JORNADA
Actualización en LUPUS
ALICANTE 16 y 17 NOV
2018

LES & Artritis Refractaria

Francisco Ortiz Sanjuán

Alicante, 16 Noviembre 2018

1869

Jaccoud´s artropathy

1940

Slocumb Mayo Clinic

1958

Armas-Cruz

Erosive LES arthropaty

1963 - 1969

Rhupus

CCPA

Ac Anti-SSA/Ro

Eco

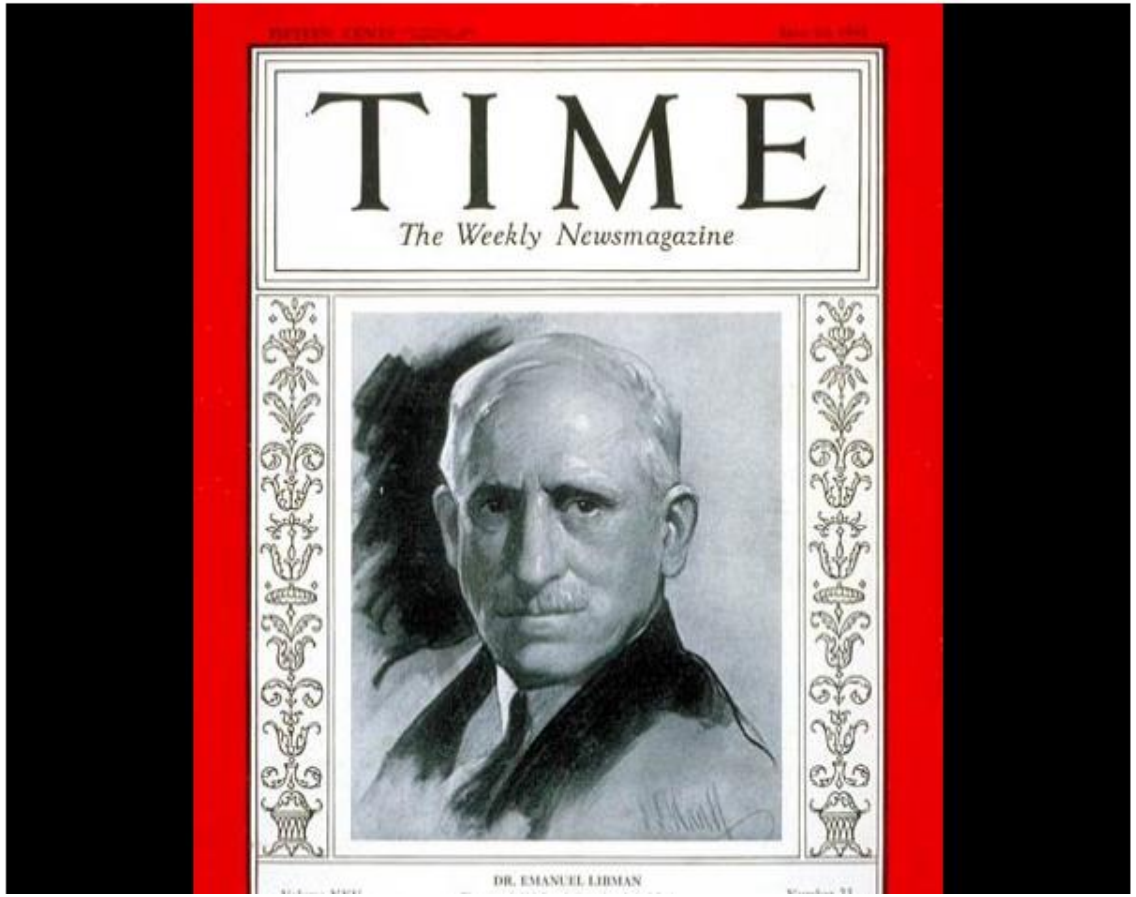
RMN

LES & Artritis refractaria

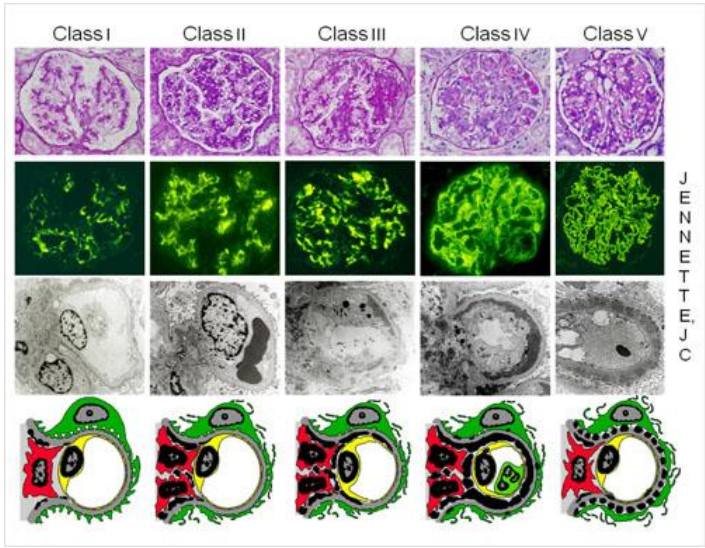
TIME

Dr. Emanuel Libman | **June 10, 1935**

PREVIOUS WEEK'S COVER | FOLLOWING WEEK'S COVER



Dr.Benjamin Sacks



Clin Rheumatol (2016) 35:227–231
DOI 10.1007/s10067-015-3127-3

BRIEF REPORT

Chronic arthritis in systemic lupus erythematosus: distinct features in 336 paediatric and 1830 adult patients

Natali W. S. Gormezano[1,2] · Clovis A. Silva[2] · Nadia E. Aikawa[1,2] · Diego L. Barros[1] · Mariana A. da Silva[1] · Carini I. Otsuzi[1] · Katia Kozu[2] · Luciana Parente Seguro[1] · Rosa M. R. Pereira[1] · Eloisa Bonfá[1]

Received: 29 July 2015 / Revised: 20 November 2015 / Accepted: 21 November 2015 / Published online: 28 November 2015

Abstract The objectives of this study are to assess the frequency of chronic arthritis and compare the clinical and laboratory features in a large population of childhood-onset systemic lupus erythematosus (cSLE) and adult-onset (aSLE) patients. This historical study evaluated 336 cSLE and 1830 aSLE patients. Chronic arthritis was defined as synovitis of at least 6 weeks of duration. Rhupus was characterised as the association of SLE and chronic inflammatory arthritis with erosion and positive rheumatoid factor. Jaccoud's arthropathy (25 vs. 0 %, p=0.009), nephritis (37 vs. 3 % , p=0.006), haematuria (37 vs. 1.4 %, p=0.002), lupus anticoagulant (40 vs. 1.6 %, p=0.012), anticardiolipin IgM (40 vs. 1.5 %, p=0.012) and median Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) [10.5(1–20) vs. 6(4–16), p=0.029] were higher in cSLE. Frequency of rhupus, (12 vs. 17 %, p=1.0), Jaccoud's arthropathy (0 vs. 17 %, p=0.343) and treatments were similar in cSLE and aSLE. We determined that chronic arthritis in SLE has distinct features in

Gormezano et al. Clin Rheumatol. 2016; 35:227–231

Table 1 Demographic data, clinical manifestations and disease activity score at chronic arthritis (CA) diagnosis in childhood-onset systemic lupus erythematosus (cSLE) and adult-onset SLE (aSLE) patients

Variables	cSLE (n=8)	aSLE (n=69)	p value
Demographic data			
Age at chronic arthritis diagnosis, years	10.8 (4.2–14.6)	40 (21–67)	<0.001
Disease duration until chronic arthritis diagnosis, years	0 (−2.2–0)	10 (0.3–36)	<0.001
Duration of chronic arthritis, weeks	17 (6–104)	12 (6–720)	0.092
Chronic arthritis characteristics			
Monoarthritis	1 (12)	9 (13)	1.0
Oligoarthritis	1 (12)	38 (55)	0.028
Polyarthritis	6 (75)	22 (32)	0.024
Number of joints with arthritis	8.5 (1–18)	3 (1–9)	0.017
Number of limited joints	1.5 (0–24)	0 (0–4)	0.004
Rhupus syndrome	1 (12)	12 (17)	1.000
Jaccoud's arthropathy	0 (0)	12 (17)	0.343
Myositis	0 (0)	0 (0)	1.000
Site of arthritis			
Hands	5 (62)	40 (58)	1.000
Wrists	5 (62)	33 (48)	0.480
Knees	4 (50)	12 (17)	0.053
Ankles	8 (100)	11 (16)	<0.001

Materials and methods

This historical study evaluated 336 cSLE and 1830 aSLE patients followed from 1983 to 2014 at the paediatric and adult lupus outpatient clinics at the same tertiary public hospital in an urban area of São Paulo. All patients fulfilled the American College of Rheumatology criteria for SLE [7].

