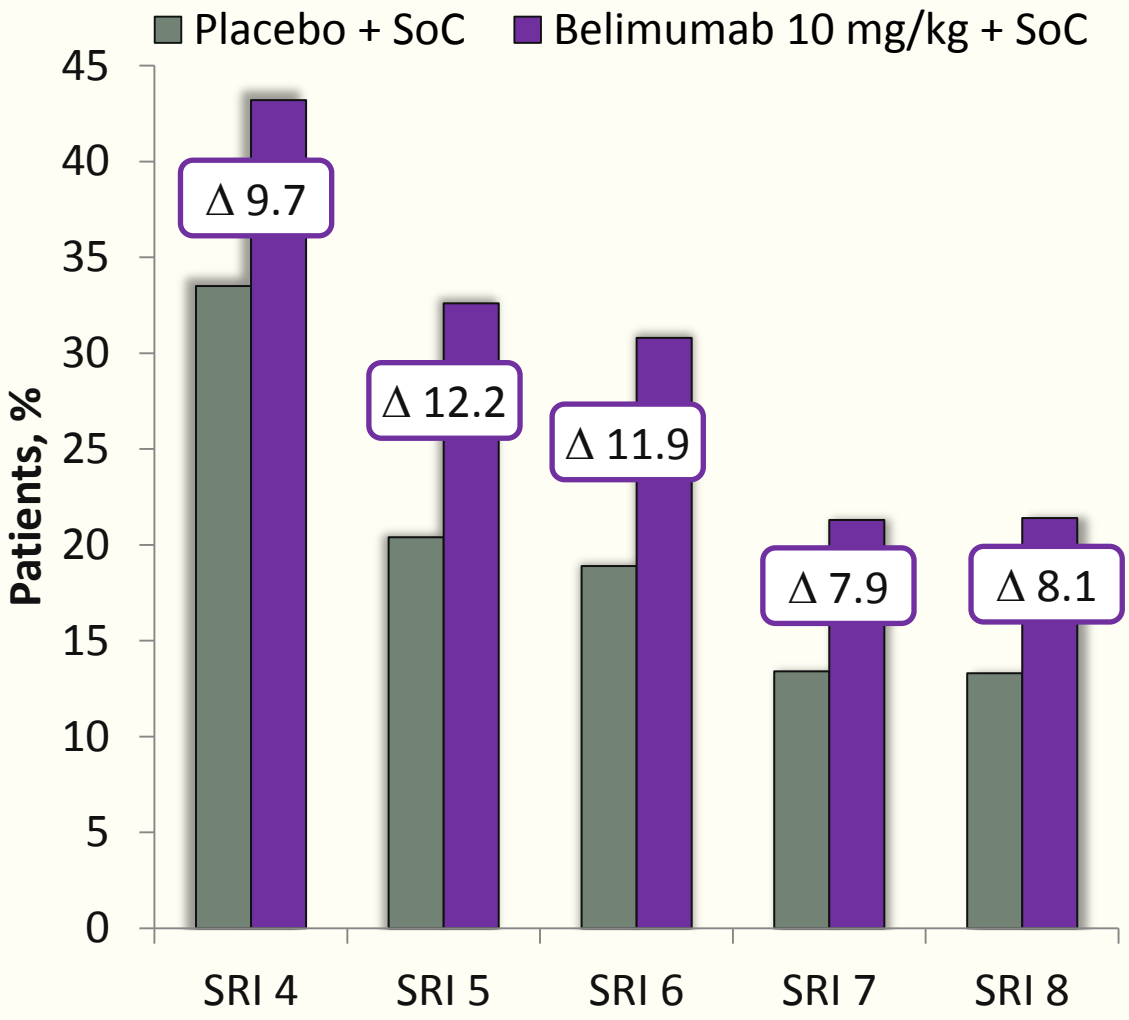
1. Benlysta® (belimumab) SmPC. GlaxoSmithKline (UK). May 2012;
2. Navarra SV, *et al. Lancet* 2011; 377:721–731;
3. Furie RA, *et al. Arthritis Rheum* 2011; 63:3918–3930;
4. van Vollenhoven RF, *et al. Ann Rheum Dis* 2012; 71:1343–1349.

Restrictions in the use of SoC therapies



1. Navarra SV, *et al. Lancet* 2011; 377:721–731;
2. Furie RA, *et al. Arthritis Rheum* 2011; 63:3918–3930.

BLISS-76: Modified SRI data at Week 52

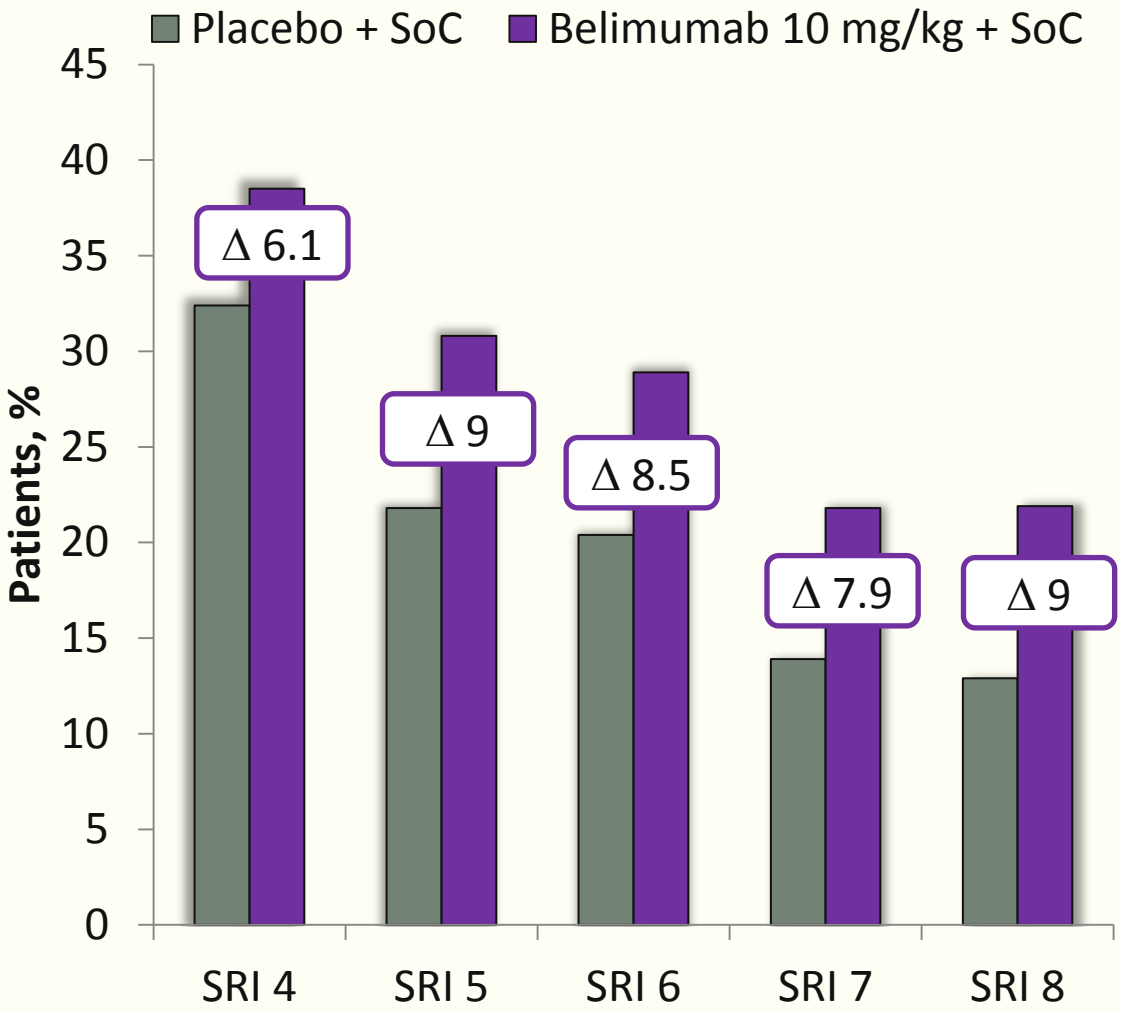


Clinical data summary
SRI at Week 52

Trial	Placebo + SoC	Belimumab + SoC	Δ	*P*-value
BLISS-52[1]	43.6%	57.6%	14	0.0006
BLISS-76[2]	33.5	43.2	9.7	0.02
Pooled[3]	38.8	50.6	11.8	<0.001

1. Navarra SV, *et al. Lancet* 2011; 377:721–731;
2. Furie RA, *et al. Arthritis Rheum* 2011; 63:3918–3930;
3. van Vollenhoven RF, *et al. Ann Rheum Dis* 2012; 71:1343–1349.

