II curs de malalties autoimmunes SCR 2014
Curs Societat Catalana de Reumatologia
26 i 27 de setembre de 2014

EXPERIENCIA CLÍNICA CON BELIMUMAB EN EL TRATAMIENTO DEL LES

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Sección de Enfermedades Sistémicas Autoinmunes
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H.U. Puerta de Hierro Majadahonda. Majadahonda (Madrid)

ÍNDICE

- Necesidades no cubiertas en lupus
- Perfil de paciente respondedor
- Seguridad y eficacia a largo plazo
- Efectividad en práctica clínica habitual

NECESIDADES NO CUBIERTAS EN LUPUS

OBJETIVOS DEL TRATAMIENTO

- Eliminar la actividad inflamatoria
- Preservar la función de los órganos

- Mantener la esperanza de vida
- Mantener la calidad de vida

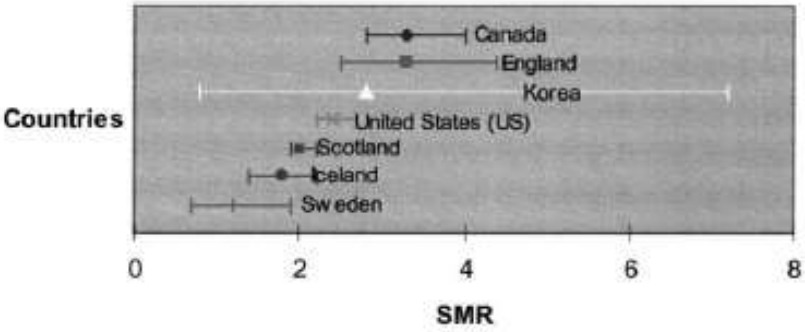
- Evitar efectos secundarios
- Minimizar el daño acumulado

Mortality in Systemic Lupus Erythematosus

S. Bernatsky,[1] J.-F. Boivin,[2] L. Joseph,[3] S. Manzi,[4] E. Ginzler,[5] D. D. Gladman,[6] M. Urowitz,[6] P. R. Fortin,[6] M. Petri,[7] S. Barr,[8] C. Gordon,[9] S.-C. Bae,[10] D. Isenberg,[11] A. Zoma,[12] C. Aranow,[13] M.-A. Dooley,[14] O. Nived,[15] G. Sturfelt,[15] K. Steinsson,[16] G. Alarcón,[17] J.-L. Senécal,[18] M. Zummer,[19] J. Hanly,[20] S. Ensworth,[21] J. Pope,[22] S. Edworthy,[8] A. Rahman,[11] J. Sibley,[23] H. El-Gabalawy,[24] T. McCarthy,[24] Y. St. Pierre,[1] A. Clarke,[1] and R. Ramsey-Goldman[25]

Table 2. Unadjusted SMR estimates, stratified by sex, age, and SLE duration*

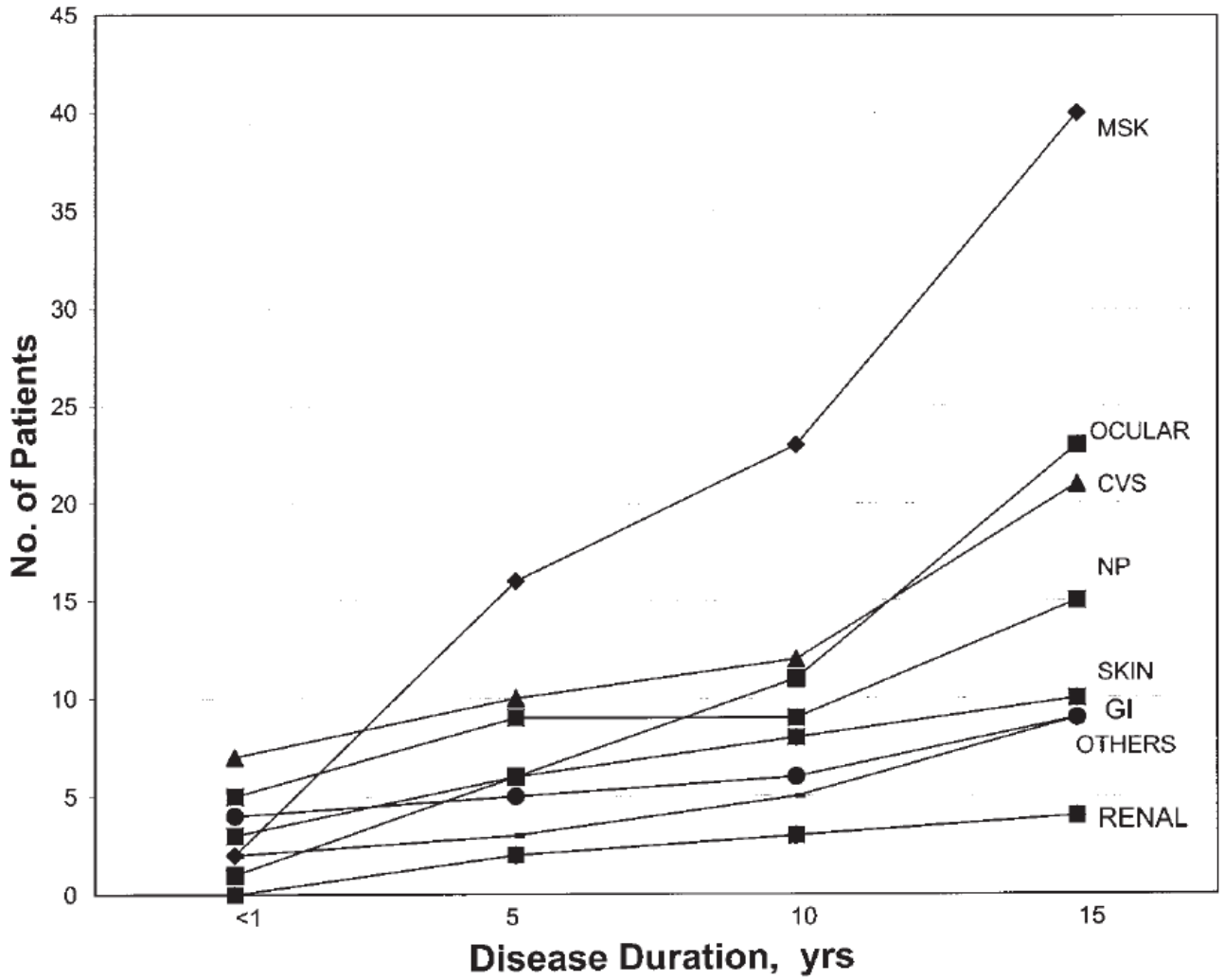
	SMR (95% CI)
Sex	
Female	2.5 (2.3–2.7)
Male	1.9 (1.7–2.2)
Age, years	
<40†	10.7 (9.5–11.9)
40–59	3.7 (3.3–4)
≥60	1.4 (1.3–1.5)
SLE duration, years	
<1	5.4 (4.7–6.3)
1–4	2.5 (2.2–2.8)
5–9	2.1 (1.9–2.4)
10–19	2.0 (1.8–2.3)
≥20	2.0 (1.7–2.4)



ARTHRITIS & RHEUMATISM
Vol. 54, No. 8, August 2006, pp 2550–2557

Accrual of Organ Damage Over Time in Patients with Systemic Lupus Erythematosus

DAFNA D. GLADMAN, MURRAY B. UROWITZ, PROTON RAHMAN, DOMINIQUE IBAÑEZ, and LAI-SHAN TAM

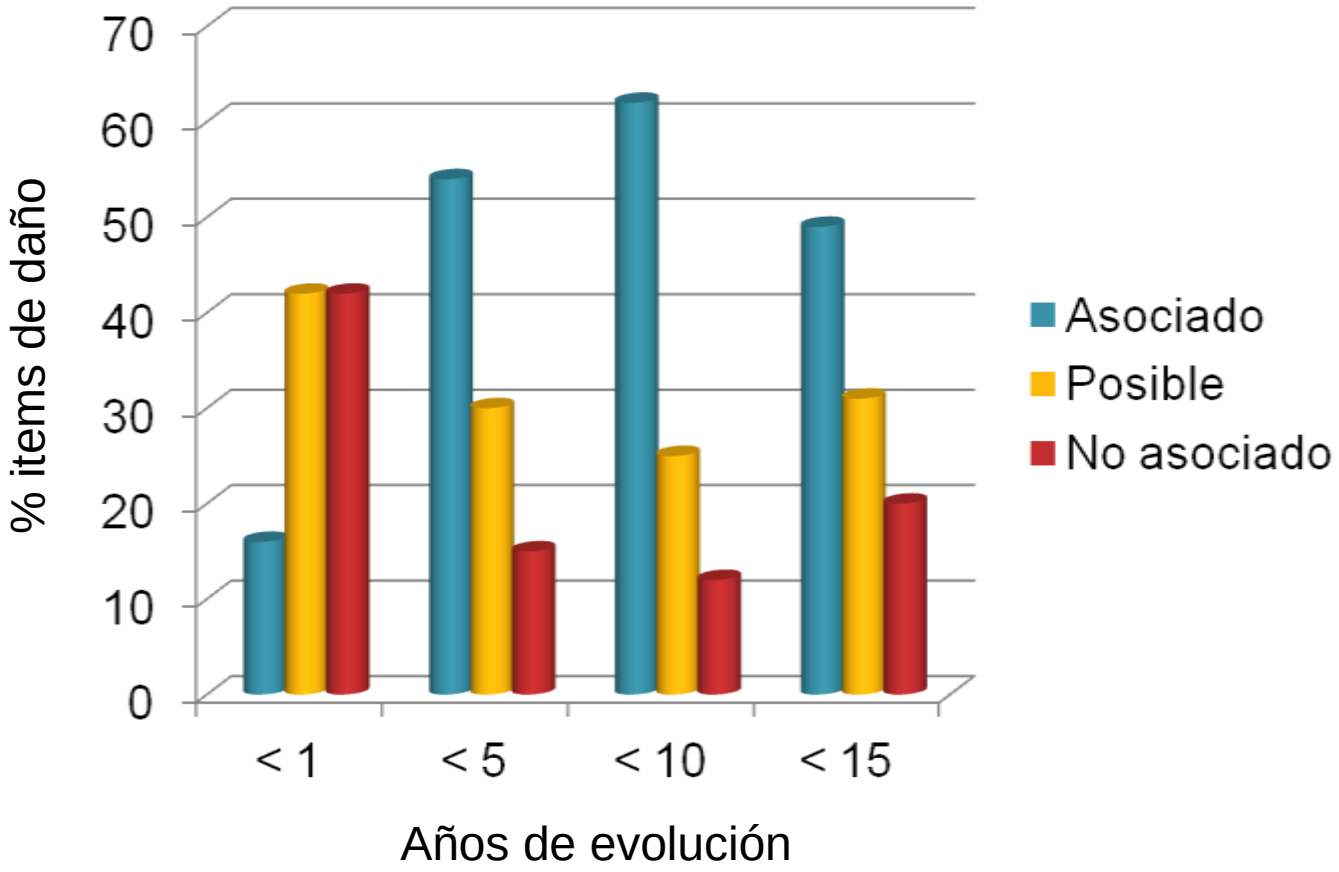


J Rheumatol 2003;30:1955.

Accrual of Organ Damage Over Time in Patients with Systemic Lupus Erythematosus

DAFNA D. GLADMAN, MURRAY B. UROWITZ, PROTON RAHMAN, DOMINIQUE IBAÑEZ, and LAI-SHAN TAM

Asociación del daño acumulado al uso de GC



J Rheumatol 2003;30:1955.

ABRAHAM ZONANA-NACACH, SUSAN G. BARR, LAURENCE S. MAGDER, and MICHELLE PETRI

Table 2. Prednisone use in the Hopkins Lupus Cohort during different periods after diagnosis

	Years after SLE diagnosis		
Prednisone use	0–5 years*	6–10 years†	11–15 years‡
Percentage of time			
Never	56 (17%)	37 (21%)	15 (18%)
1–49%	57 (18%)	19 (11%)	10 (12%)
50–99%	90 (27%)	19 (11%)	10 (12%)
Always	119 (37%)	101 (57%)	46 (57%)
Mean daily dose			
1–10 mg	96 (36%)	63 (45%)	40 (60%)
11–20 mg	104 (39%)	52 (37%)	18 (27%)
21–30 mg	43 (16%)	18 (13%)	7 (11%)
≥31 mg	23 (9%)	6 (4%)	1 (2%)

ABRAHAM ZONANA-NACACH, SUSAN G. BARR, LAURENCE S. MAGDER, and MICHELLE PETRI

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ABRAHAM ZONANA-NACACH, SUSAN G. BARR, LAURENCE S. MAGDER, and MICHELLE PETRI

Table 4. Risk of organ damage associated with cumulative corticosteroid dose*

Damage item	No. of events	Adjusted RR (95% CI)†	*P*
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

Relationship between Prednisone, Lupus Activity and Permanent Organ Damage

Mae Thamer, PhD[1], Miguel A. Hernán, MD[2], Yi Zhang, MS[1], Dennis Cotter, MSE[1], and Michelle Petri, MD, MPH[3]

Hazard ratio of organ damage (n = 141) by cumulative average dose of prednisone.