Chronic arthritis was defined according to the presence of swelling or effusion or two or more of the following: limitation of motion, tenderness or pain on motion and increased heat for at least 6 weeks. Arthritis features were also evaluated

Variables	cSLE (n=8)	aSLE (n=69)	p value
Other clinical manifestations			
Constitutional involvement			
Fever	2 (25)	2 (3)	0.051
Adenomegaly	1 (12)	1 (1.4)	0.198
Hepatomegaly	2 (25)	0 (0)	0.009
Splenomegaly	2 (25)	0 (0)	0.009
Mucocutaneous involvement			
Malar rash	2 (25)	8 (11)	0.276
Discoid rash	0 (0)	0 (0)	1.000
Photosensitivity	2 (25)	9 (13)	0.319
Mucosal ulcers	1 (12)	0 (0)	0.103
Alopecia	3 (37)	1 (1.4)	0.002
Raynaud's phenomenon	1 (12)	19 (27)	0.672
Serosal involvement			
Pleuritis	0 (0)	1 (1.4)	1.000
Pericarditis	2 (25)	0 (0)	0.009
Neuropsychiatric involvement			
Central nervous system	1 (12)	0 (0)	0.103
Peripheral nervous system	0 (0)	0 (0)	1.000
Renal involvement	3 (37)	2 (3)	0.006
Disease activity at chronic arthritis diagnosis			
SLEDAI-2K	10.5 (1–20)	6 (4–16)	0.029
Treatment at chronic arthritis diagnosis			
Non-steroidal anti-inflammatory drugs	4 (50)	27 (39)	0.707
Glucocorticoid use	8 (100)	55 (80)	0.338
Intravenous methylprednisolone	2 (25)	3 (4)	0.081
Antimalarial drugs	8 (100)	55 (80)	0.668
Immunosuppressive agents	5 (62)	49 (71)	0.689
Azathioprine	1 (12)	14 (20)	1.000
Cyclosporin	1 (12)	0 (0)	0.103
Methotrexate	3 (37)	39 (56)	0.456
Mycophenolate mofetil	0 (0)	5 (7)	1.000
Intravenous cyclophosphamide	1 (12)	1 (1.4)	0.198
Others			
Intravenous immunoglobulin	0 (0)	0 (0)	1.000
Rituximab	0 (0)	1 (1.4)	0.103

Results are presented in n (%) median (range). *SLEDAI-2K* Systemic

Results are presented in n (%), median (range). *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein

Discussion

This was the first study comparing adults and children to identify a low frequency of chronic arthritis in SLE patients with

Seminars in Arthritis and Rheumatism 47 (2017) 53–64

Contents lists available at ScienceDirect

Seminars in Arthritis and Rheumatism

journal homepage: www.elsevier.com/locate/semarthrit

Joint involvement in systemic lupus erythematosus: From pathogenesis to clinical assessment

Fulvia Ceccarelli, MD, PhD[a,*,1], Carlo Perricone, MD, PhD[a,1], Enrica Cipriano, MD[a], Laura Massaro, MD[a], Francesco Natalucci, MD[a], Giuseppe Capalbo, MD[a], Ilaria Leccese, MD[a], Dimitrios Bogdanos, MD[b], Francesca Romana Spinelli, MD, PhD[a], Cristiano Alessandri, MD[a], Guido Valesini, MD[a], Fabrizio Conti, MD[a]

[a] Lupus Clinic, Dipartimento di Medicina Interna e Specialità Mediche, Università di Roma "La Sapienza," Viale del Policlinico 155, 00161 Roma, Italy
[b] Department of Medicine, Faculty of Medicine, School of Health Sciences, University of Thessaly, Larissa, Greece

ARTICLE INFO

Keywords:
Systemic lupus erythematosus
Joint involvement
Pathogenesis
Biomarkers
Clinimetry
Imaging

ABSTRACT

Objective: In the present review, the different phenotypes, clinimetric and imaging tools able to assess joint involvement in patients affected by Systemic Lupus Erythematosus (SLE) have been described and summarized. Furthermore, the current knowledge about the pathogenic mechanism and the potential biomarkers of this feature is reported.

Methods: A literature search was done in PubMed, accessed via the National Library of Medicine PubMed interface (http://www.ncbi.nlm.nih.gov/pubmed). Firstly, PubMed was searched using the term "systemic lupus erythematosus" OR "lupus" in combination with (AND) "joint" OR "articular".

Secondly, the same PubMed research was combined with other terms, such as "pathogenesis" OR "genetic" OR "antibodies" OR "biomarkers" OR "cytokines" OR "imaging" OR "ultrasonography" OR "magnetic resonance" OR "clinimetry".