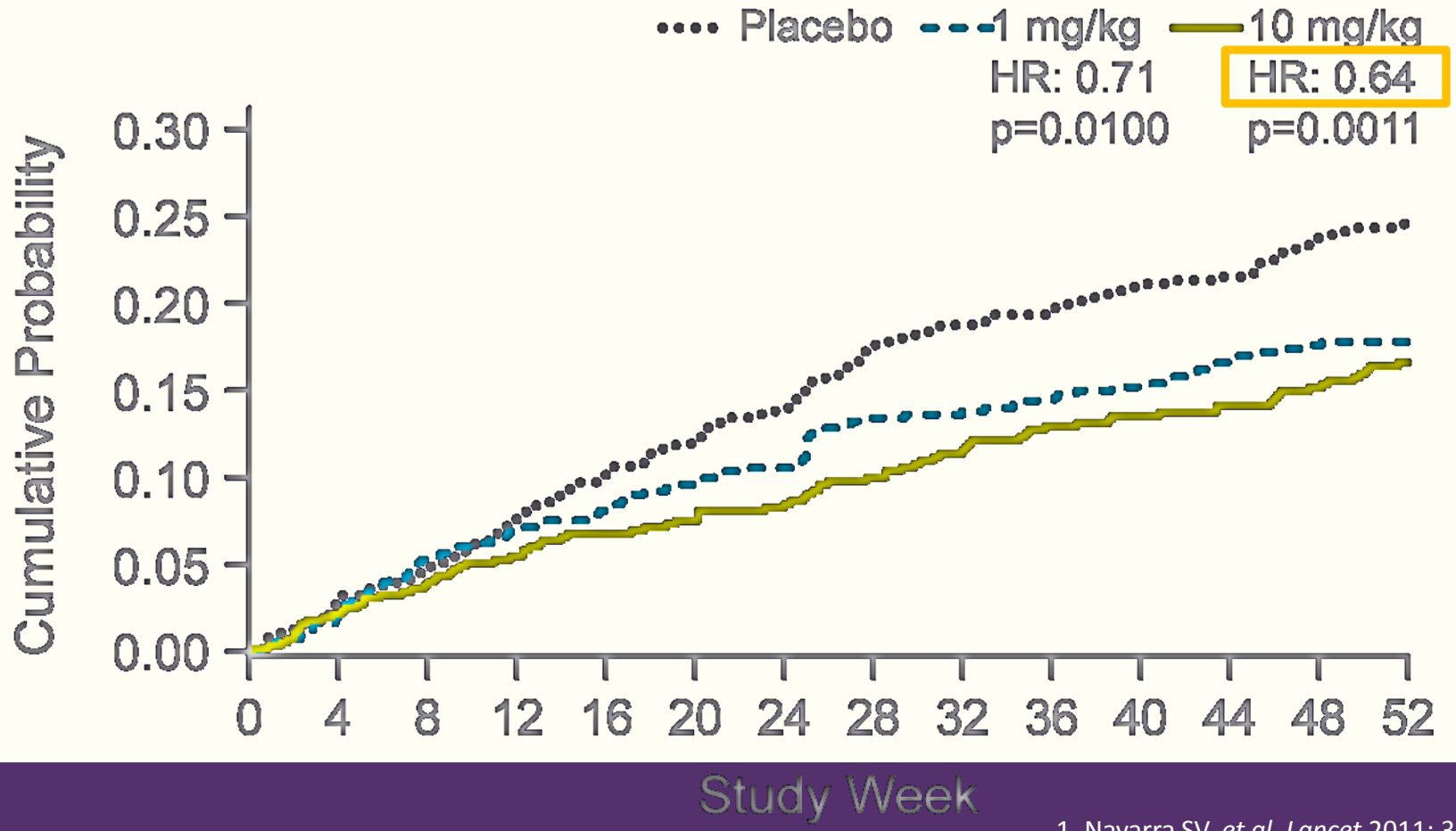
BLISS-76: Modified SRI data at Week 76



Furie RA, *et al. Arthritis Rheum* 2011; 63:3918–3930.

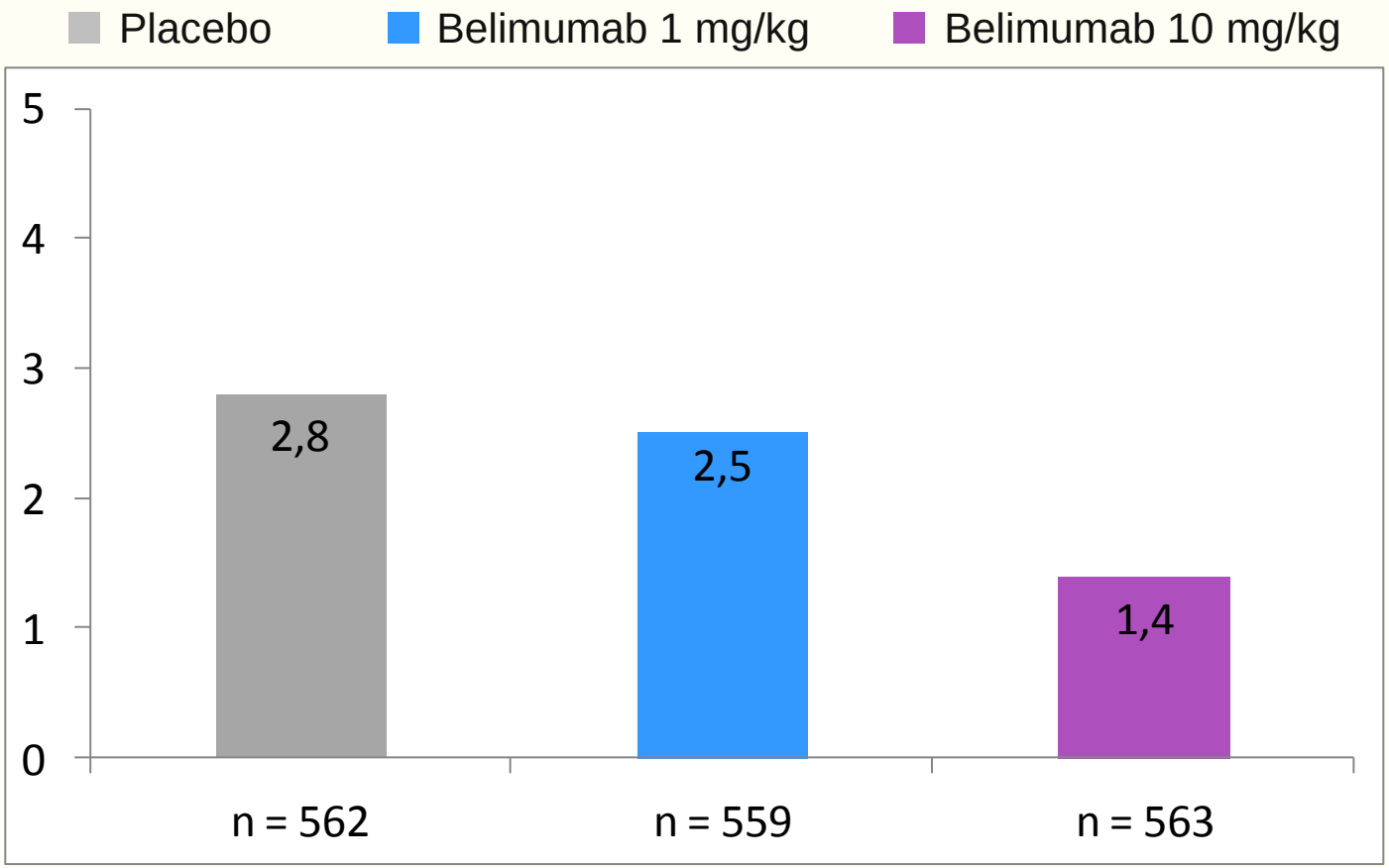
Benlysta reduces flares

- ✓ Μειωμένος κίνδυνος εξάρσεων ανεξάρτητα της κλινικής ανταπόκρισης SRI
- ✓ Κατά το 2ο μισό μέρος των μελετών η μείωση των σοβαρών εξάρσεων στην ομάδα του belimumab προσέγγισε το 50%