Cumulative average prednisone dose (mg/month)			Unadjusted model			Conventionally-adjusted model*		
	% of patient months	no. of events	HR	95 % CI		HR	95 % CI	
0	35.9	34	*Ref*			*Ref*		
>0–180	37.0	49	1.58	1.00	2.50	**2.01**	**1.11**	**3.63**
>180–360	14.9	29	**2.10**	**1.24**	**3.55**	**2.46**	**1.17**	**5.16**
>360–540	6.7	18	**3.04**	**1.67**	**5.53**	**3.54**	**1.55**	**8.12**
>540	5.5	21	**4.19**	**2.35**	**7.47**	**4.10**	**1.74**	**9.65**

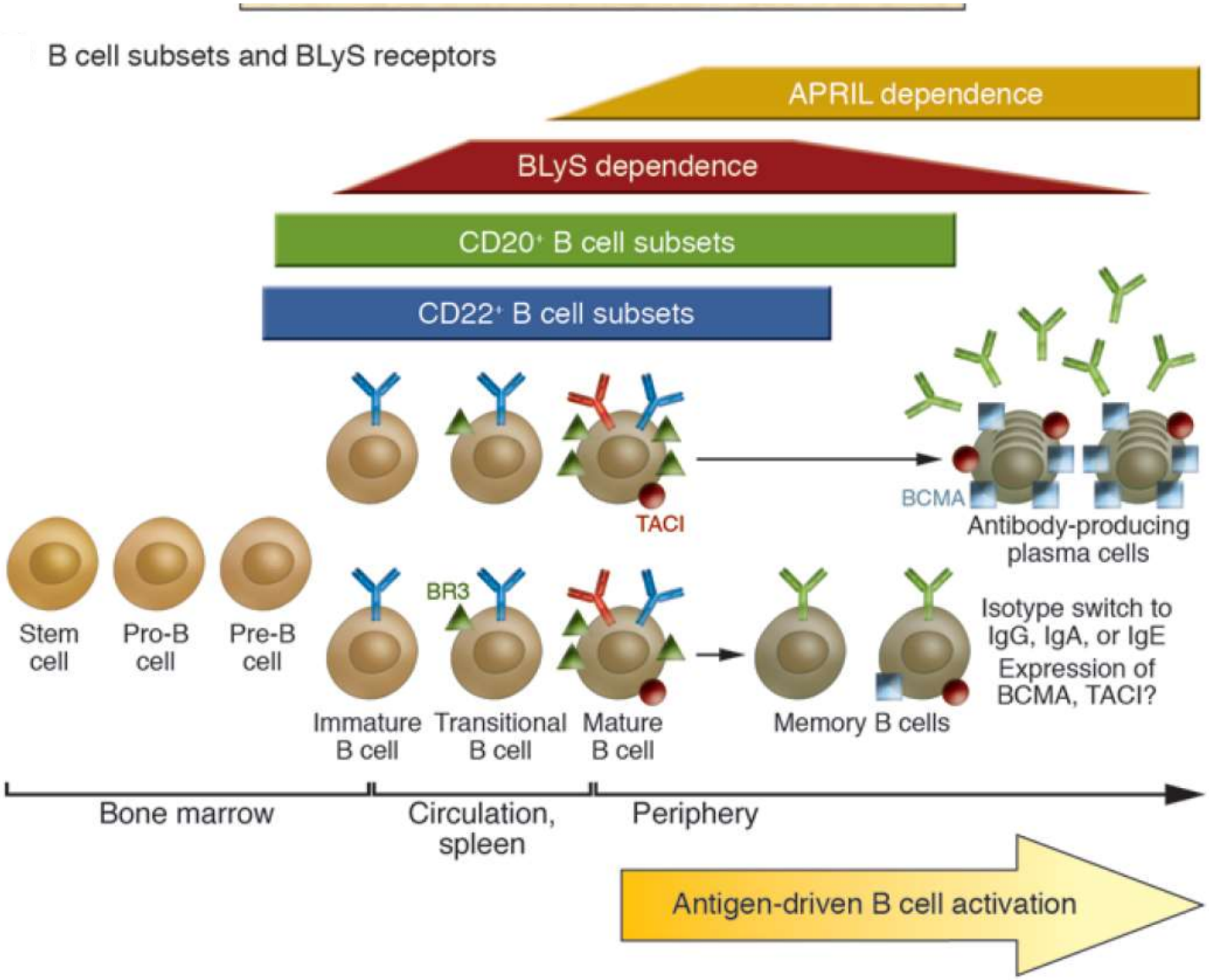
*Adjusted for age, sex, race/ethnicity, baseline prednisone dose, baseline SLE activity, baseline organ damage, and time-varying covariates.

J Rheumatol. 2009 March ; 36(3): 560–564.

P of prednisone in lupus stands for…

P of prednisone in lupus stands for…

POISON!

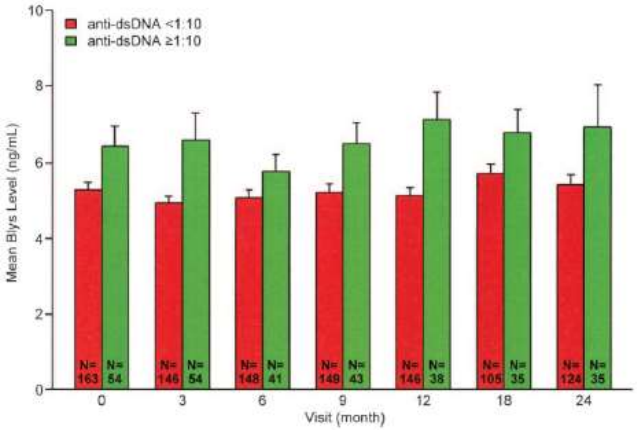


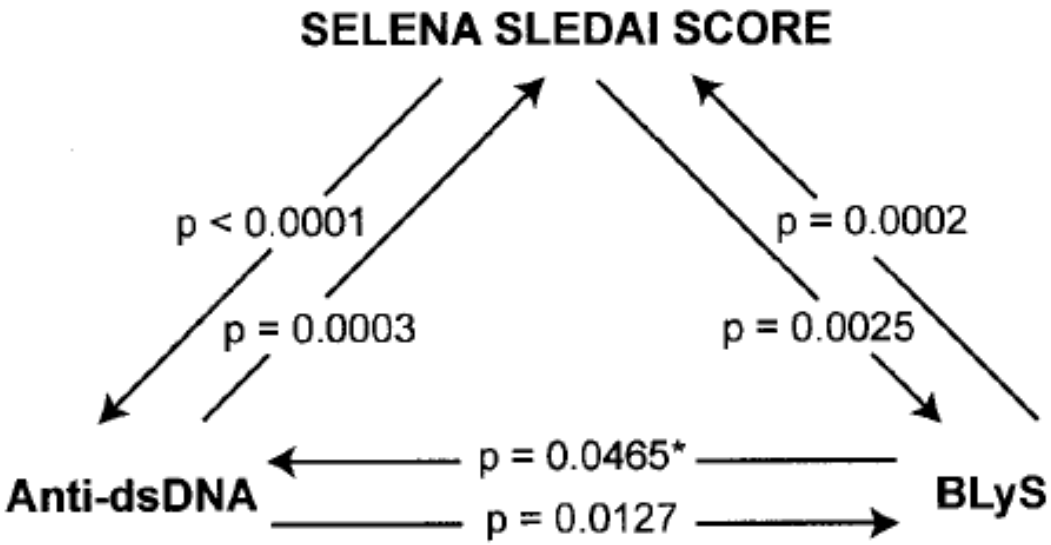
Cancro et al. 2009

Association of Plasma B Lymphocyte Stimulator Levels and Disease Activity in Systemic Lupus Erythematosus

ARTHRITIS & RHEUMATISM
Vol. 58, No. 8, August 2008, pp 2453–2459
DOI 10.1002/art.23678

Michelle Petri,[1] William Stohl,[2] Winn Chatham,[3] W. Joseph McCune,[4] Marc Chevrier,[5] Jeff Ryel,[5] Virginia Recta,[5] John Zhong,[5] and William Freimuth[5]





A Phase II, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study of Belimumab in Patients With Active Systemic Lupus Erythematosus

DANIEL J. WALLACE,[1] WILLIAM STOHL,[2] RICHARD A. FURIE,[3] JEFFREY R. LISSE,[4] JAMES D. McKAY,[5] JOAN T. MERRILL,[6] MICHELLE A. PETRI,[7] ELLEN M. GINZLER,[8] W. WINN CHATHAM,[9] W. JOSEPH McCUNE,[10] VIVIAN FERNANDEZ,[11] MARC R. CHEVRIER,[11] Z. JOHN ZHONG,[11] AND WILLIAM W. FREIMUTH[11]

- Estudio fase II, aleatorizado, doble-ciego, controlado con placebo, multicéntrico.

- > 18 años
- Criterios ACR para LES
- SELENA-SLEDAI ≥4
- Antecedente de ANA, anti -DNA, -Sm, -cardiolipina, -RNP, -Ro, -La.

- Se excluyeron pacientes con nefritis lúpica activa o afectación de SNC

- Cambio en SELENE-SLEDAI a la semana 24
- Tiempo a brote en 52 semanas

Arthritis & Rheumatism (Arthritis Care & Research)
Vol. 61, No. 9, September 15, 2009, pp 1168–1178

A Phase II, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study of Belimumab in Patients With Active Systemic Lupus Erythematosus

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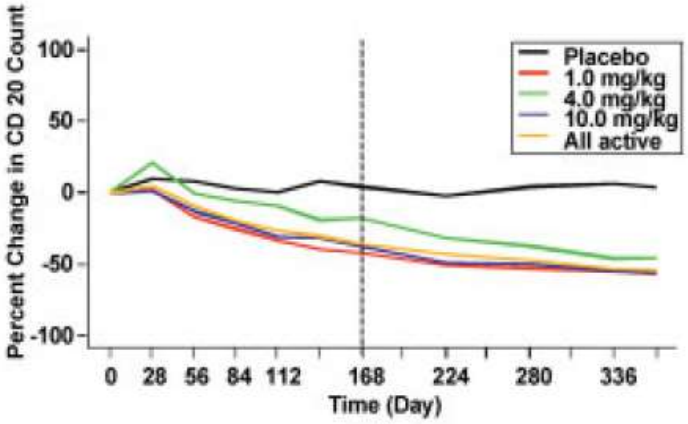

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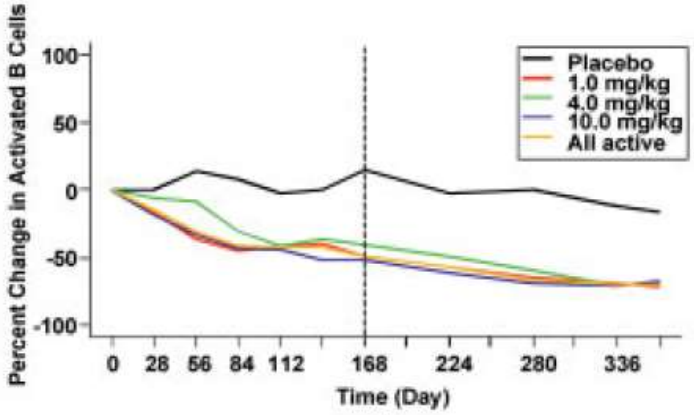

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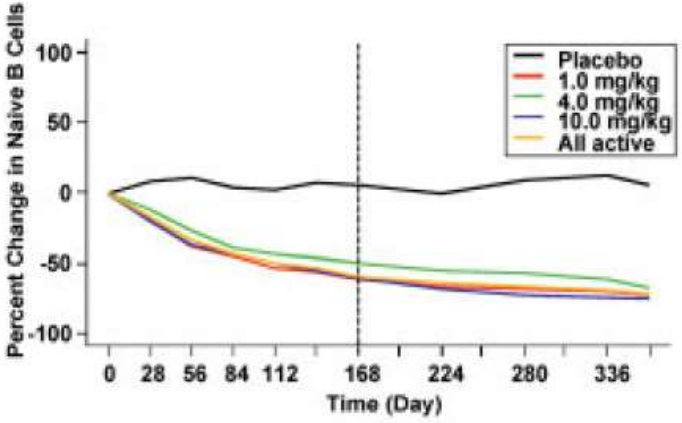

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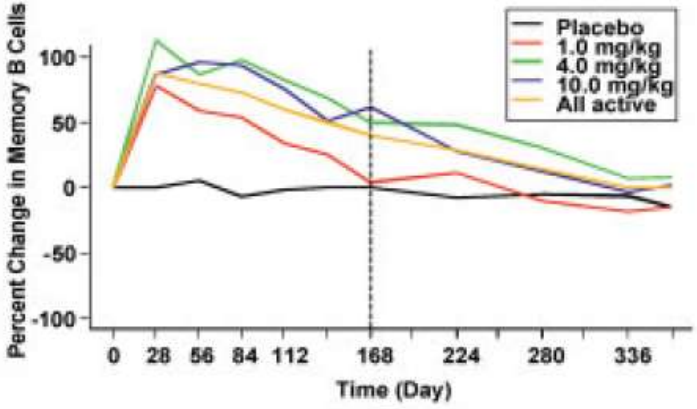

D

Arthritis & Rheumatism (Arthritis Care & Research)
Vol. 61, No. 9, September 15, 2009, pp 1168–1178

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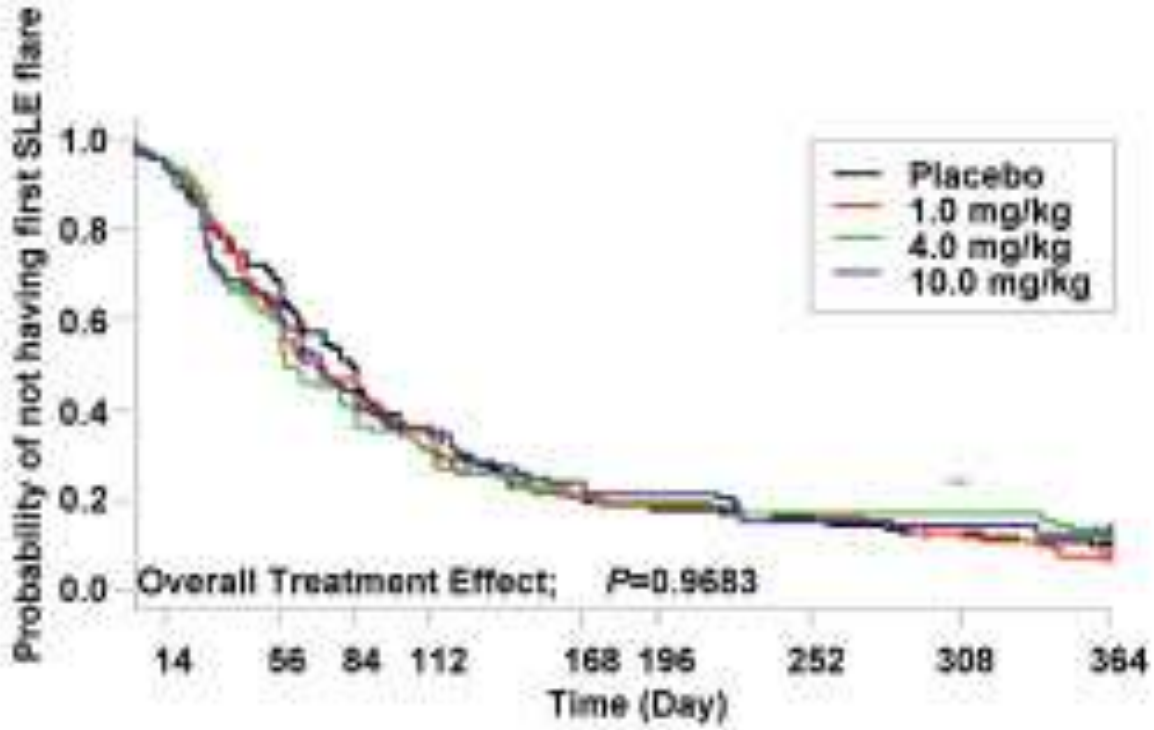