Results: After a stringent selection, we evaluated in the present review 13 papers concerning clinical

Ceccarelli et al. Seminars in Arthritis and Rheumatism 47 (2017) 53–6454

LES & Artritis refractaria

Table 1
Definitions of joint involvement in some of the most frequently used disease activity indices

Activity index	Definition of joint involvement	Referring period (d)	Score
BILAG 2004 [43]	Arthritis (severe) Arthritis (moderate)/tendonitis/tenosynovitis Arthritis (mild)/arthralgia/myalgia	28	Improved, same, worse, new
SLEDAI-2000 [41]	Arthritis: ≥ 2 joints with pain and signs of inflammation (i.e., tenderness, swelling, or effusion)	28	4
ECLAM [42]	Arthritis: non-erosive arthritis involving at least two peripheral joints Evolving arthralgia: new onset or worsening of specific localized pain without objective symptoms in at least two peripheral joints	28	1

¿ Artritis ? → ≥ 2 → ¿ Refractaria ? → ≥ 6w

LES & Artritis refractaria

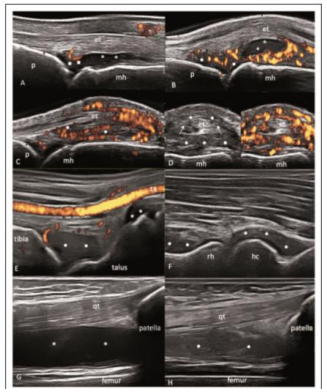


Table 2
Ultrasonographyc studies in SLE patients with joint involvement

Study	*N* patients	Joint assessed	Inflammatory features	Bone erosion	Association with clinical and serological parameters
Iagnocco et al. [56]	26 SLE 15 HC	Bilateral wrist	Synovitis: 57.7% pts (SH: 19.2%; JE: 25%; PD: 9.6% of the joints) Tenosynovitis: 57.7% pts	3.8%	No correlation
Wright et al. [57]	17 SLE	Bilateral wrist, II/III MCP III PIP Bilateral digitorum II/III/IV flexor tendons	94% JE/SH wrist 71% JE/SH II or III MCP 65% tenosynovitis	47% pts (II or III MCP)	Not evaluated
Delle Sedie et al. [58]	50 SLE 50 HC	Bilateral wrist, II/III MCP II/III PIP Bilateral digitorum II III flexor tendons	Synovitis: 80% wrist 50% MCP or PIP 22% tenosynovitis	2% pts (joint not specified)	No significant correlation between joint or tendon involvement and disease activity parameters, systemic involvement or disease duration
Demirkaya et al. [59]	30 juvenile SLE 32 HC	Non-dominant knee, ankle, elbow, wrist, MCP Tendon thickness measurements and tenosynovitis (quadriceps, patellar, Achilles, triceps, III flexor and extensor tendons)	JE: knee 60%, ankle 27.6%, elbow 6.7%, wrist 10.3% Tenosynovitis: III flexor tendon 3.3%, extensor tendons 23.3%	0%	Tendon thickness values did not correlate with disease duration and SLE disease activity index scores
Ossandon et al. [60]	26 SLE 25 RA 15 HC	Bilateral knee	Synovitis in 58% of SLE pts (JE: 23%, SH: 23%, PD: 10% of joints) Gastrocnemius-semimembranosus bursitis 15% SLE pts	0%	Not evaluated

US

Ceccarelli et al. Seminars in Arthritis and Rheumatism 47 (2017) 53–6454

LES & Artritis refractaria

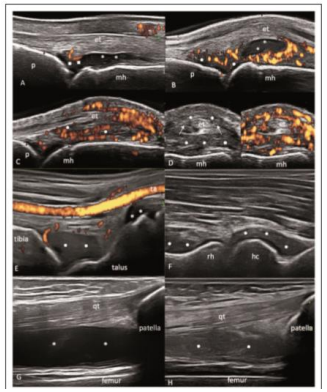


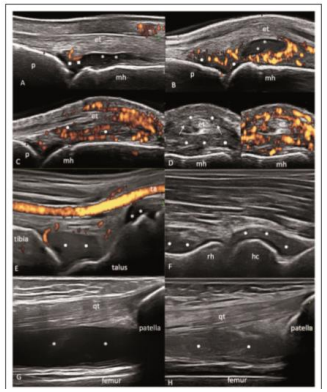
Table 2
Ultrasonographyc studies in SLE patients with joint involvement