1. Navarra SV, *et al. Lancet* 2011; 377:721–731;
2. Furie RA, *et al. Arthritis Rheum* 2011; 63:3918–3930.

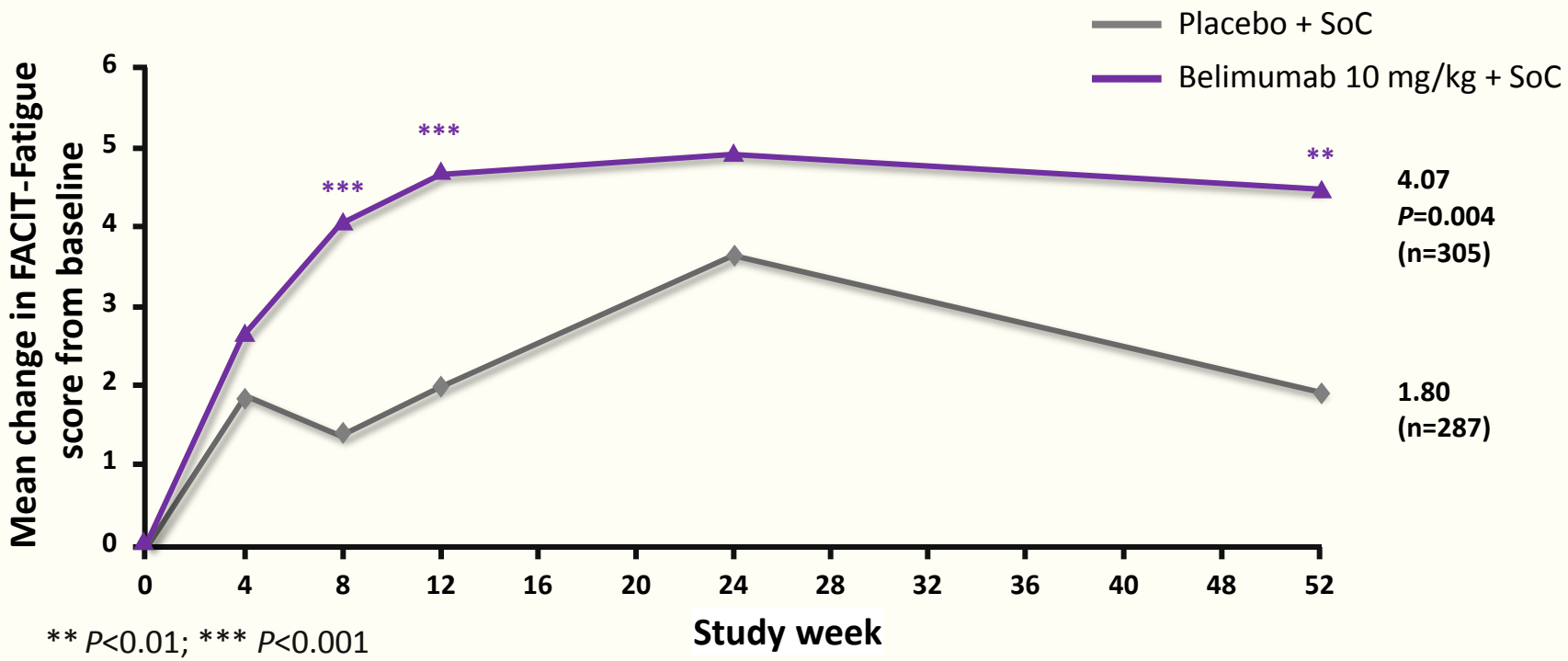
Renal Flare Rate Over 52 Weeks



[a]Renal flares as defined by Alarcón-Segovia D *et al.* Arthritis Rheum. 2003; 48: 442-54
Dooley MA *et al. Lupus* 2013 22: 63

Benlysta reduces fatigue

- Fatigue is one of the symptoms most commonly reported by patients with SLE
- FACIT-Fatigue scores were significantly improved with Benlysta 10 mg/kg

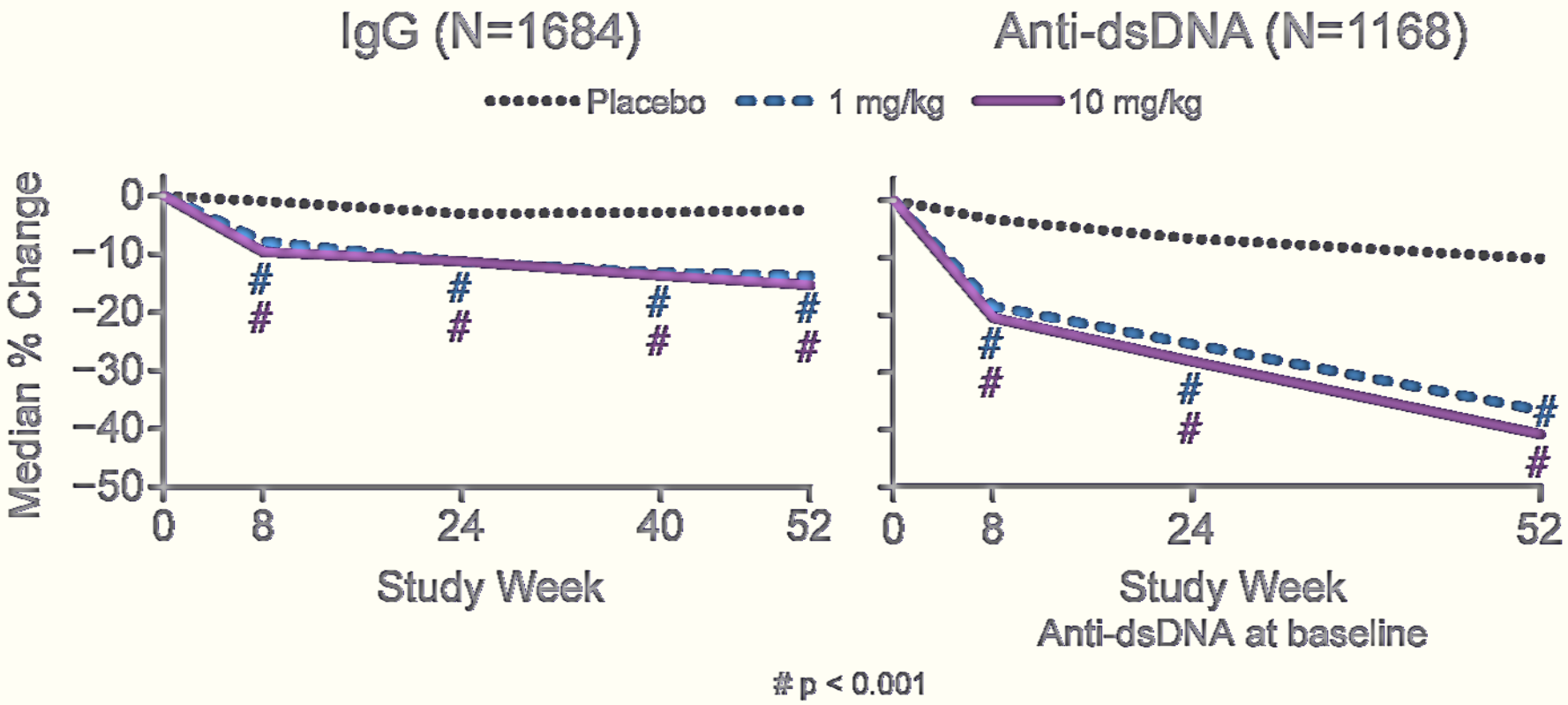


** *P*<0.01; *** *P*<0.001

HDA = patients with high disease activity at baseline, low complement factor 3 (<90 mg/dL) and/or complement factor 4 (<16 mg/dL) and anti-dsDNA ≥30 IU/mL at baseline.