Arthritis & Rheumatism (Arthritis Care & Research)
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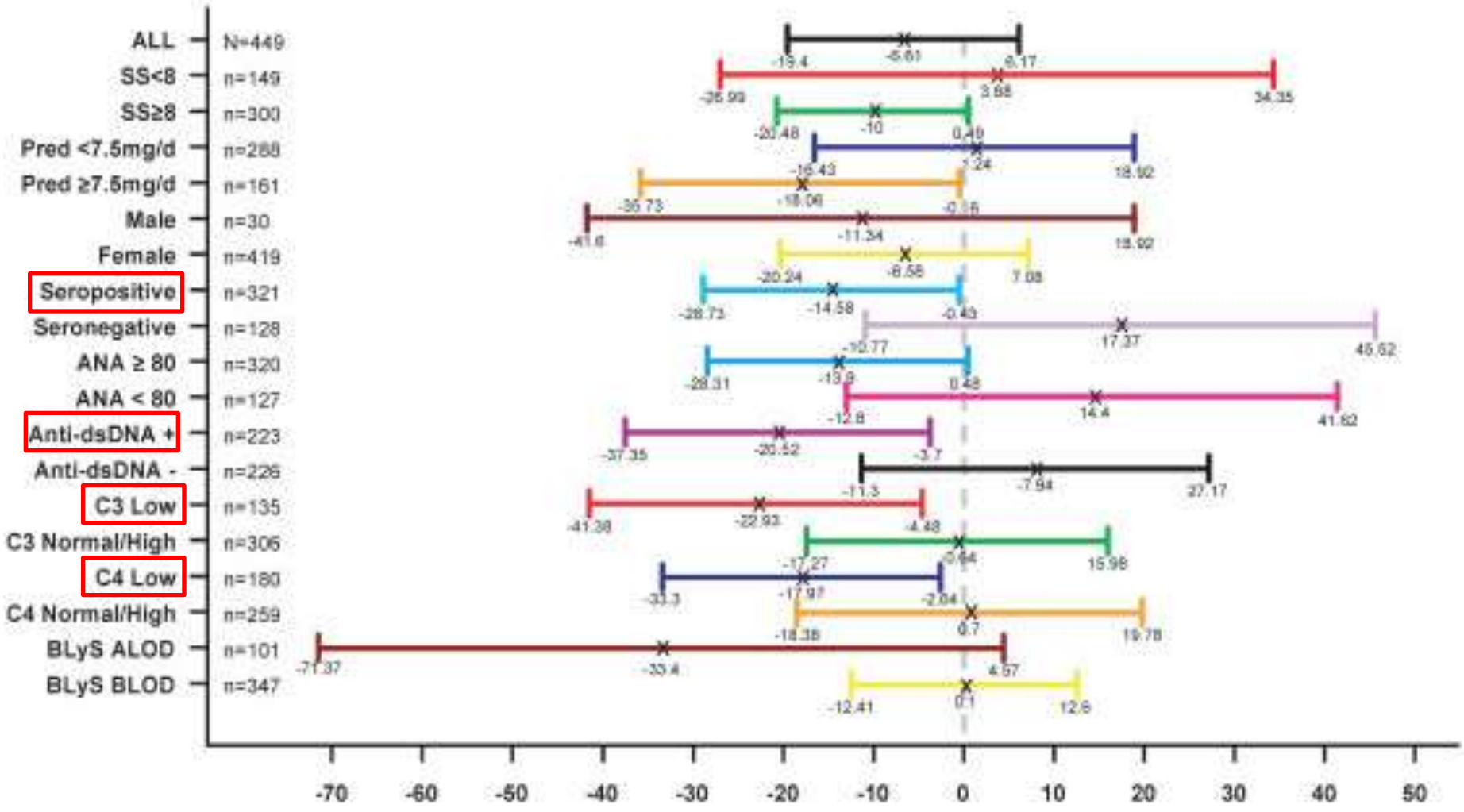
ANA titer ≥1:80	74.3	70.2	73.9	66.7	70.2
Anti-dsDNA ≥30 IU/ml	51.3	51.8	47.7	47.7	49.1
Serologically active‡	76.1	68.4	71.2	70.3	69.9
C3, mean ± SEM mg/dl	114.6 ± 3.4	110.0 ± 3.6	109.4 ± 3.0	112.7 ± 3.5	110.7 ± 2.0
C4, mean ± SEM mg/dl	20.2 ± 1.0	18.3 ± 1.0	18.3 ± 0.9	19.8 ± 1.0	18.8 ± 0.6
IgG, mean ± SEM mg/dl	1,366.8 ± 55.1	1,372.7 ± 48.4	1,385.4 ± 48.8	1,407.3 ± 54.3	1,388.3 ± 29.1
IgA, mean ± SEM mg/dl	300.8 ± 18.6	285.2 ± 15.4	278.2 ± 15.3	303.8 ± 14.9	289.0 ± 8.8
IgM, mean ± SEM mg/dl	101.5 ± 6.9	117.7 ± 8.1	127.6 ± 9.7	103.2 ± 7.1	116.2 ± 4.9
IgE, mean ± SEM KU/liter	70.8 ± 13.4	114.1 ± 22.9	127.7 ± 31.9	91.4 ± 18.4	111.1 ± 14.4

Arthritis & Rheumatism (Arthritis Care & Research)
Vol. 61, No. 9, September 15, 2009, pp 1168–1178



Wallace et al. 2009

SRI (*SLE RESPONDER INDEX*)

- Reducción SELENA-SLEDAI ≥ 4

Y

- Ausencia de un nuevo BILAG A o 2 nuevos BILAG B

Y

- No deterioro de la opinión global del médico mayor de 0,3 puntos

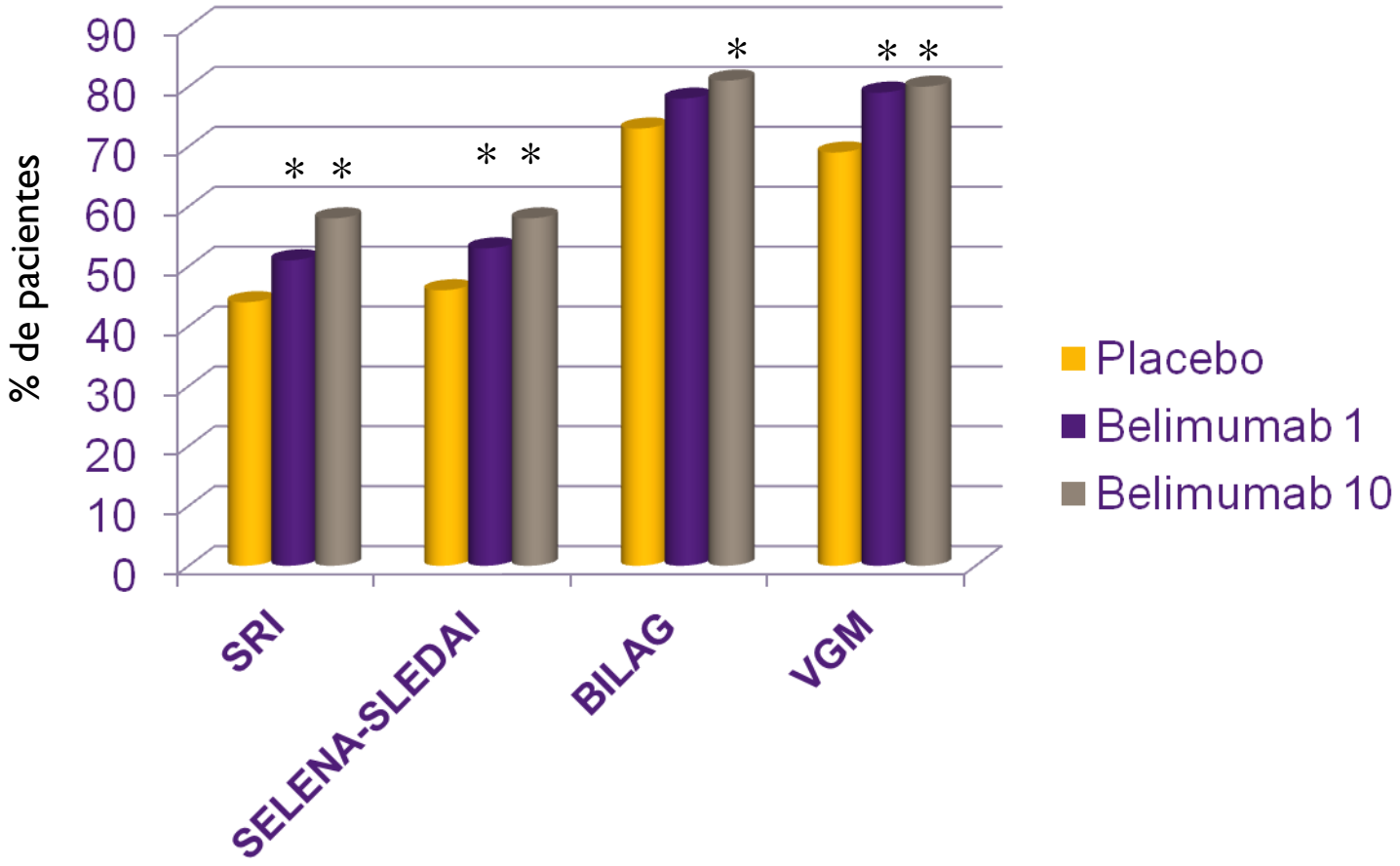
Efficacy and safety of belimumab in patients with active systemic lupus erythematosus: a randomised, placebo-controlled, phase 3 trial

Sandra V Navarra, Renato M Guzmán, Alberto E Gallacher, Stephen Hall, Roger A Levy, Renato E Jimenez, Edmund K-M Li, Mathew Thomas, Ho-Youn Kim, Manuel G León, Coman Tanasescu, Eugeny Nasonov, Joung-Liang Lan, Lilia Pineda, Z John Zhong, William Freimuth, Michelle A Petri, for the BLISS-52 Study Group

- ≥18 años
- Criterios ACR de LES
- SELENA-SLEDAI ≥6
- ANA ≥1:80 o anti-DNAn ≥30 IU/mL
- Tratamiento estable con dosis fija de prednisona (0–40 mg/día), AINE, antipalúdicos o inmunosupresores en el mes previo.

CRITERIOS DE EXCLUSIÓN

- Nefritis activa
- Afectación activa de SNC
- Embarazo
- Uso previo de agentes anti-linfocito B
- Ciclofosfamida IV en los 6 meses previos
- IgIV en los 3 meses previos
- Prednisona > 100 mg/día en los 3 meses previos

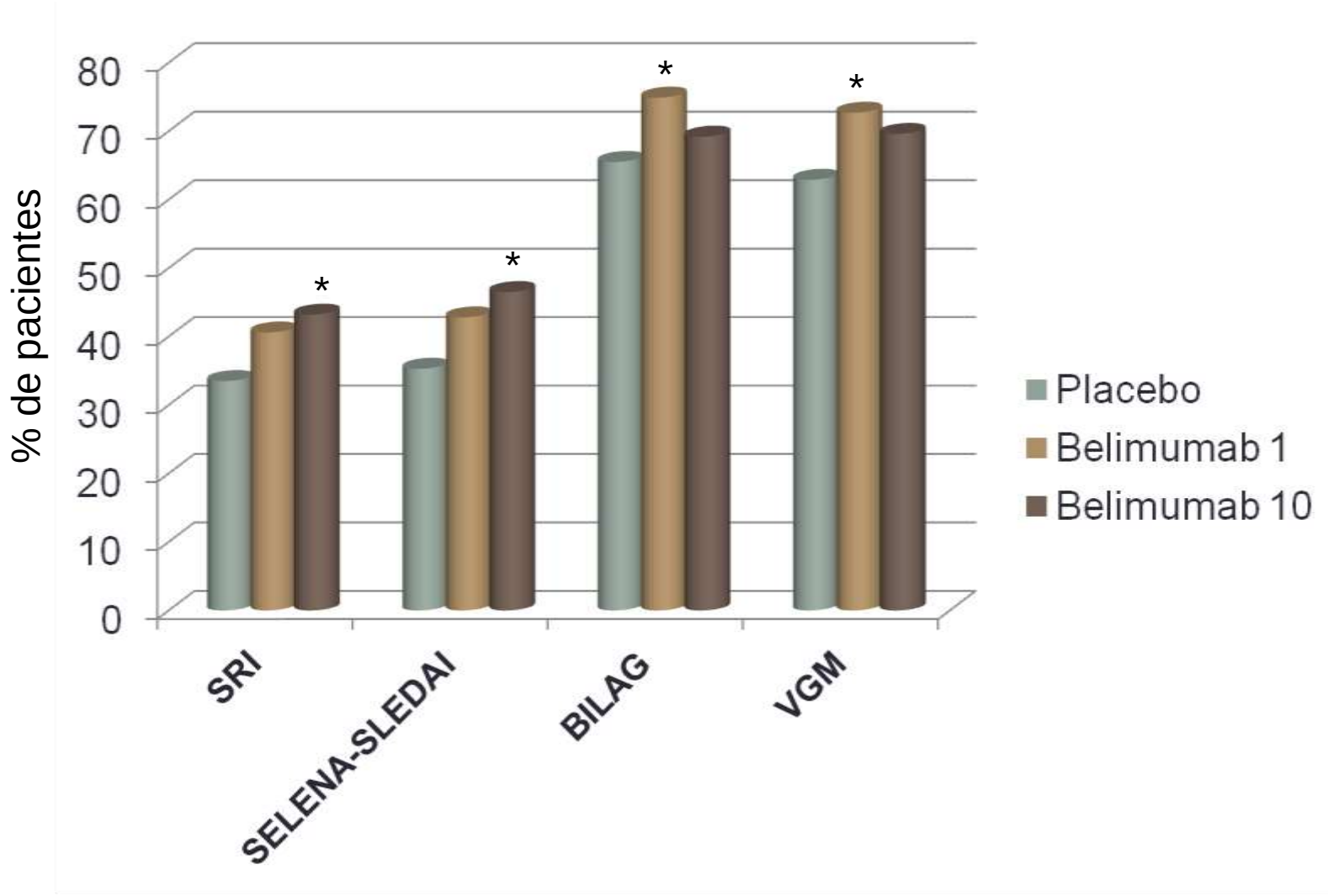


Navarra et al. 2011

A Phase III, Randomized, Placebo-Controlled Study of Belimumab, a Monoclonal Antibody That Inhibits B Lymphocyte Stimulator, in Patients With Systemic Lupus Erythematosus

Richard Furie,[1] Michelle Petri,[2] Omid Zamani,[3] Ricard Cervera,[4] Daniel J. Wallace,[5] Dana Tegzová,[6] Jorge Sanchez-Guerrero,[7] Andreas Schwarting,[8] Joan T. Merrill,[9] W. Winn Chatham,[10] William Stohl,[11] Ellen M. Ginzler,[12] Douglas R. Hough,[13] Z. John Zhong,[13] William Freimuth,[13] and Ronald F. van Vollenhoven,[14] for the BLISS-76 Study Group

Characteristic	Placebo (n = 275)	Belimumab 1 mg/kg (n = 271)	Belimumab 10 mg/kg (n = 273)
Female, no. (%)	252 (91.6)	253 (93.4)	259 (94.9)
Race, no. (%)†			
Indigenous American‡	36 (13.1)	33 (12.2)	34 (12.5)
White/Caucasian	188 (68.4)	192 (70.8)	189 (69.2)
Black/African American	39 (14.2)	40 (14.8)	39 (14.3)
Asian	11 (4.0)	6 (2.2)	11 (4.0)
Hispanic or Latino origin, no. (%)§	55 (20.0)	62 (22.9)	56 (20.5)
Age, years	40.0 ± 11.9	40.0 ± 11.4	40.5 ± 11.1
SLE disease activity			
Disease duration, years	7.4 ± 6.7	7.9 ± 7.1	7.2 ± 7.5
SELENA–SLEDAI score	9.8 ± 4.0	9.7 ± 3.7	9.5 ± 3.6
SELENA–SLEDAI score ≥10, no. (%)	140 (50.9)	144 (53.1)	136 (49.8)
≥1 BILAG A or 2 BILAG B scores, no. (%)	187 (68.0)	173 (63.8)	160 (58.6)
PGA score (0–3 VAS)	1.5 ± 0.5	1.4 ± 0.5	1.4 ± 0.5