Study	*N* patients	Joint assessed	Inflammatory features	Bone erosion	Association with clinical and serological parameters
Iagnocco et al. [56]	26 SLE 15 HC	Bilateral wrist	Synovitis: 57.7% pts (SH: 19.2%; JE: 25%; PD: 9.6% of the joints) Tenosynovitis: 57.7% pts	3.8%	No correlation
Wright et al. [57]	17 SLE	Bilateral wrist, II/III MCP III PIP Bilateral digitorum II/III/IV flexor tendons	94% JE/SH wrist 71% JE/SH II or III MCP 65% tenosynovitis	47% pts (II or III MCP)	Not evaluated
Delle Sedie et al. [58]	50 SLE 50 HC	Bilateral wrist, II/III MCP II/III PIP Bilateral digitorum II III flexor tendons	Synovitis: 80% wrist 50% MCP or PIP 22% tenosynovitis	2% pts (joint not specified)	No s… te… pa… dise…
Demirkaya et al. [59]	30 juvenile SLE 32 HC	Non-dominant knee, ankle, elbow, wrist, MCP Tendon thickness measurements and tenosynovitis (quadriceps, patellar, Achilles, triceps, III flexor and extensor tendons)	JE: knee 60%, ankle 27.6%, elbow 6.7%, wrist 10.3% Tenosynovitis: III flexor tendon 3.3%, extensor tendons 23.3%	0%	Tendon thickness values did not correlate with disease duration and SLE disease activity index scores
Ossandon et al. [60]	26 SLE 25 RA 15 HC	Bilateral knee	Synovitis in 58% of SLE pts (JE: 23%, SH: 23%, PD: 10% of joints) Gastrocnemius-semimembranosus bursitis 15% SLE pts	0%	Not evaluated

US

Ceccarelli et al. Seminars in Arthritis and Rheumatism 47 (2017) 53–6454

LES & Artritis refractaria

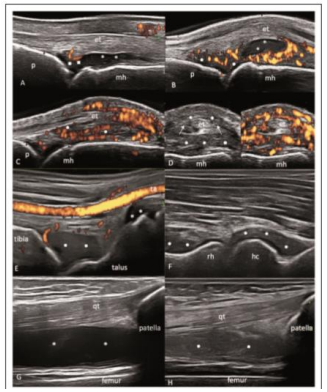


Gabba et al. [33]	108 SLE 8 Rhupus 6 JA 94 NDNE	Bilateral wrist, II/III MCP Hand and wrist flexor tendons Wrist extensor tendons	Wrist synovitis: 12.9% pts Hand synovitis: 15.7% pts PD: joints: 17% of pts; tendons: 12% pts	Bone erosions: Total pts 25.9% (hand: 24.1%; wrist 4.6%); Rhupus: 87%; JA: 17%; NDNE: 21%	Joint synovitis was independently associated with higher SLEDAI score
Torrente-Segarra et al. [61]	58 SLE (28 with arthralgia, 30 without arthralgia)	Bilateral hand and wrist	Pt with arthralgia 39.2% tenosynovitis 25% JE/SH 14.2% wrist active synovitis		Correlation between PDUS and SLEDAI, anti-dsDNA. Correlation between worsening in SF-12 and mHAQ
Ball et al. [55]	50 SLE 40 RA 15 HC	Dominant: wrist II/III/V MCP, PIP, digitorum flexor and extensor tendons. Application of semiquantitative score (0–3) for each US modifications	US activity score: SLE with erosion ($N = 18$): 10.7 ± 8.1 SLE without erosion ($N = 20$): 6.1 ± 5.6	36.0% pts	Association between erosive damage and anti-SSA, CRP Correlation between PD, tenosynovitis, total US inflammatory score and IL-6
Yoon et al. [62]	50 SLE without musculoskeletal symptoms 18 HC	Non-dominant, wrist, II/III MCP, II/III/IV digitorum flexor tendons Application of semiquantitative score (0–3) for each US modifications	Synovitis 58.3% pts (II MCP 29.2%, III MCP 31.3%, wrist 33.3%), PD 6.3%, tenosynovitis in 4.2% pts USSI score = 1.0 ± 1.01	Not evaluated	Positive correlation between USSI score and ESR, anti-dsDNA titer Positive correlation between PD and ESR
Iagnocco et al. [63]	62 SLE (40% joint involvement at the time of US assessment)	Bilateral wrist, MCP, PIP, MTP Application of semiquantitative score (0–3) for each US modifications	Inflammatory US-features in 87.1% pts: MTP (at least 1) 72.6% pts (JE 50%; SH 16%; PD 4.8%) MCP (at least 1) 46.7% pts (JE 24.2%; SH 9.7%; PD 9.7%) PIP (at least 1) 19.3% pts (JE 9.7%; SH 6.5%; PD 3.2%) Wrist 53% pts (JE 22.6%; SH 17.7%; PD 11.3%)	Not evaluated	Significant correlation between US total score and CRP levels