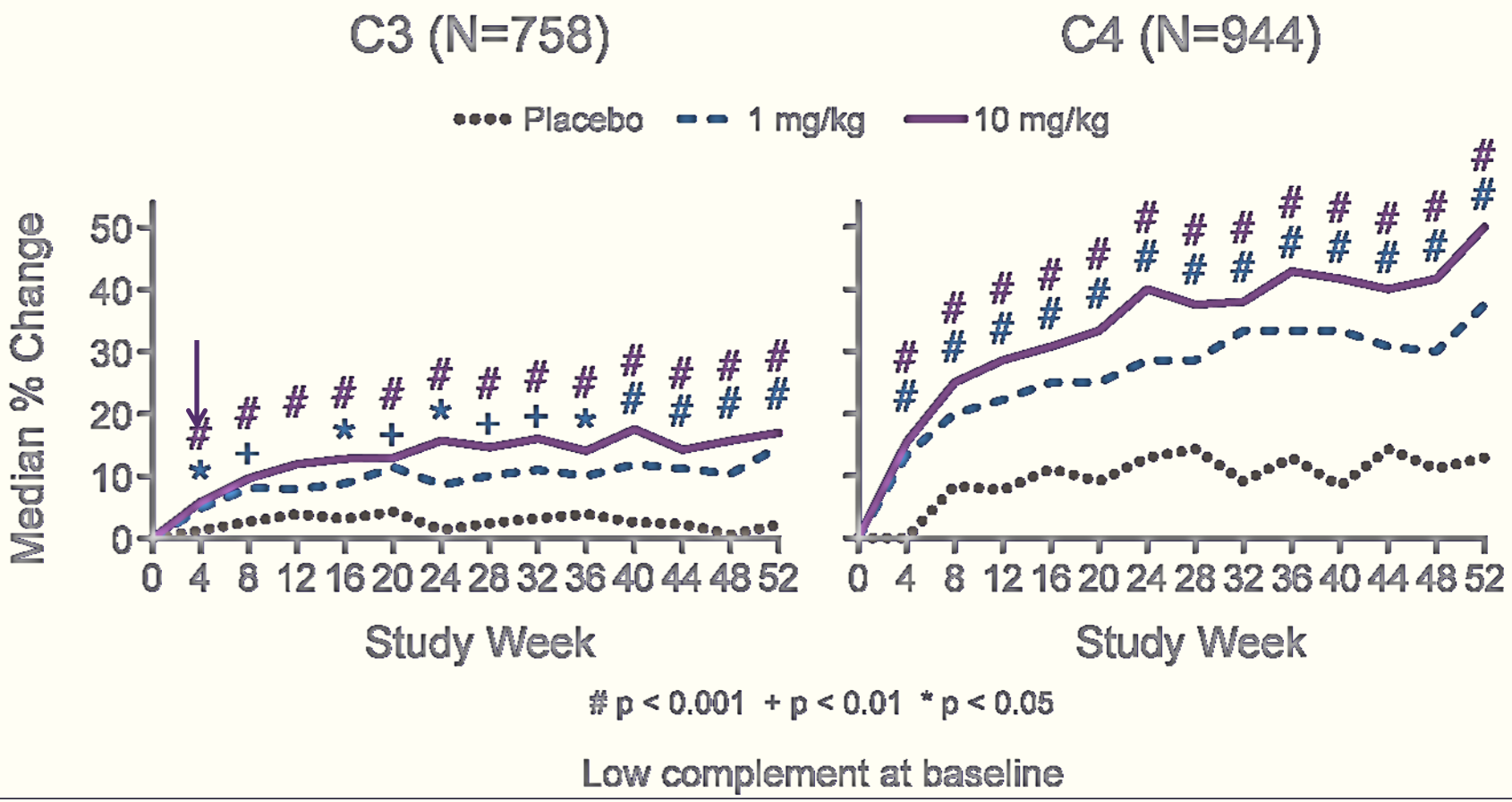
van Vollenhoven RF, et al. *Ann Rheum Dis* 2012; 71:1343–1349.

Immunoglobulin and Anti-dsDNA



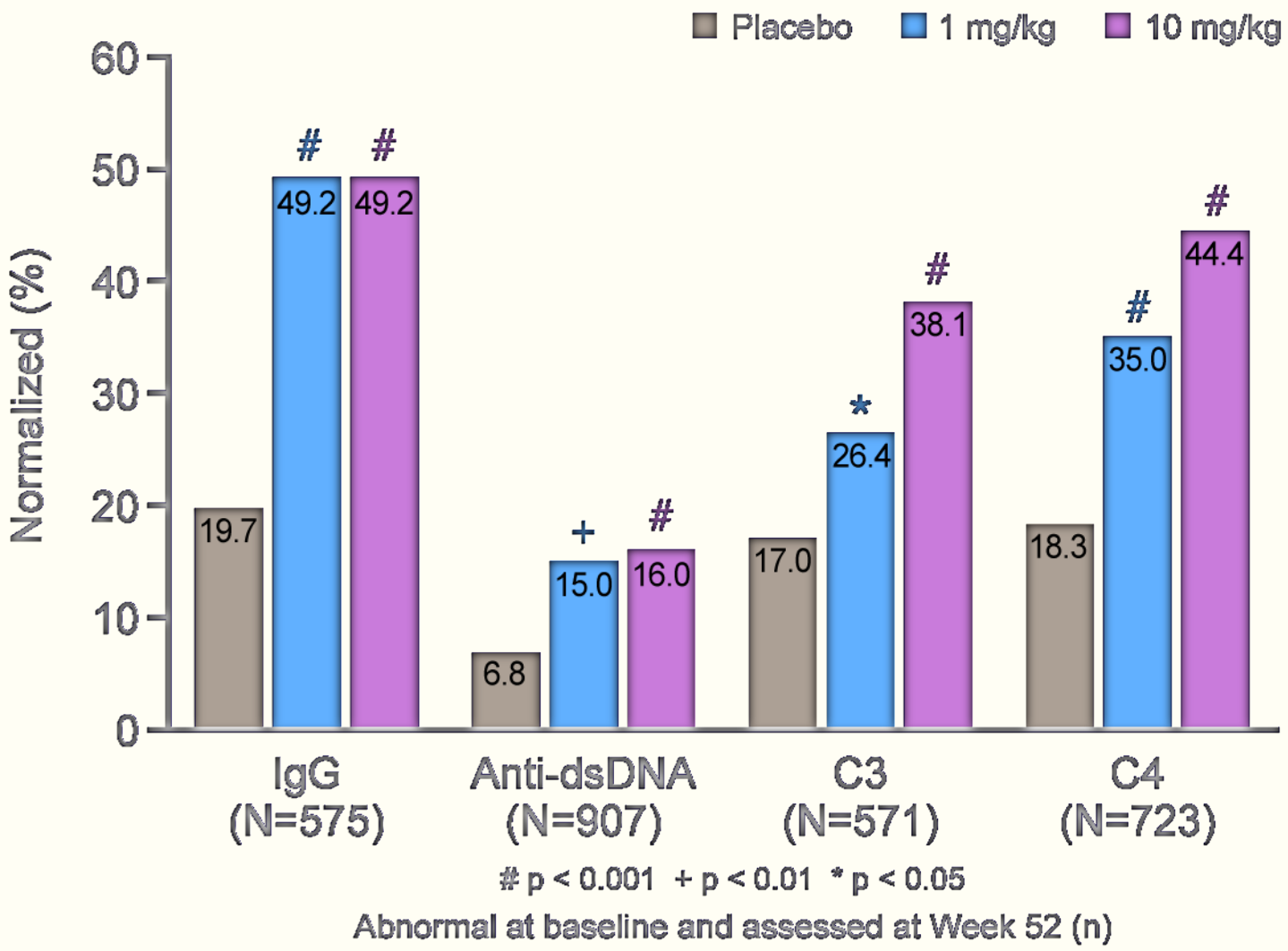
1. Navarra SV, *et al. Lancet* 2011; 377:721–731;
2. Furie RA, *et al. Arthritis Rheum* 2011; 63:3918–3930.