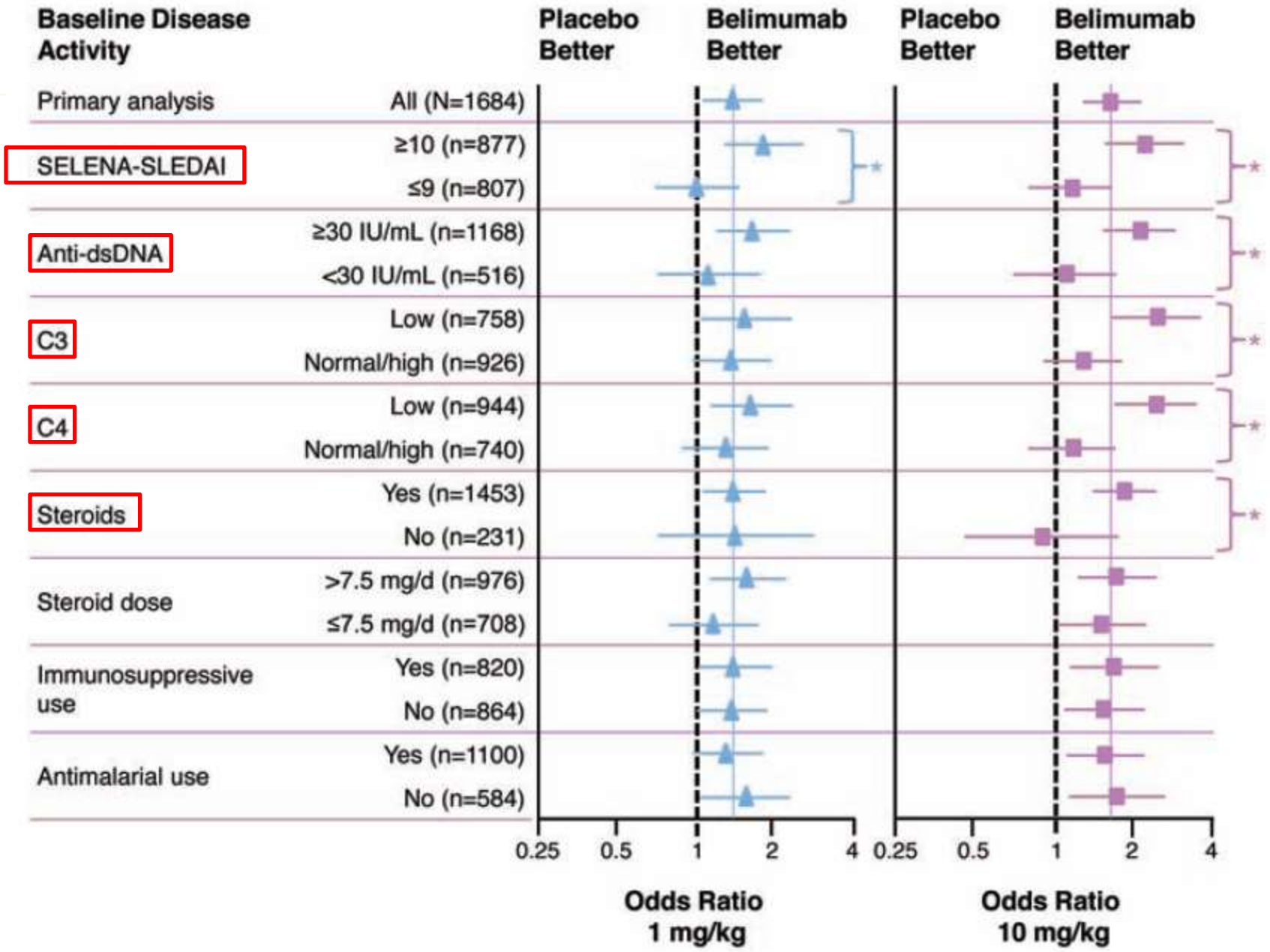


Furie et al. 2012

Ficha técnica EMA

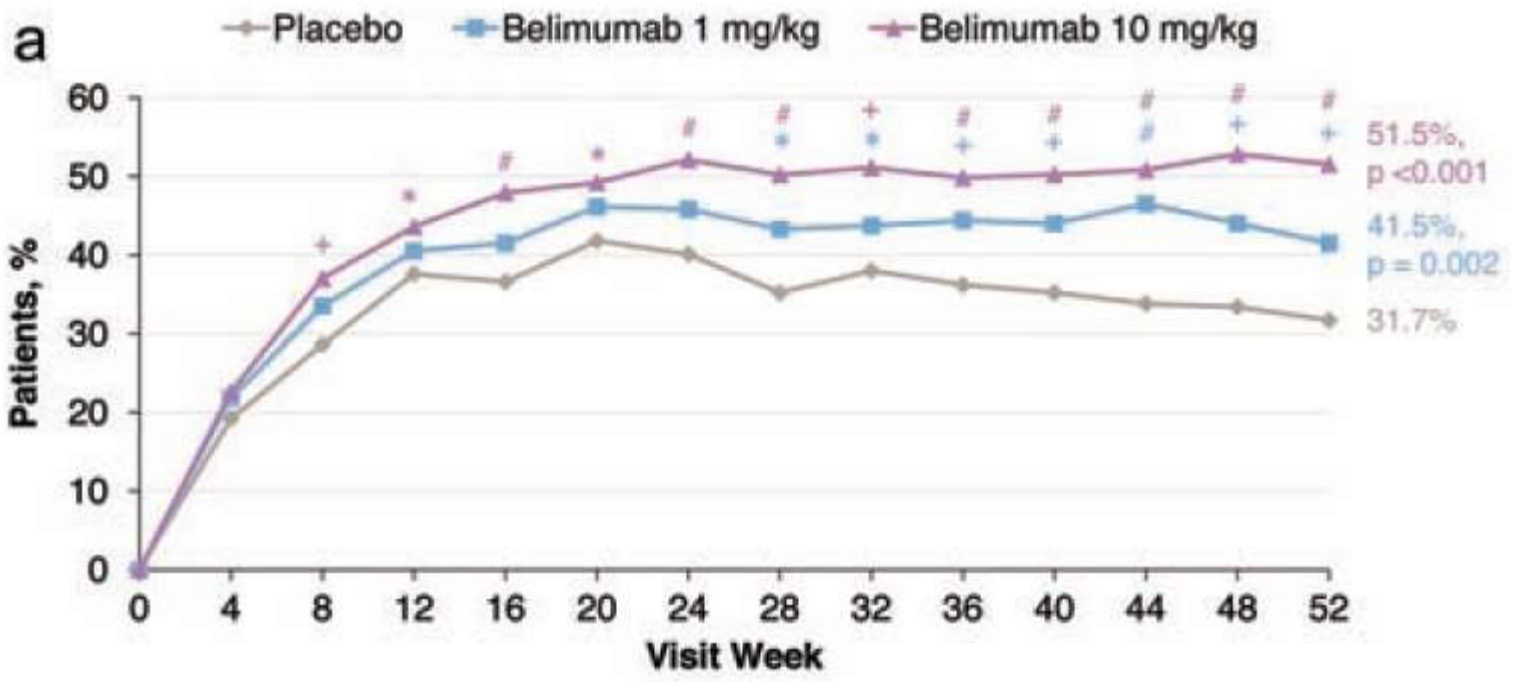
- **Benlysta está indicado como**
  - tratamiento adyuvante
  - en pacientes adultos
  - con lupus eritematoso sistémico (LES)
  - activo
  - con autoanticuerpos positivos
  - con un alto grado de actividad de la enfermedad (p.ej. anti-ADNdc positivo y bajo nivel de complemento)
  - a pesar del tratamiento estándar

PERFIL DE PACIENTE RESPONDEDOR



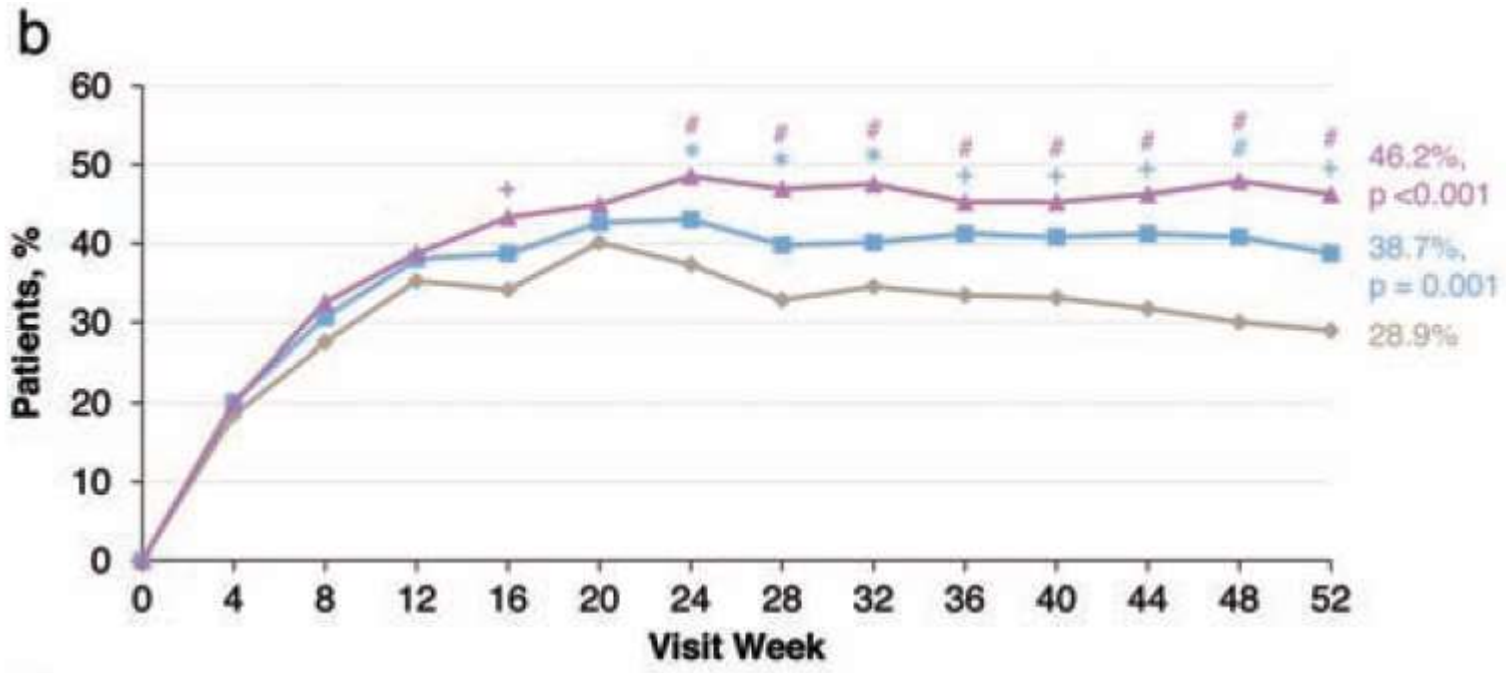
Van Vollenhoven et al. 2012

Pacientes anti-DNA e hipocomplementémicos que alcanzan SRI BLISS-52 + BLISS-76



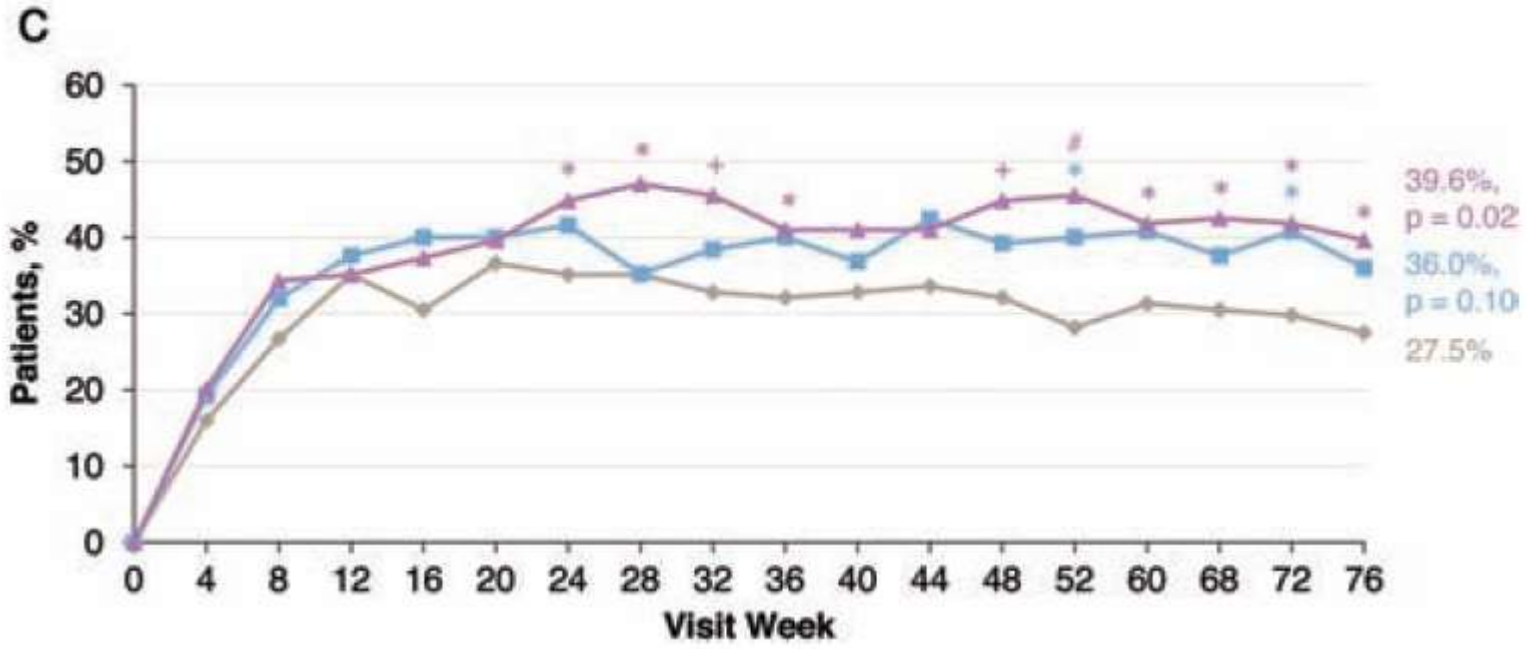
Van Vollenhoven et al. 2012

Pacientes anti-DNA e hipocomplementémicos que alcanzan SRI BLISS-52 + BLISS-76, excluyendo las mejorías serológicas del SELENA-SLEDAI