US

Ceccarelli et al. Seminars in Arthritis and Rheumatism 47 (2017) 53–6454

LES & Artritis refractaria



Gabba et al. [33]	108 SLE 8 Rhupus 6 JA 94 NDNE	Bilateral wrist, II/III MCP Hand and wrist flexor tendons Wrist extensor tendons	Wrist synovitis: 12.9% pts Hand synovitis: 15.7% pts PD: joints: 17% of pts; tendons: 12% pts	Bone erosions: Total pts 25.9% (hand: 24.1%; wrist 4.6%); Rhupus: 87%; JA: 17%; NDNE: 21%	Joint synovitis was independently associated with higher SLEDAI score
Torrente-Segarra et al. [61]	58 SLE (28 with arthralgia, 30 without arthralgia)	Bilateral hand and wrist	Pt with arthralgia 39.2% tenosynovitis 25% JE/SH 14.2% wrist active synovitis		Correlation between PDUS and SLEDAI, anti-dsDNA. Correlation between worsening in SF-12 and mHAQ
Ball et al. [55]	50 SLE 40 RA 15 HC	Dominant: wrist II/III/V MCP, PIP, digitorum flexor and extensor tendons. Application of semiquantitative score (0–3) for each US modifications	US activity score: SLE with erosion ($N = 18$): 10.7 ± 8.1 SLE without erosion ($N = 20$): 6.1 ± 5.6	36.0% pts	Association between [illegible] anti-SSA, CRP Correlation between [illegible] total US inflammato
Yoon et al. [62]	50 SLE without musculoskeletal symptoms 18 HC	Non-dominant, wrist, II/III MCP, II/III/IV digitorum flexor tendons Application of semiquantitative score (0–3) for each US modifications	Synovitis 58.3% pts (II MCP 29.2%, III MCP 31.3%, wrist 33.3%), PD 6.3%, tenosynovitis in 4.2% pts USSI score = 1.0 ± 1.01	Not evaluated	Positive correlation between USSI score and ESR, anti-dsDNA titer Positive correlation between PD and ESR
Iagnocco et al. [63]	62 SLE (40% joint involvement at the time of US assessment)	Bilateral wrist, MCP, PIP, MTP Application of semiquantitative score (0–3) for each US modifications	Inflammatory US-features in 87.1% pts: MTP (at least 1) 72.6% pts (JE 50%; SH 16%; PD 4.8%) MCP (at least 1) 46.7% pts (JE 24.2%; SH 9.7%; PD 9.7%) PIP (at least 1) 19.3% pts (JE 9.7%; SH 6.5%; PD 3.2%) Wrist 53% pts (JE 22.6%; SH 17.7%; PD 11.3%)	Not evaluated	Significant correlation between US total score and CRP levels