Complement

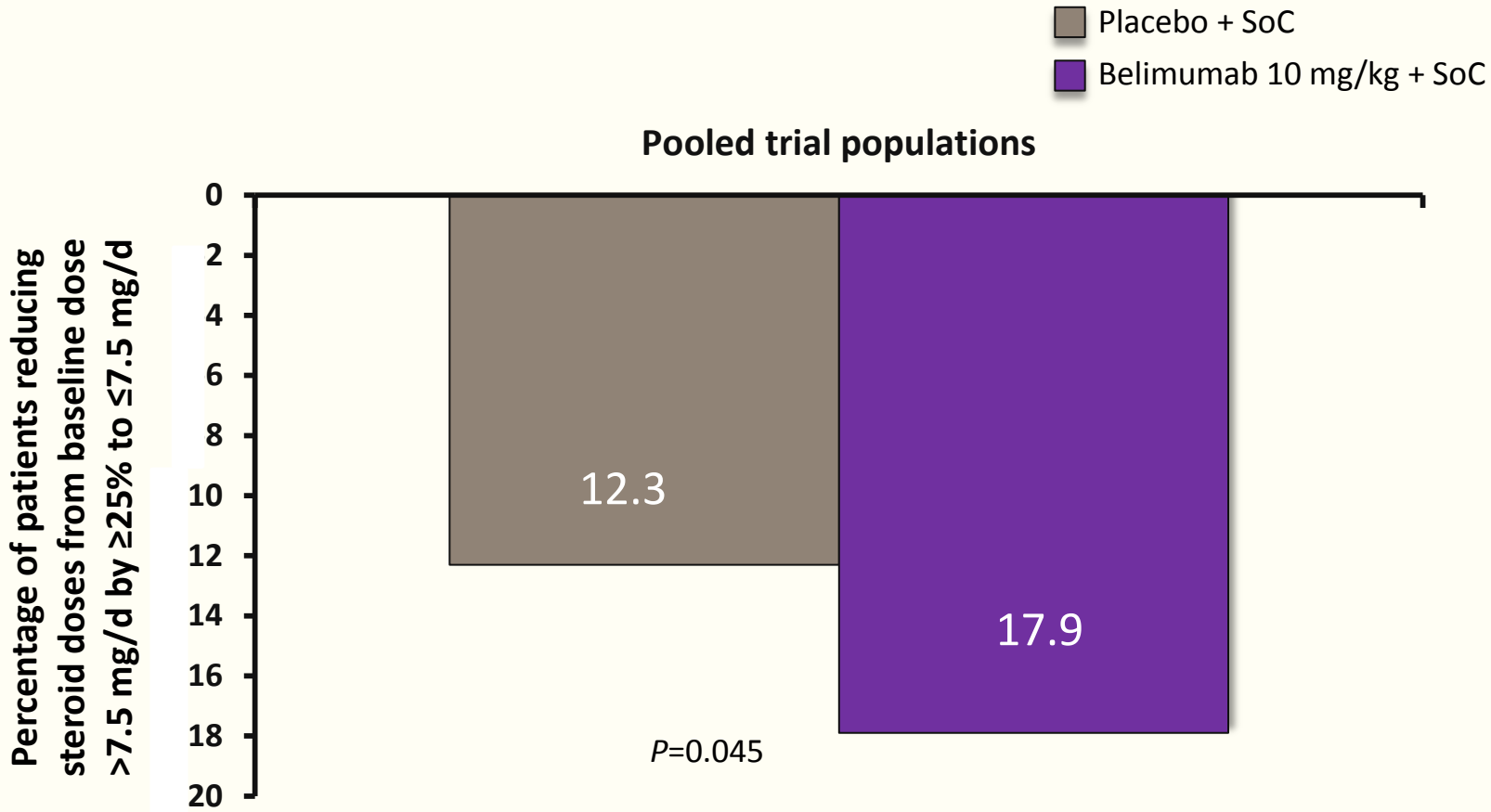


1. Navarra SV, *et al. Lancet* 2011; 377:721–731;
2. Furie RA, *et al. Arthritis Rheum* 2011; 63:3918–3930.

Normalization of Serological Activity



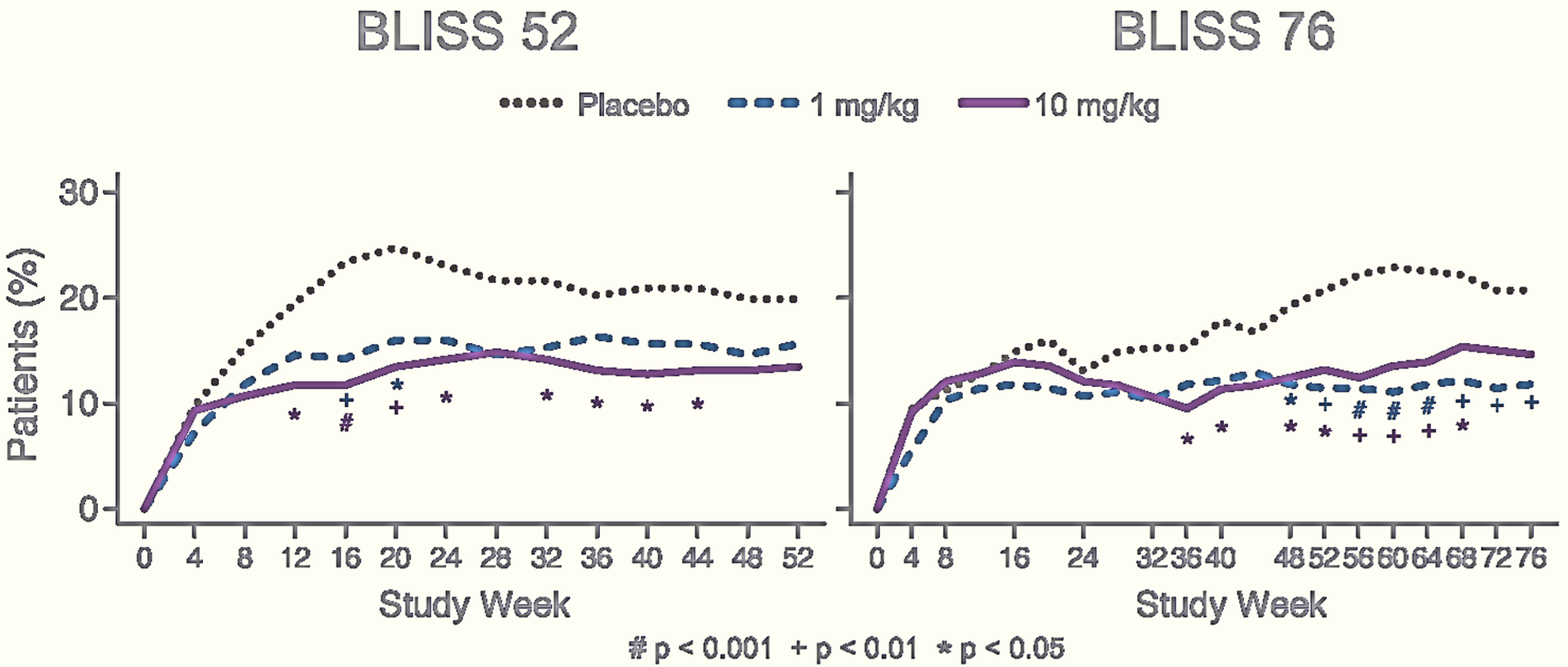
Changes in corticosteroid use during Weeks 40–52



- Corticosteroid tapering was not mandated in the study protocol and was performed at the investigators' discretion[1,2]
- Dose increases beyond defined limits resulted in patients being defined as a treatment failure[1,2]

1. Benlysta® (belimumab) SmPC. GlaxoSmithKline (UK). May 2012;
2. van Vollenhoven RF, *et al. Ann Rheum Dis* 2012; **71**:1343–1349.

Increase in Steroid Use Over Time



Clinically meaningful improvement in the BLISS trials

Outcome	Week	Placebo + SoC n (%)	Belimumab 10 mg/kg + SoC n (%)	P-value
SELENA-SLEDAI reduction of 7 from baseline	16	67 (15.3)	95 (21.2)	0.01
SELENA-SLEDAI reduction of 4 in high disease activity subgroup	8	91 (31.7)	120 (39.3)	0.01
FACIT-Fatigue, n (median improvement)	8	553 (1.5)	547 (3.0)	0.005

BL = baseline; SS = SELENA-SLEDAI.