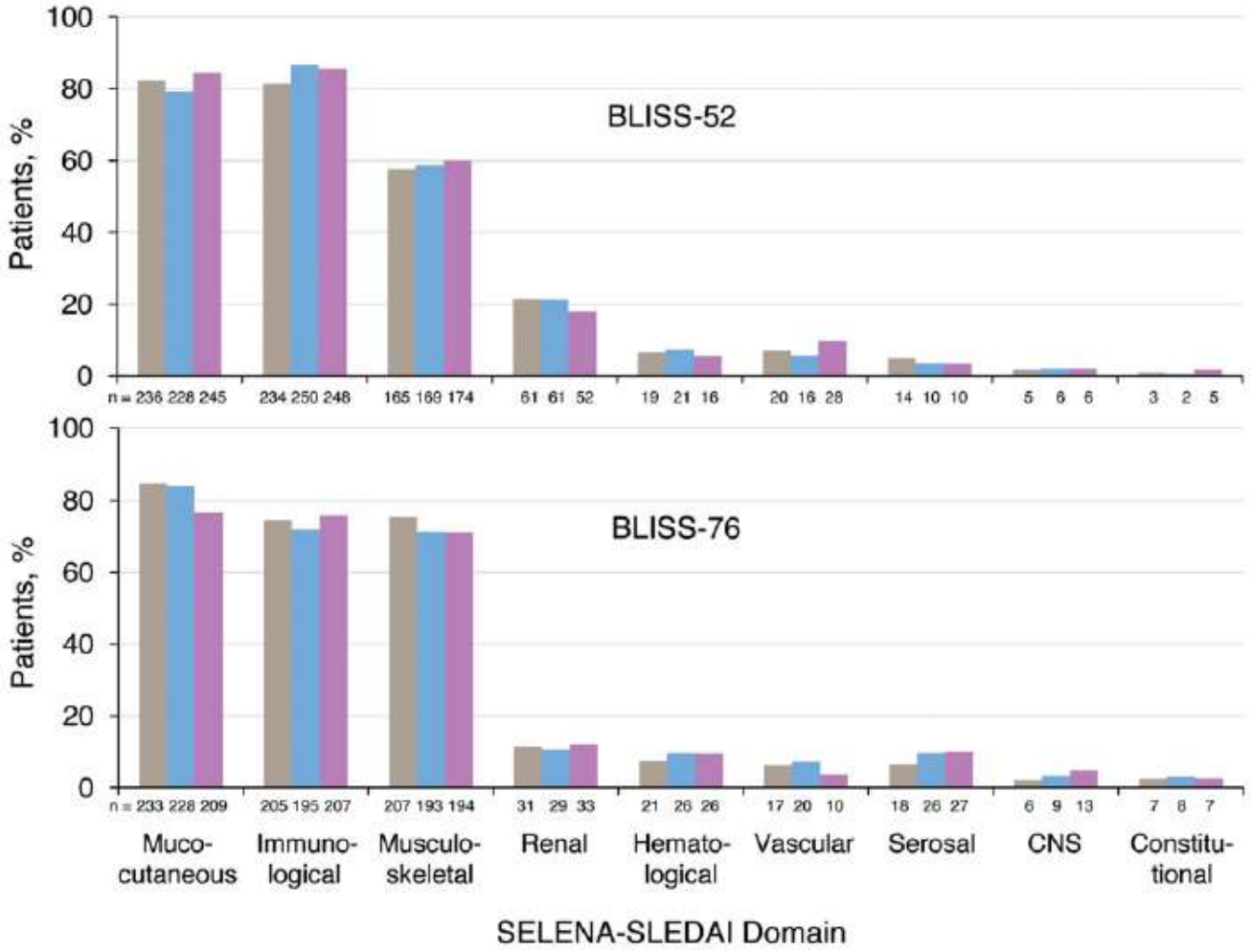


Van Vollenhoven et al. 2012

Pacientes anti-DNA e hipocomplementémicos que alcanzan SRI Estudio BLISS-76



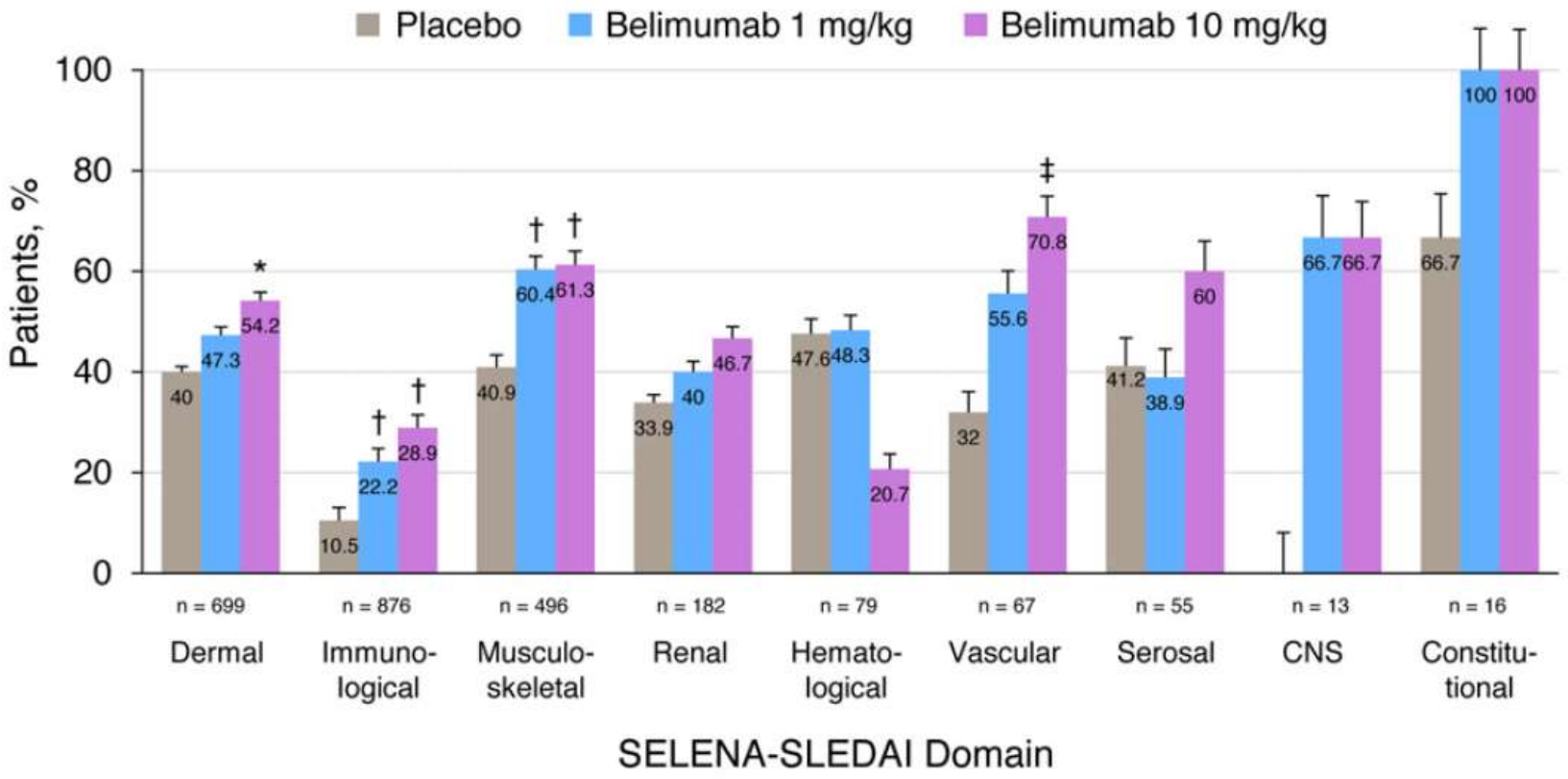
Van Vollenhoven et al. 2012



Manzi et al. 2012

Effects of belimumab, a B lymphocyte stimulator-specific inhibitor, on disease activity across multiple organ domains in patients with systemic lupus erythematosus: combined results from two phase III trials

Susan Manzi,[1] Jorge Sánchez-Guerrero,[2] Joan T Merrill,[3] Richard Furie,[4] Dafna Gladman,[5] Sandra V Navarra,[6] Ellen M Ginzler,[7] David P D'Cruz,[8] Andrea Doria,[9] Simon Cooper,[10] Z John Zhong,[10] Douglas Hough,[10] William Freimuth,[10] Michelle A Petri[11]



Manzi et al. 2012

Reumatol Clin. 2013;9(5):281–290

Reumatología Clínica

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Original

Consenso de la Sociedad Española de Reumatología sobre el uso de terapias biológicas en el lupus eritematoso sistémico

Jaime Calvo-Alén[a], Lucía Silva-Fernández[b,*], Eduardo Úcar-Angulo[c], José María Pego-Reigosa[d], Alejandro Olivé[e], Carmen Martínez-Fernández[f], Víctor Martínez-Taboada[g], José Luis Marenco[h], Estíbaliz Loza[i], Javier López-Longo[j], Juan Jesús Gómez-Reino[k], María Galindo-Izquierdo[l], Antonio Fernández-Nebro[m], María José Cuadrado[n], María Ángeles Aguirre-Zamorano[o], Antonio Zea-Mendoza[p] e Íñigo Rúa-Figueroa[q]

El panel recomienda la utilización de BLM en pacientes **adultos** con **LES activo**, con **autoanticuerpos positivos** y **alto grado de actividad** de la enfermedad **a pesar de tratamiento estándar** (NE 1; GR A; GA 93%).

A día de hoy, los pacientes con **manifestaciones clínicas no mayores** (como artritis o afectación cutánea) **refractarias** y con **datos analíticos de actividad** parecen ser el escenario clínico mas adecuado para el uso de este agente.

Actualmente, **no se puede recomendar** el uso de BLM en pacientes con LES y afectación **grave** del **sistema nervioso central** (SNC) y/o **nefritis** lúpica **grave** (NE 1; GR A; GA 93%).

SEGURIDAD Y EFICACIA A LARGO PLAZO

Long-Term Safety Profile of Belimumab Plus Standard Therapy in Patients With Systemic Lupus Erythematosus

Joan T. Merrill,[1] Ellen M. Ginzler,[2] Daniel J. Wallace,[3] James D. McKay,[4] Jeffrey R. Lisse,[5] Cynthia Aranow,[6] Frank R. Wellborne,[7] Michael Burnette,[8] John Condemi,[9] Z. John Zhong,[10] Lilia Pineda,[10] Jerry Klein,[10] and William W. Freimuth,[10] on behalf of the LBSL02/99 Study Group

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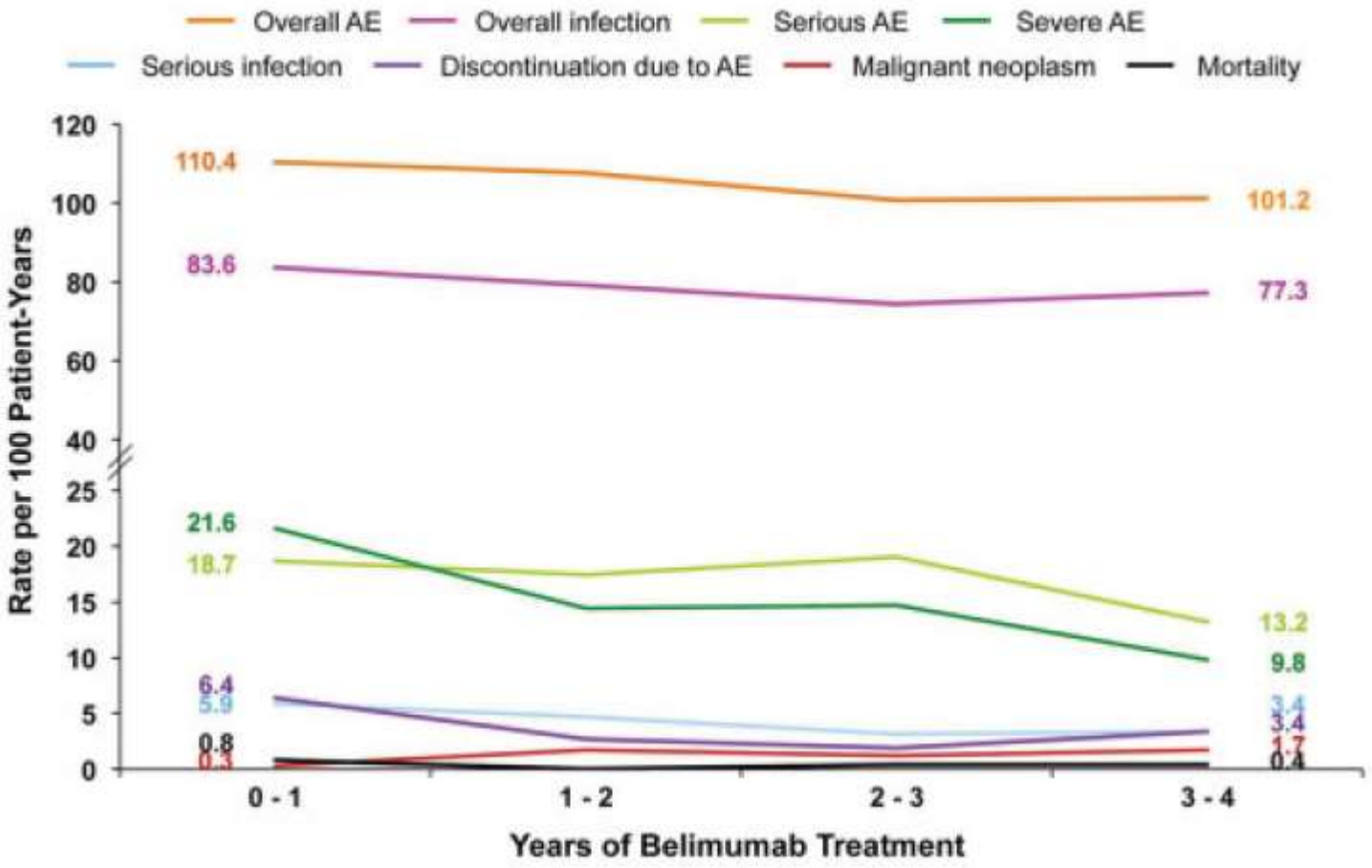
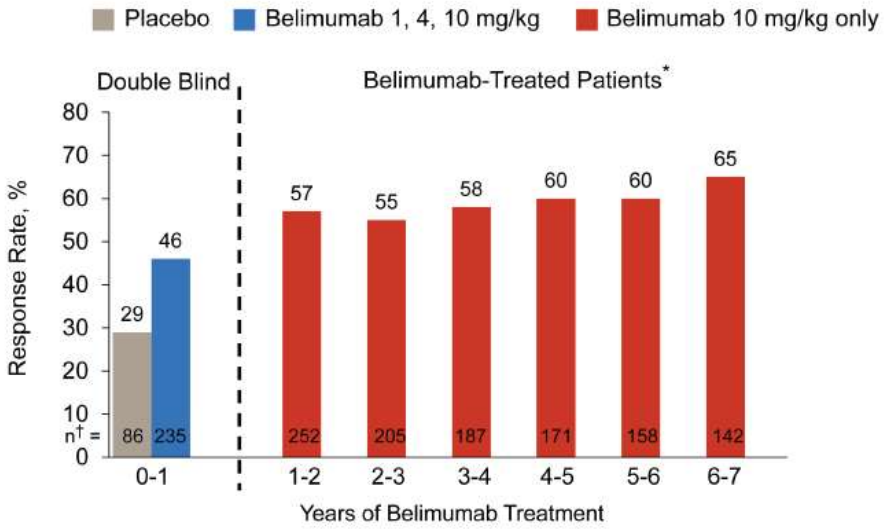