US

Ceccarelli et al. Seminars in Arthritis and Rheumatism 47 (2017) 53–6454

LES & Artritis refractaria

Fig. 1 Coronal MRI MCP joint images of an SLE patient

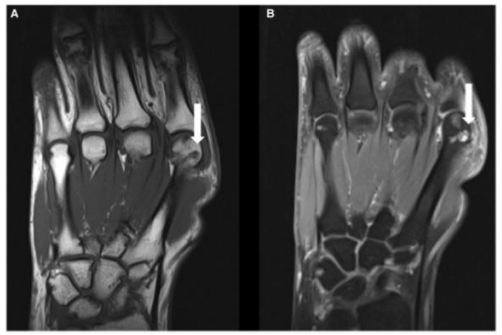


Table 3
MRI evaluation in SLE patients with joint involvement

Study	*N* patients	Joint assessed	Inflammatory features	Frequency of bone erosion	Association with clinical and serological parameters
Ostendorf et al. [66]	14 SLE (28.6% JA)	Bilateral hands	Capsular swelling: 100% pts JE 50% pts SH 71.4% pts Bony cysts 14.3% pts	57.2% pts	Not evaluated
Boutry et al. Radiology (2005) [110]	14 SLE 5 SjS 28 RA	Bilateral wrist, MCP and carpal joints. Application of semiquantitative score (synovitis 0–3, erosion 0–10)	Wrist/MCP synovitis 100% of SLE/SjS pts Wrist bone edema 16% of SLE/SjS pts MCP bone edema 5% of SLE/SjS pts Wrist tenosynovitis 47% of SLE/SjS pts MCP tenosynovitis 79% of SLE/SjS pts	Wrist 84% of SLE/SjS pts MCP 47% of SLE/SjS pts	Not evaluated
Sa Ribeiro et al. [32]	20 JA	Bilateral hand (PIP, MCP and carpometacarpal) Application of semiquantitative score 0–3	Synovitis in at least one joint: 100% Bone edema 40% pts Tenosynovitis 95% pts	50% pts	Association between swan neck deformity and ulnar deviation and synovitis/flexor tenosynovitis
Ball et al. [67]	34 SLE with arthralgia/ arthritis 15 RA	Bilateral hand and wrist	Synovitis: MCP 93% of patients, wrist 100% of patients Edema: 7.3% of MCP, 3.4% of PIP, 13.3% of wrist Tenosynovitis: 20.3% of extensor tendon, 10.2 felxor tendon	42.4% of MCP (61.8% pts) 11% of PIP 45% of carpal 36.6% distal ulna 33.3% distal radius	No association between anti-RA33 and ACPA and erosive damage
Mosca et al. [65]	102 SLE (10% Rhupus, 10% JA)	Non-dominant II/III/IV/V MCP and wrist	Bone marrow edema: Hand 7.5% of patients Wrist 35.5% of patients	Hand: 47.3% of patients Wrist: 98.9% of patients	No correlation
Tani et al. [68]	50 SLE 22 RA 48 HC	Non-dominant II/III/IV/V MCP and wrist	Bone marrow edema: Hand 4% of patients Wrist 13% of patients	Hand 48% of patients Wrist 82% of patients	No correlation

HC, healthy control; JA, Jaccoud's arthropathy; JE, joint effusion; MCP, metacarpophalangeal; PIP, proximal interphalangeal; RA, rheumatoid arthritis; SH, synovial hypertrophy; SjS, Sjögren syndrome; SLE, systemic lupus erythematosus.

RMN

Ceccarelli et al. Seminars in Arthritis and Rheumatism 47 (2017) 53–6454

LES & Artritis refractaria

Fig. 1 Coronal MRI MCP joint images of an SLE patient

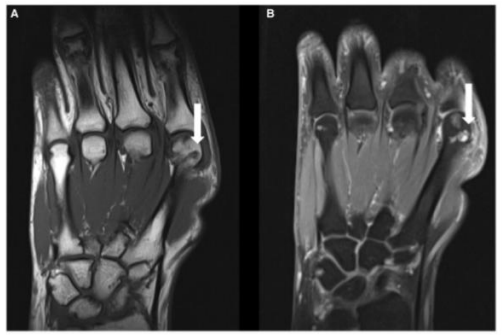


Table 3
MRI evaluation in SLE patients with joint involvement

Study	*N* patients	Joint assessed	Inflammatory features	Frequency of bone erosion	Association with clinical and serological parameters
Ostendorf et al. [66]	14 SLE (28.6% JA)	Bilateral hands	Capsular swelling: 100% pts JE 50% pts SH 71.4% pts Bony cysts 14.3% pts	57.2% pts	Not evaluated
Boutry et al. Radiology (2005) [110]	14 SLE 5 SjS 28 RA	Bilateral wrist, MCP and carpal joints. Application of semiquantitative score (synovitis 0–3, erosion 0–10)	Wrist/MCP synovitis 100% of SLE/SjS pts Wrist bone edema 16% of SLE/SjS pts MCP bone edema 5% of SLE/SjS pts Wrist tenosynovitis 47% of SLE/SjS pts MCP tenosynovitis 79% of SLE/SjS pts	Wrist 84% of SLE/SjS pts MCP 47% of SLE/SjS pts	Not
Sa Ribeiro et al. [32]	20 JA	Bilateral hand (PIP, MCP and carpometacarpal) Application of semiquantitative score 0–3	Synovitis in at least one joint: 100% Bone edema 40% pts Tenosynovitis 95% pts	50% pts	Association between swan neck deformity and ulnar deviation and synovitis/flexor tenosynovitis
Ball et al. [67]	34 SLE with arthralgia/ arthritis 15 RA	Bilateral hand and wrist	Synovitis: MCP 93% of patients, wrist 100% of patients Edema: 7.3% of MCP, 3.4% of PIP, 13.3% of wrist Tenosynovitis: 20.3% of extensor tendon, 10.2 felxor tendon	42.4% of MCP (61.8% pts) 11% of PIP 45% of carpal 36.6% distal ulna 33.3% distal radius	No association between anti-RA33 and ACPA and erosive damage
Mosca et al. [65]	102 SLE (10% Rhupus, 10% JA)	Non-dominant II/III/IV/V MCP and wrist	Bone marrow edema: Hand 7.5% of patients Wrist 35.5% of patients	Hand: 47.3% of patients Wrist: 98.9% of patients	No correlation
Tani et al. [68]	50 SLE 22 RA 48 HC	Non-dominant II/III/IV/V MCP and wrist	Bone marrow edema: Hand 4% of patients Wrist 13% of patients	Hand 48% of patients Wrist 82% of patients	No correlation