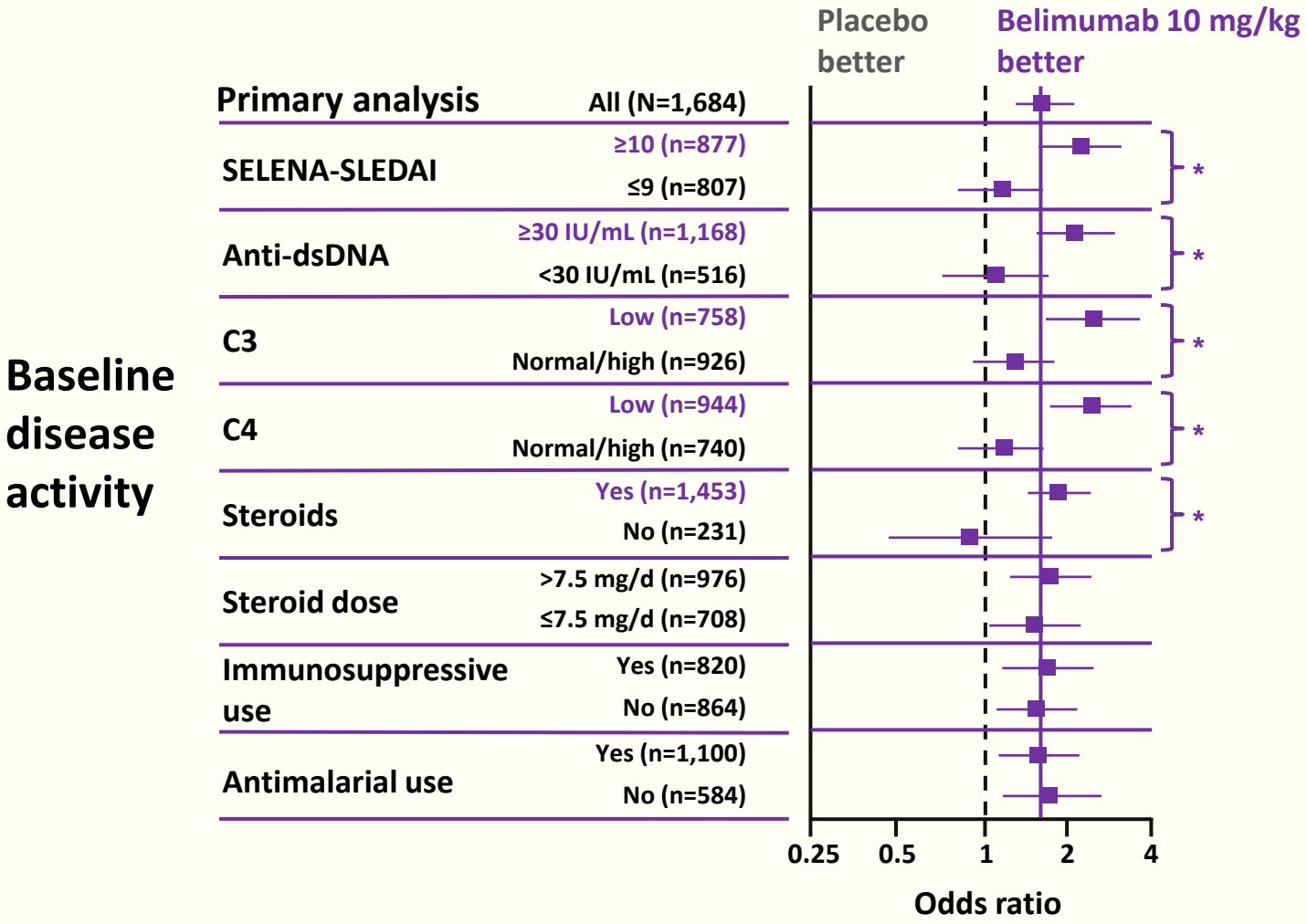
Doria A, *et al. Ann Rheum Dis* 2012; 71(Suppl3):535.

Which patients achieved greatest clinical benefit?

Univariate and multivariate analyses of pre-specified subgroups were performed to identify baseline disease characteristics associated with the SRI response

van Vollenhoven RF, *et al. Ann Rheum Dis* 2012; **71**:1343–1349.

Patients with high disease activity show better response



* $P<0.1$

SELENA-SLEDAI = Safety of Estrogens in Lupus Erythematosus National Assessment–Systemic Lupus Erythematosus Disease Activity Index; SRI = Systemic Lupus Erythematosus Responder Index.

van Vollenhoven RF, *et al. Ann Rheum Dis* 2012; **71**:1343–1349.

Safety

Adverse event profiles were comparable in both treatment arms

Pooled 52&76 Phase II

	Placebo + SoC, % (n=675) [1–3]	Belimumab 10 mg/kg + SoC, % (n=674) [1–3]
At least one:		
Adverse event	92.4	92.7
Serious adverse event	15.9	17.4
Severe adverse event	15.4	15.3
Discontinuation due to adverse event	7.1	6.7
Common adverse events (occurring in >10%)		
Headache	20.7	21.1
Upper respiratory tract infection	19.3	17.5
Arthralgia	16.6	16.2
Nausea	12.1	14.7
Urinary tract infection	12.1	12.9
Diarrhoea	9.2	11.9
Fatigue	10.4	9.8
Serious adverse events (occurring in >1%)		
Pneumonia	1.5	0.9
Pyrexia	0.4	1.3
Urinary tract infection	0.6	0.7
Cellulitis	0.3	0.1
Other events of special interest		
Depression	3.7	5.2
Suicidality†	0.1	0.1

† Based on Karassa FB *et al. Ann Rheum Dis* 2003; **62**:58–60.

1. Benlysta® (belimumab) SmPC. GlaxoSmithKline (UK). March 2012;
2. Wallace DJ, *et al. Ann Rheum Dis* 2011; **70**:318;
3. Wallace D, *et al. ACR* 2010 Annual Meeting; Poster.

Similar rates of infection were reported in both treatment arms

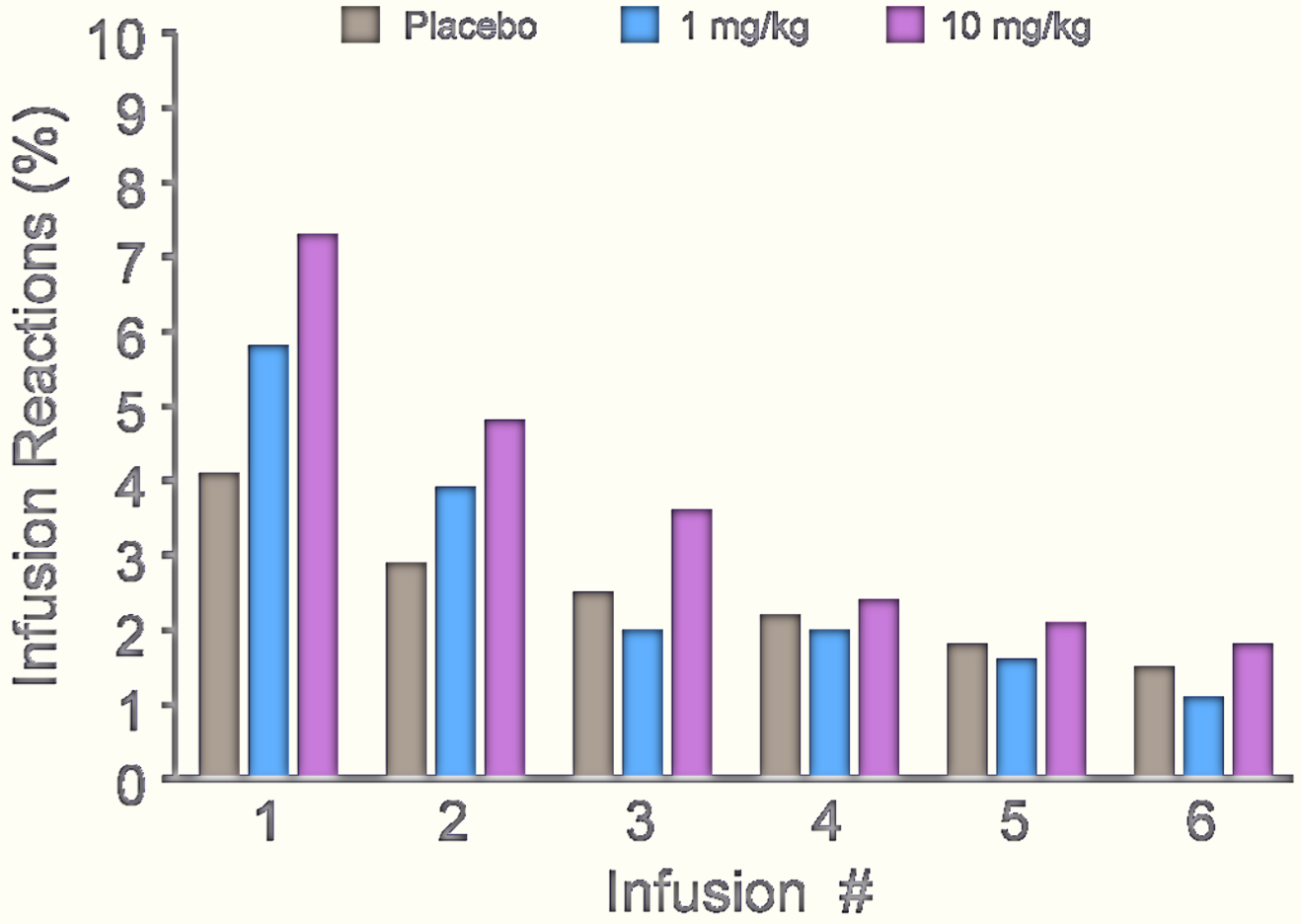
Pooled 52&76 Phase II

	Placebo + SoC, % (n=675)[1–3]	Belimumab 10 mg/kg + SoC, % (n=674)[1–3]
Patients with ≥1:		
Adverse event infection in general	66.7	69.9
Adverse event infection resulting in discontinuation	1.0	0.6
Serious and/or severe adverse event infection	6.7	5.9
Adverse event infection of special interest		
Cellulitis	6.4	6.4
Sepsis	0.4	0.9
Fungal	3.3	2.5
Herpes infections	8.0	6.5
All respiratory	48.4	51.9
Lower respiratory	8.6	12.0
Possible opportunistic	0	0.3†

† One report of *Acinetobacter* bacterium and one of disseminated cytomegalovirus.