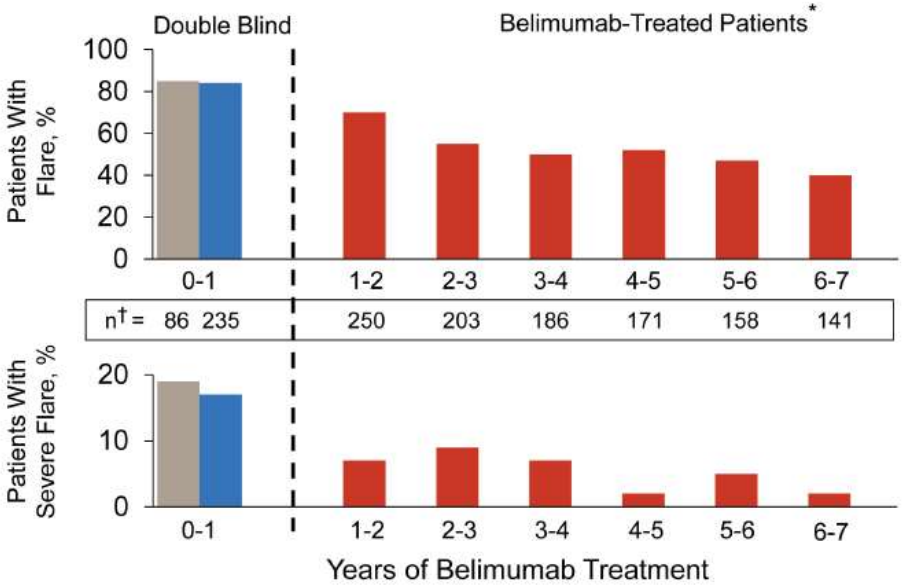
Disease Control and Safety of Belimumab Plus Standard Therapy Over 7 Years in Patients with Systemic Lupus Erythematosus

Ellen M. Ginzler, Daniel J. Wallace, Joan T. Merrill, Richard A. Furie, William Stohl, W. Winn Chatham, Arthur Weinstein, James D. McKay, W. Joseph McCune, Z. John Zhong, William W. Freimuth, and Michelle A. Petri; and the LBSL02/99 Study Group

SRI



Brotes



J Rheumatol First Release Nov 1 2013; doi:10.3899/jrheum.121368

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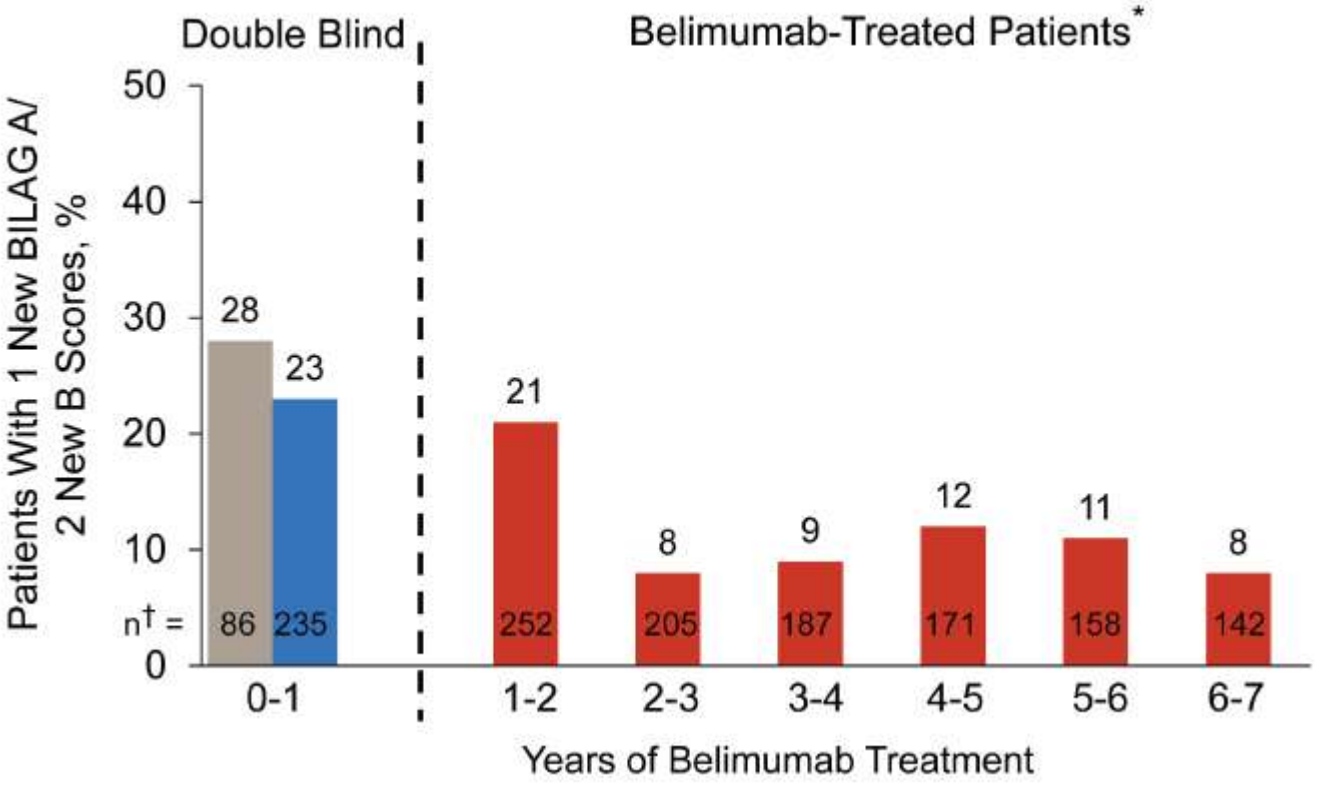
1 BILAG A/2 BILAG B



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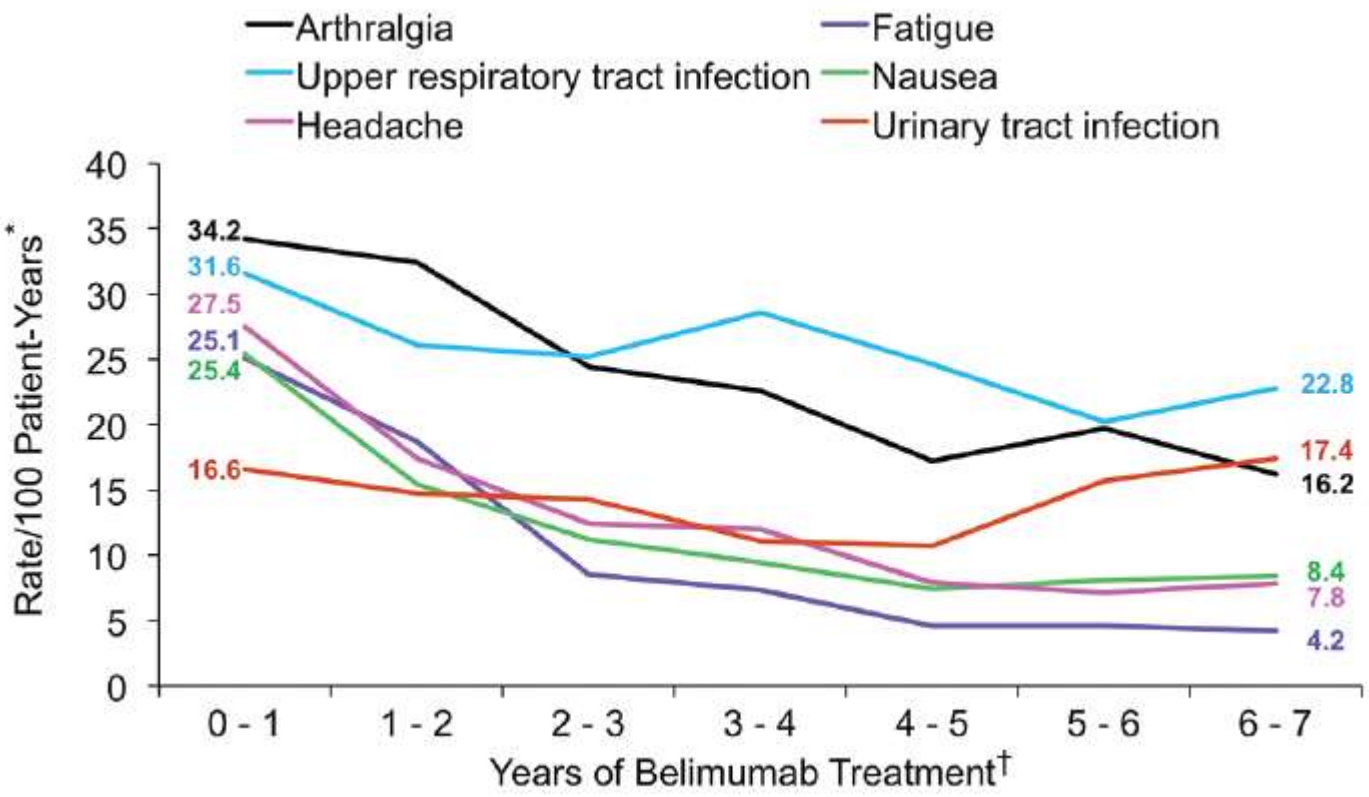

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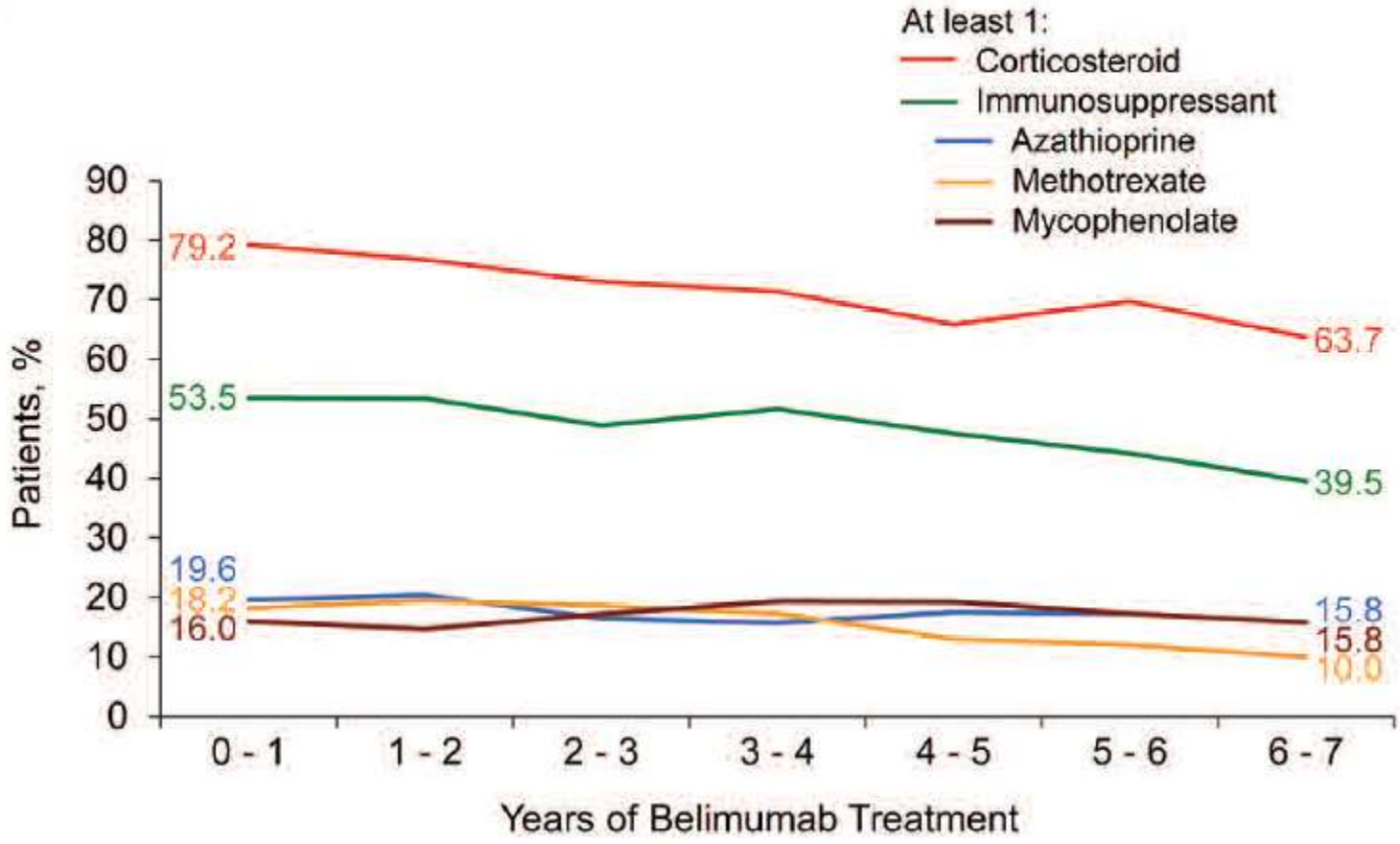

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EFECTIVIDAD EN PRÁCTICA CLÍNICA HABITUAL

Estudio OBSErve:

Resultados a 12 meses en Pacientes con Lupus Eritematoso Sistémico tratados con belimumab en la Práctica Clínica

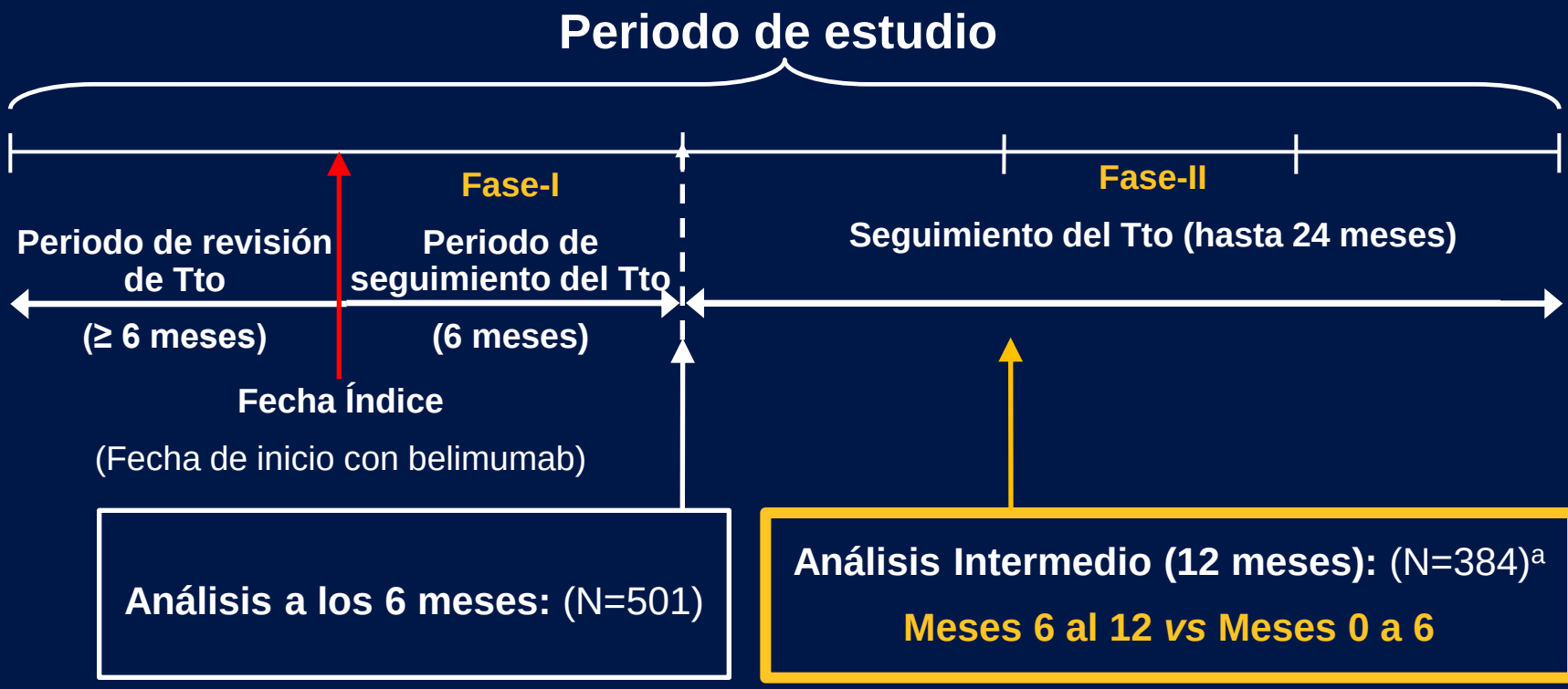
Collins CE[1], Dall'Era M[2], Oglesby A[3], Mcguire MB[4], Pappu R[3], Kan H[3], Molta C[3]
[1]MedStar Washington Hospital Center, Washington, DC, USA; [2]University of California, San Francisco, CA, USA;
[3]GlaxoSmithKline, Research Triangle Park, NC, USA; [4]Medical Data Analytics, Parsippany, NJ, USA.