1. Benlysta® (belimumab) SmPC. GlaxoSmithKline (UK). March 2012;
2. Wallace DJ, *et al. Ann Rheum Dis* 2011; **70**:318;
3. Wallace D, *et al. ACR* 2010 Annual Meeting; Poster.

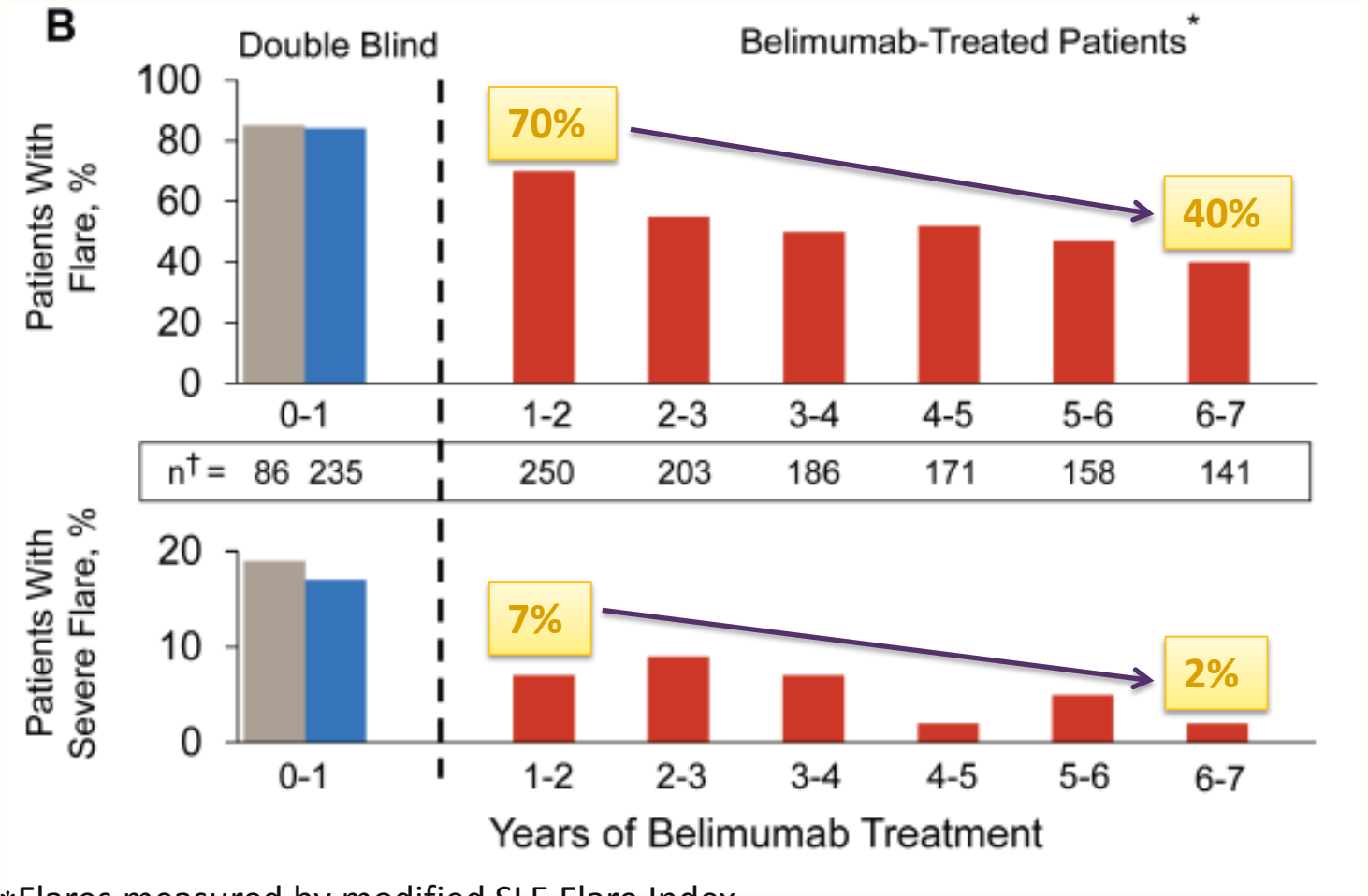
Infusion Reactions for the First 6 Infusions



Belimumab Plus Standard Therapy Over 7 Years in Patients with SLE

Ginzler EM *et al*, J Rheumatol 2013

Decreased frequency of flares



*Flares measured by modified SLE Flare Index

Real-world data: OBSERVE study

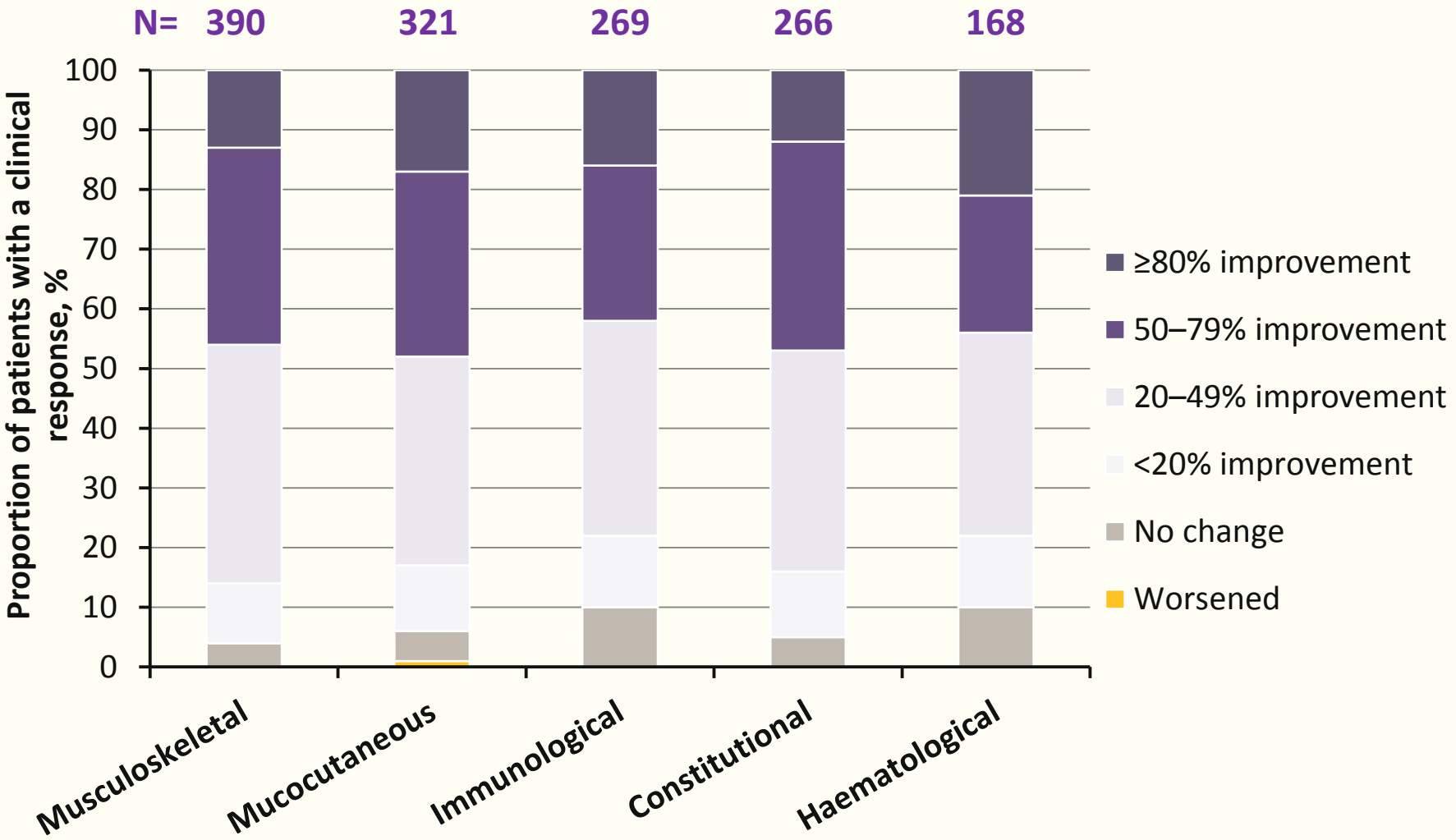
Baseline patient characteristics

Baseline characteristics		(N=501)
Mean age, years		41.3
Gender, %	Female	89
Ethnicity, %	Caucasian	53
	Black/African-American	24
	Hispanic	18
	Other	5
Diagnosed with SLE <5 yrs ago, %		56
Severity* of SLE at belimumab initiation, %	Mild	3
	Moderate	77
	Severe	20
Concomitant SLE medications, %	Oral steroids	78
	Antimalarials	70
	Immunosuppressants	61
	NSAIDs	16
Mean prednisone equivalent dose at belimumab initiation		19.9 mg/day

* Severity was assessed by physicians using clinical judgment.