OBSErve:"Evaluation Of Use of Belimumab in Clinical Practice Settings"

Collins CE, *et al*, The Observe Study Arthritis Rheum 2013;65: abstract: 1740, presentado en el Congreso Americano de Reumatología. San Diego (25-31 octubre 2013).

MÉTODOS
Diseño del estudio

- Estudio multicéntrico, de revisión retrospectiva de los historiales médicos. **N=384 pac** (89,8% mujeres)
- Los datos fueron recogidos durante los 6 meses previos al inicio del tratamiento con belimumab, y cada 6 meses hasta llegar al mes 24.



Tto, tratamiento.

[A] Descenso del tamaño de la muestra de 117 pacientes debido que los datos no estaban disponibles al comienzo del análisis.

RESULTADOS

Características demográficas y basales de los pacientes

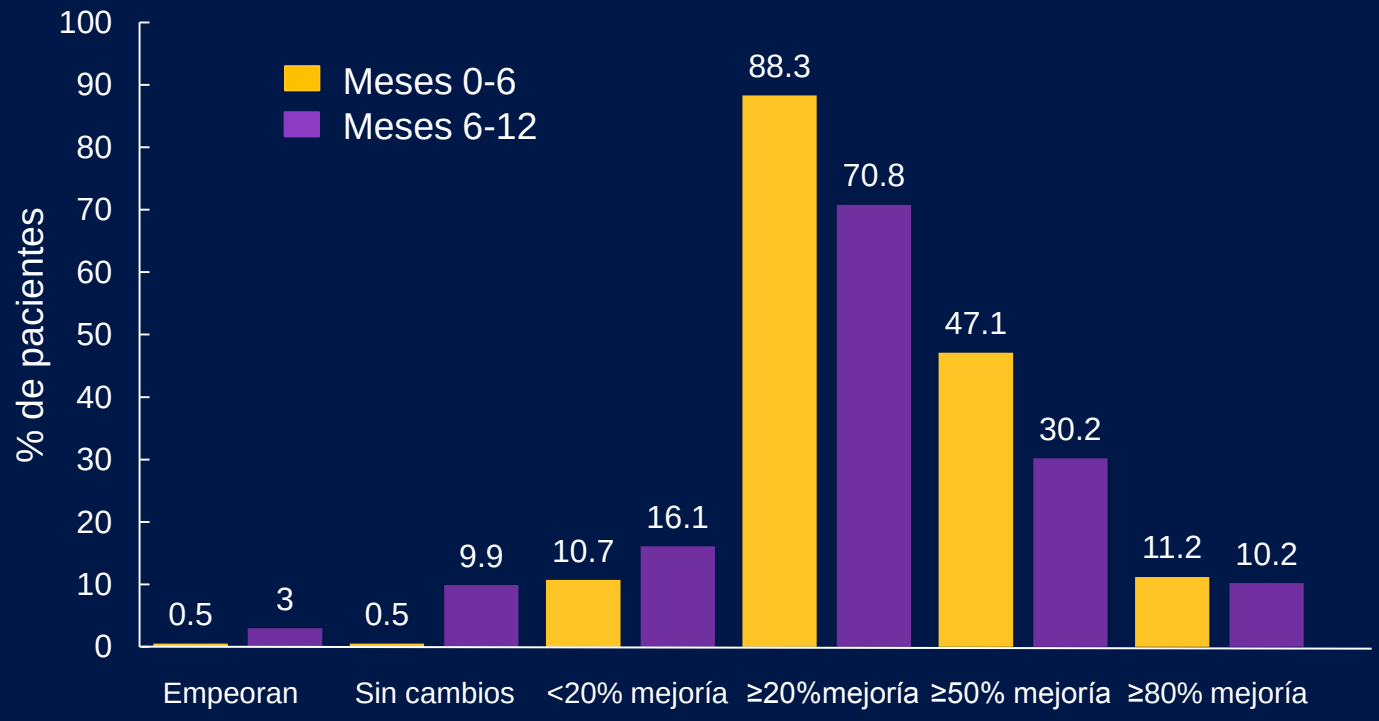
		Total pacientes con LES en el mes 12 (n=384)
Sexo, n (%):	Mujeres	345 (**89,8%**)
Etnia, n (%):	Caucásica	**198** (51,6%)
	Negros/Africanos-Americanos	98 (25,5%)
	Hispanicos	64 (16,7%)
	Otros	24 (6,3%)
Diagnosticados de LES ≤5 años atrás, n (%)		222 (**57,8%**)
Gravedad[a] de LES al comienzo de tratamiento con belimumab, n (%):		
	Leve	8 (2,1%)
	Moderado	297 (**77,3%**)
	Grave	79 (20,6%)
Medicación concomitante LES, n (%):	Esteroides orales	297 (77,3%)
	Antimaláricos	261 (68,0%)
	Inmunosupresores	227 (59,1%)
	AINEs	69 (18,0%)
Media de dosis de prednisona al comienzo, mg/día		19,4
Interrupciones belimumab, n (%)		43 (11,2%)
Razones de la interrupción n (%):	Petición del paciente	16 (37,2%)
	Falta de efectividad	12 (27,9%)
	Incumplimiento de los pacientes	9 (20,9%)
	Progresión de la enfermedad	8 (18,6%)
	Pérdida de seguridad/Reembolso	3 (7,0%)
	Abandono del seguimiento/muerte	3 (7,0%)

[A] Gravedad de la enfermedad fue evaluada según criterio clínico del médico.
AINEs, Antinflamatorios No Esteroideos; LES, Lupus Eritematoso Sistémico.

RESULTADOS

Impresión médica sobre los cambios de actividad del LES

- Tras las mejorías reportadas durante el análisis inicial de 6 meses, continuaron las mejorías durante los meses 6 a 12.



LES: Lupus Eritematoso Sistémico.

RESULTADOS
Uso de esteroides

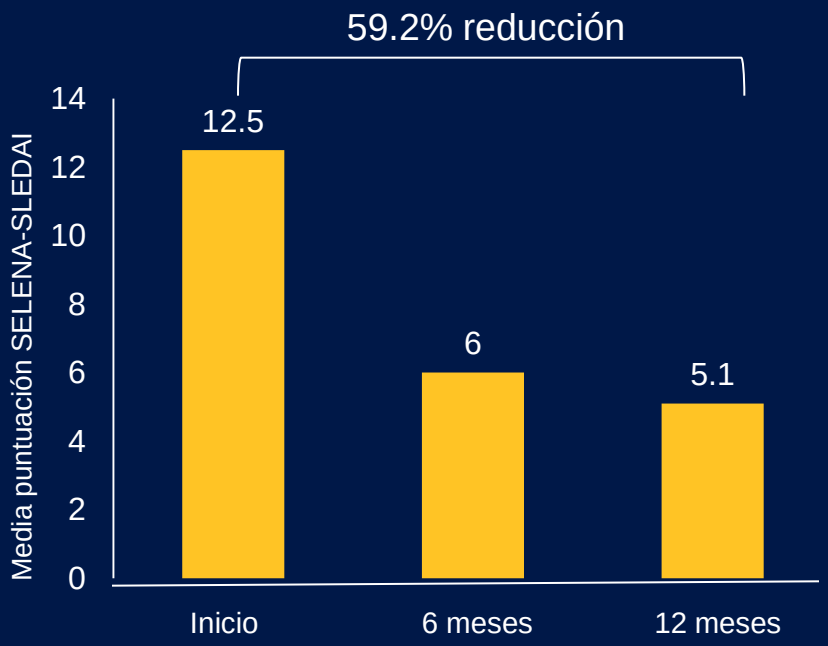
- De los **384 pacientes** analizados a los 12 meses, **el 77%** (n=297) recibían tratamiento con esteroides desde el comienzo.
  - De ellos, el **35%** (n=104) **interrumpieron** su tratamiento con **esteroides a los 12 meses**.
  - La **media** de la **dosis de esteroides**, **disminuyó** entre sus usuarios **de 19,4 mg/día** desde el inicio **a 8,4 mg/día** en el mes 12.

- Durante el periodo de 12 meses, 11 patientes iniciaron tratamiento con esteroides:
  - 6 pacientes entre los meses 0 y 6 (2 de los cuales lo interrumpieron a los 12 meses).
    - La dosis media al mes 6 fue: 6,3 mg/día.
  - 5 pacientes entre los meses 6 y 12.
    - La dosis media al mes 12 fue: 13,5 mg/día.

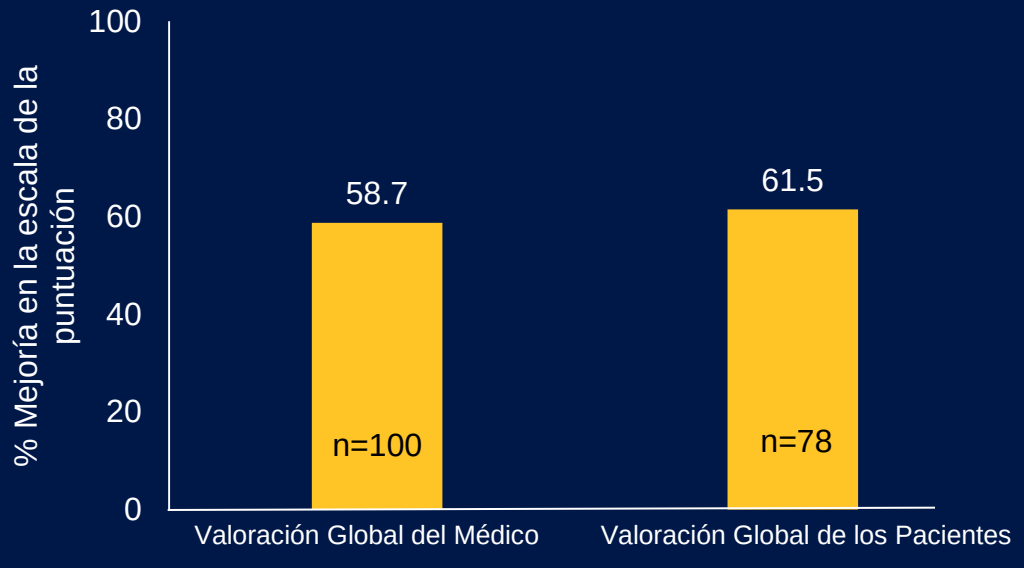
RESULTADOS

Puntuación SELENA-SLEDAI* y puntuación de la valoración global del médico y de los pacientes

Cambios en la puntuación SELENA-SLEDAI



Cambios en PGA: meses 0–12



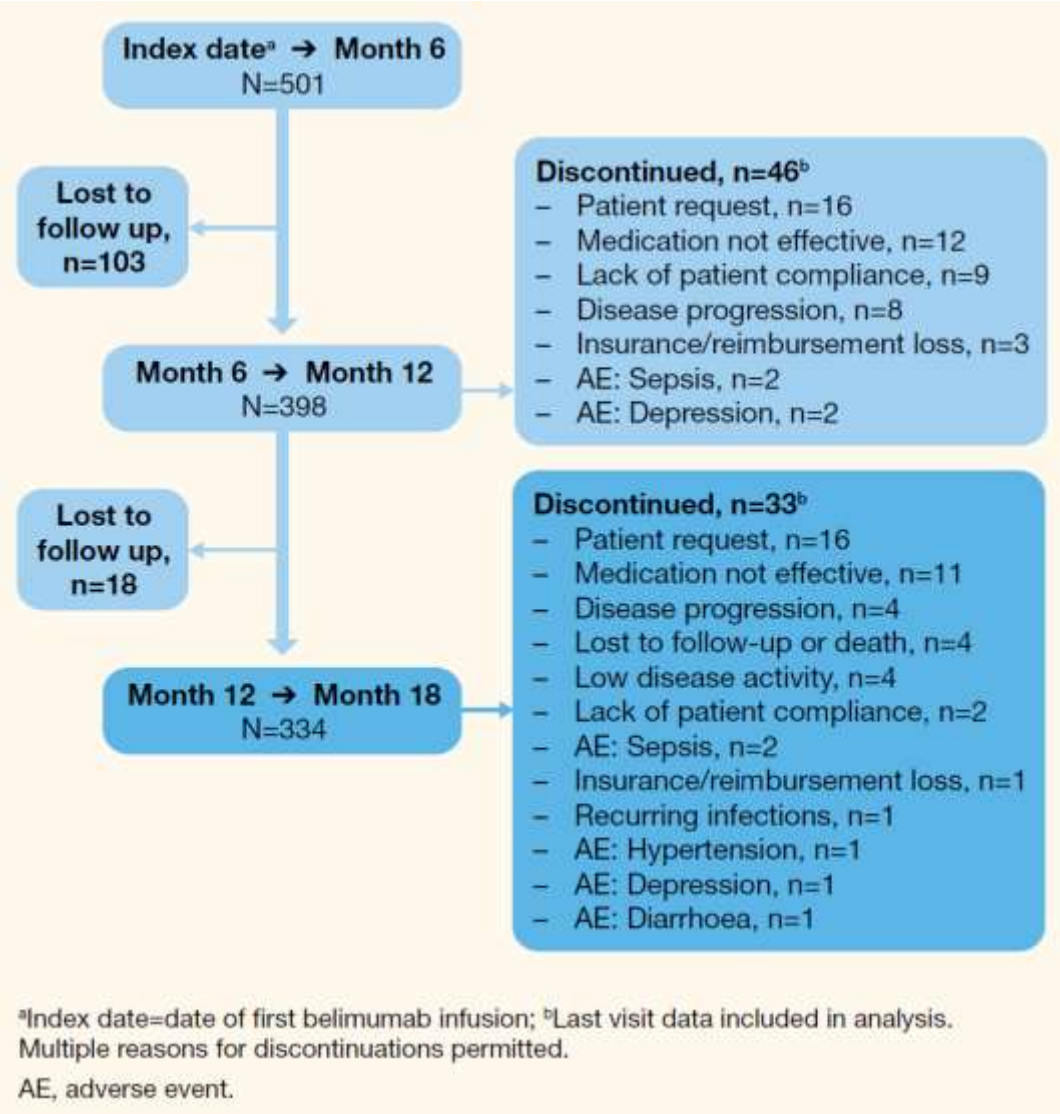
*En total, 96 pacientes tuvieron puntuación SELENA-SLEDAI disponible a los 12 meses.
SELENA-SLEDAI, Safety in Estrogen in Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index.