Collins CE, *et al. Arthritis Rheum* 2012; 64:S1109
Askanase AD et al. *Rheum Dis Clin N Am* 2014; 40 : 507–517.

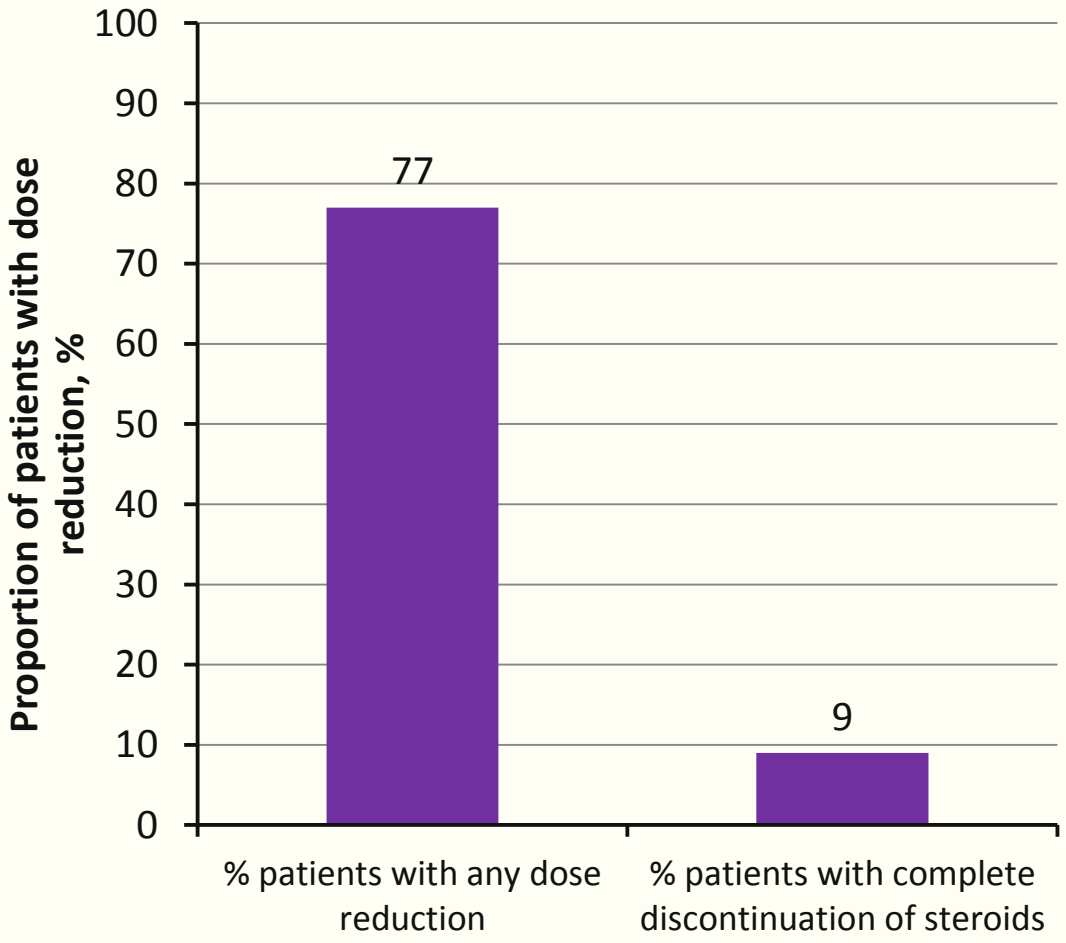
Changes in commonly involved organ domains

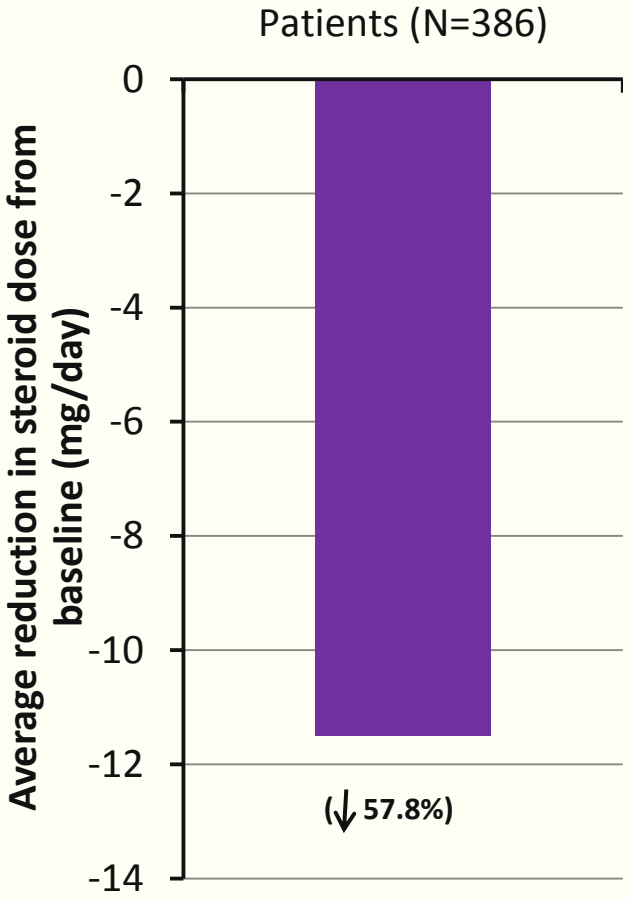


Note: Only the top 5 individual clinical manifestations are presented.

Collins CE, *et al. Arthritis Rheum* 2012; 64:S1109
Askanase AD et al. *Rheum Dis Clin N Am* 2014; 40 : 507–517.

Clinical practice evidence of steroid-sparing effect





Collins CE, *et al. Arthritis Rheum* 2012; 64:S1109
Askanase AD et al. *Rheum Dis Clin N Am* 2014; 40 : 507–517.

Συμπεράσματα

- Το Benlysta αποτελεί την 1η εγκεκριμένη βιολογική θεραπεία που στοχεύει ειδικά στην παθογένεια του ΣΕΛ
- Η προσθήκη του στη συμβατική θεραπεία οδηγεί σε
  - βελτίωση της κλινικής & ορολογικής ενεργότητας
  - μείωση του κινδύνου υποτροπών
  - μείωση της δόσης κορτικοστεροειδών και
  - βελτίωση του αισθήματος κόπωσης & ποιότητας ζωής
- Συμβάλλει στη σύγχρονη, πολυεπίπεδη διαχείριση των ασθενών με ΣΕΛ (μείωση ενεργότητας αλλά και πρόληψη υποτροπών)

Ασθενείς που είναι πιθανόν να ωφεληθούν από το Benlysta

- Εμμένουσα ενεργότητα παρά τη λήψη συμβατικής αγωγής
  - μέτρια έως υψηλή ενεργότητα
  - υψηλότερη ενεργότητα (SLEDAI ≥ 8) σχετίζεται με μεγαλύτερη ανταπόκριση, ιδίως αν σχετίζεται με ορολογική ενεργότητα (θετικά anti-dsDNA, χαμηλό συμπλήρωμα)
  - αδυναμία μείωσης κορτικοστεροειδών σε <7,5 mg/ημέρα
- Υψηλός κίνδυνος εξάρσεων
  - ιστορικό συχνών εξάρσεων
  - υπολειπόμενη κλινική + ορολογική ενεργότητα

1. Pamfil C, Fanouriakis A, Boumpas DT. *Reviews in Health Care* 2012; 3(3): 209-222.