Outcomes in systemic lupus erythematosus patients with high disease activity treated with belimumab: 18 month results from the US OBSErve study

FRI0374

CE Collins[1], M Dall'Era[2], C Macahilig[3], R Pappu[4], C Molta[4], H Kan[5], V Koscielny[6]

[1]MedStar Washington Hospital Center, Washington, DC, USA; [2]University of California, San Francisco, CA, USA; [3]Medical Data Analytics, Parsippany, NJ, USA; [4]GlaxoSmithKline, Philadelphia, PA, USA; [5]GlaxoSmithKline, Research Triangle Park, NC, USA; [6]GlaxoSmithKline, Middlesex, UK



[a]Index date=date of first belimumab infusion; [b]Last visit data included in analysis. Multiple reasons for discontinuations permitted.

AE, adverse event.

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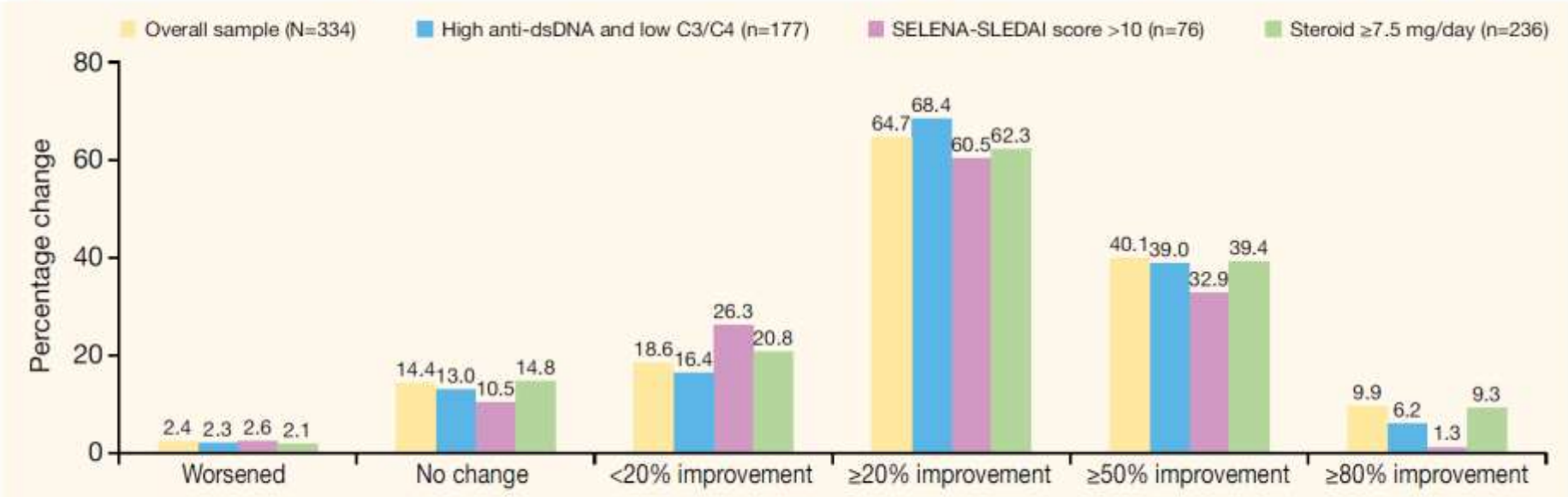
Figure 2. Overall clinical responses[a] from month 12 to 18 in the overall population and high disease activity subgroups.



[a]Levels of change were based on physician impression of overall change in SLE disease manifestations.

C, complement; dsDNA, double-stranded DNA; SELENA-SLEDAI, Safety of Estrogens in Lupus National Assessment-SLE Disease Activity Index; SLE, systemic lupus erythematosus.

Outcomes in systemic lupus erythematosus patients with high disease activity treated with belimumab: 18 month results from the US OBSErve study

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Table 2. Changes in SELENA-SLEDAI score and steroid dose in the overall population and high disease activity subgroups between index date and 18 months.

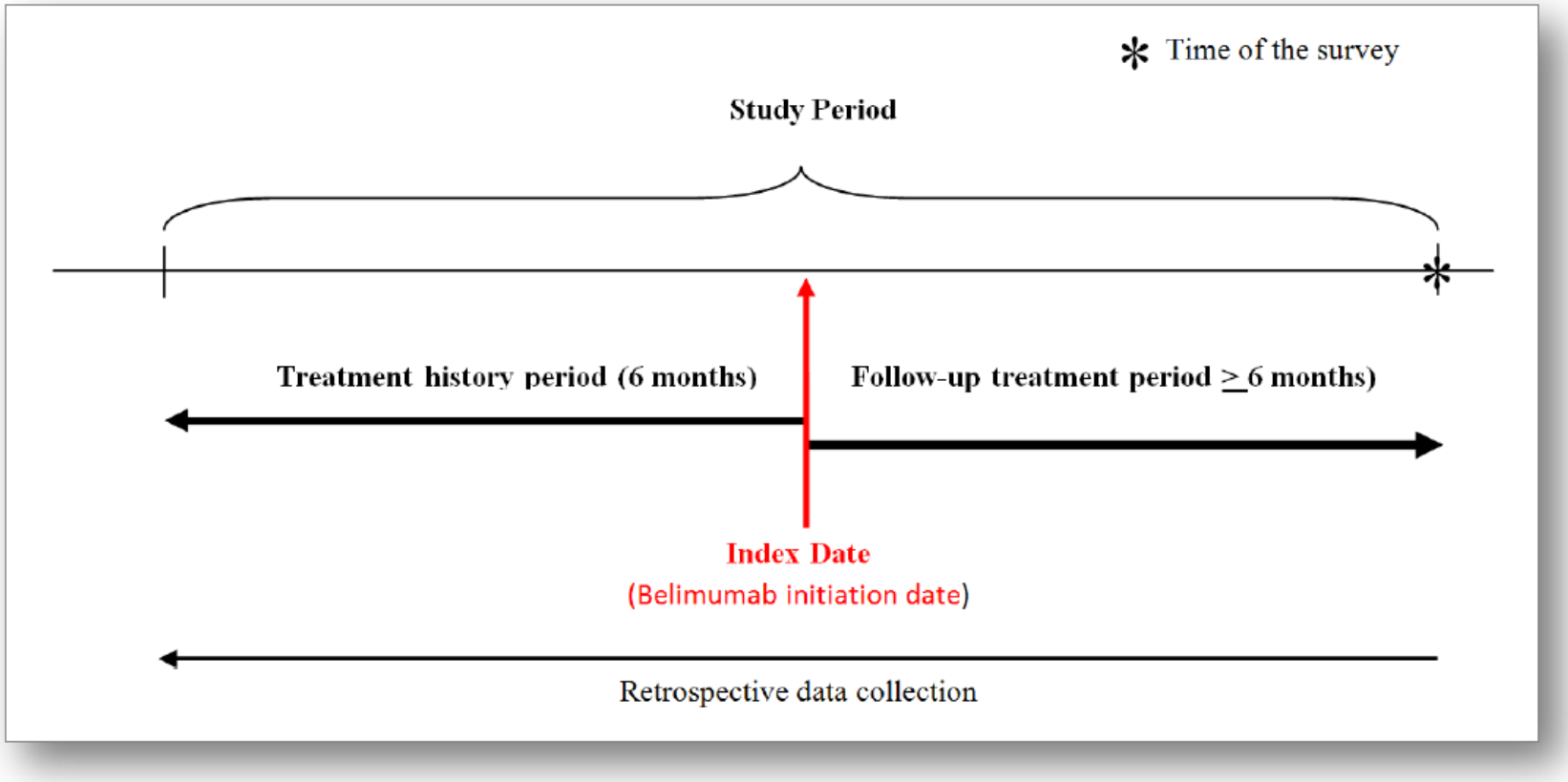
		Patients with high disease activity at index date[a]		
	Overall sample (n=334)	High anti-dsDNA and low C3/C4 (n=177)	SELENA-SLEDAI score >10 (n=76)	Steroid ≥7.5 mg/day (n=236)
SELENA-SLEDAI score[c]	**n=72**	**n=37**	**n=59**	**n=62**
Mean at index date	13.1	14.1	14.1	13.5
Mean at month 18	4.6	5.1	4.9	4.8
Mean score reduction	8.5	9.0	9.2	8.7
Steroid dose, mg/day[d]	**n=261**	**n=140**	**n=71**	**n=236**
Mean at index date	19.5	19.5	23.6	21.1
Mean at month 18	3.8	4.6	4.8	3.9
Mean dose reduction	15.7	14.9	18.8	17.2

[a]Patients may be included in multiple high disease activity subgroups; [b]Includes last visit data from discontinuations at 12–18 months (n=33); [c]Patients with scores at index date and 18 months; [d]Includes patients who discontinued steroids by 18 months.

C, complement; dsDNA, double-stranded-DNA; SELENA-SLEDAI, Safety of Estrogens in Lupus National Assessment-SLE Disease Activity Index.

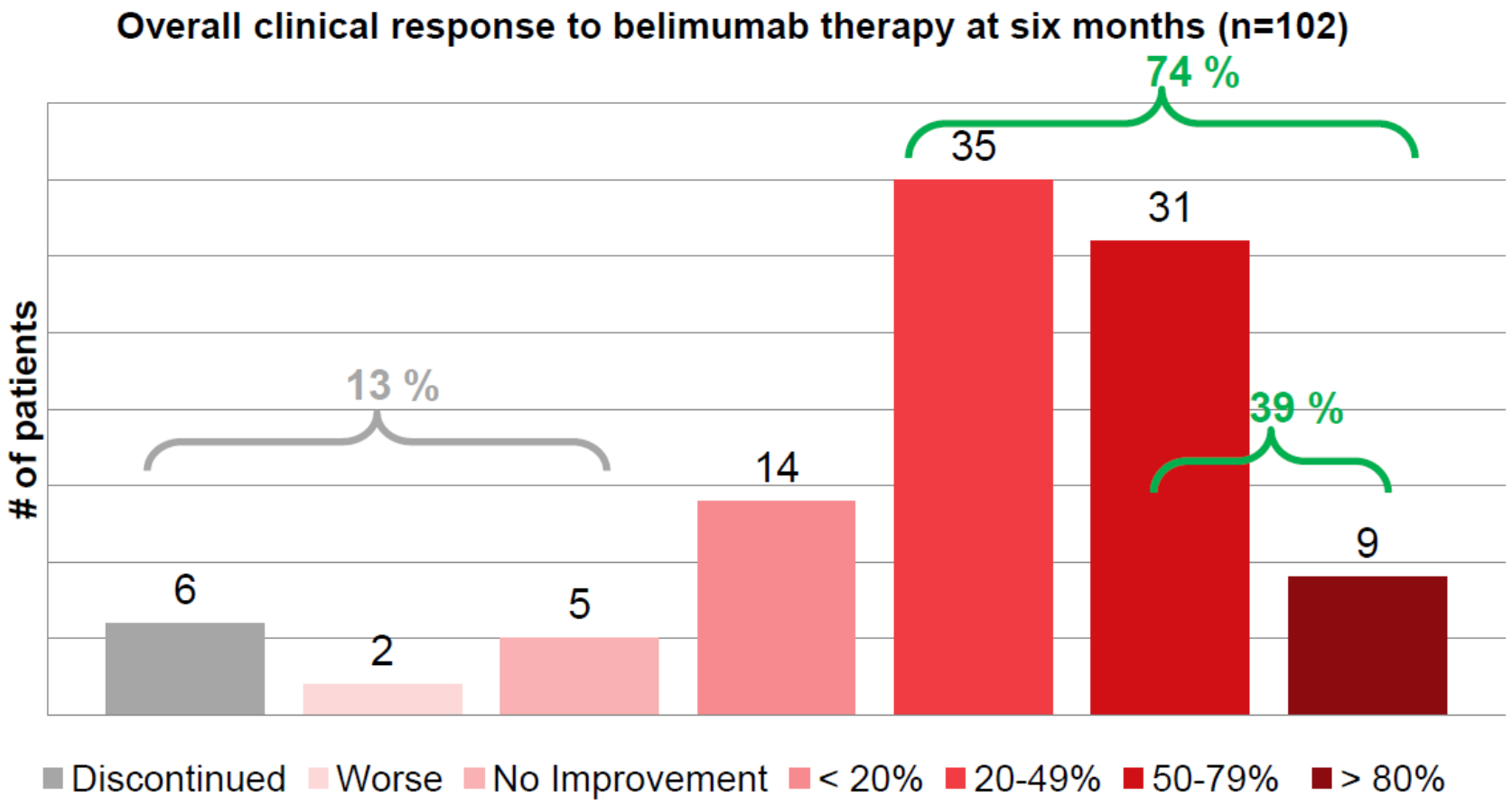
OBSErve Germany - Study Design:
Data Collection

- **Multi-center** observational cohort study, based on review of medical patient charts
- **Retrospective** data collection for three time points: at belimumab initiation, as well as 6 months before, 6 months after



OBSErve Germany - Results:

Primary Endpoint – Overall Clinical Response



OBSErve Germany - Results:

Comedication – Steroid Sparing Effect

Change of oral steroid use during belimumab therapy by initial dosage group	Total (n=91)	High dose (≥7.5 mg) (n=63)
Dosage 6 months before belimumab start [mg/day]	11.7	12.6
Dosage at belimumab start [mg/day]	13.7	17.5
Dosage 6 months after belimumab start [mg/day]	7.6	8.6
Change of dosage from belimumab start to 6 months after [mg/day]	- 6.1	-8.9

OBSERVE EN ESPAÑA

- Datos embargados (Aceptación ACR).
- Resultados muy similares en efectividad percibida y en reducción de dosis de prednisona durante el tratamiento.

MOLTES GRÀCIES PER LA SEVA ATENCIÓ
MUCHAS GRACIAS POR VUESTRA ATENCIÓN

II curs de malalties autoimmunes SCR 2014
Curs Societat Catalana de Reumatologia
26 i 27 de setembre de 2014