HC, healthy control; JA, Jaccoud's arthropathy; JE, joint effusion; MCP, metacarpophalangeal; PIP, proximal interphalangeal; RA, rheumatoid arthritis; SH, synovial hypertrophy; SjS, Sjögren syndrome; SLE, systemic lupus erythematosus.

RMN

Ceccarelli et al. Seminars in Arthritis and Rheumatism 47 (2017) 53–6454

LES & Artritis refractaria

oncerning the evaluation of anti-citrullinated peptide antibodies (ACPA) and rheumatoid factor (RF) in SLE patients with joint involvement

	N pts	ACPA (%)	RF (%)	Other results
Mediwake et al. [26]	231 (4.3% EA)	4.4% all SLE* (20% EA, 2% non-EA)	21.2% all SLE (60% EA, 18% non-EA)	–
Chan et al. [89]	104 (11.5% EA)	8% all SLE (50% EA, 3% non-EA)	17% all SLE (42% EA, 10% non-EA)	Significant association between ACPA and EA (X-ray). ALL HLA-DQB1*0302 carriers had EA
Damian Abrego et al. [90]	34 (41.2% w/DA)	5.8% all SLE (7% w/DA, 5% wo/DA)	35.3% all SLE (15% w/DA, 65% wo/DA)	ACPA and RF frequency significantly lower in SLE compared with RA
Amezcua-Guerra et al. [34]	11 (45.4% EA)	27.3% all SLE (60% EA, 0% non-EA)	45.4% all SLE (60% EA, 33% non-EA)	Significant higher CRP values in EA compared with non-EA
Qing et al. [92]	267 (4.4% EA)	27.3% all SLE (42.1% EA, 5.6% non-EA)	45.3% all SLE (44.7% EA, 46.3% non-EA)	Higher ACPA titer in EA than in non-EA
Zhao et al. [93]	138	13.8% all SLE (20% A-SLE, 7.4% nonA-SLE)	26.8% all SLE (28.6% A-SLE, 25% nonA-SLE)	Higher ACPA median levels in A-SLE compared with nonA-SLE Association between ACPA and X-ray erosive damage
Kakumanu et al. [94]	329	16.7% all SLE	–	High ACPA (> 10 units) in 12% of SLE with deforming/erosive arthritis.
Taraborelli et al. [95]	198 (EA 4%)	7% all SLE (44% EA, 9% w/DA, 5% wo/DA)	19% all SLE (55% EA, 31% w/DA, 15% wo/DA)	No significant differences among 3 groups in terms of ACPA levels Association between EA and positivity for ACPA (OR = 6.87)
Skare et al. [96]	109	13.7% all SLE	18.2% all SLE	Only 1 ACPA+ pt (6.7%) showed radiographic erosive damage (right 5th MTP)

A-SLE, SLE with arthritis at the time of evaluation; EA, erosive arthritis; MTP, metatarsophalangeal; nonA-SLE, SLE without arthritis at the time of evaluation; w/DA, with deforming arthropathy; wo/DA, without deforming arthropathy.

* Evaluation on 66 SLE patients; $P = 0.005$.

Ceccarelli et al. Seminars in Arthritis and Rheumatism 47 (2017) 53–6454

LES & Artritis refractaria

oncerning the evaluation of anti-citrullinated peptide antibodies (ACPA) and rheumatoid factor (RF) in SLE patients with joint involvement

	N pts	ACPA (%)	RF (%)	Other results
Mediwake et al. [26]	231 (4.3% EA)	4.4% all SLE* (20% EA, 2% non-EA)	21.2% all SLE (60% EA, 18% non-EA)	–
Chan et al. [89]	104 (11.5% EA)	8% all SLE (50% EA, 3% non-EA)	17% all SLE (42% EA, 10% non-EA)	Significant association between ACPA and EA (X-ray). ALL HLA-DQB1*0302 carriers had EA
Damian Abrego et al. [90]	34 (41.2% w/DA)	5.8% all SLE (7% w/DA, 5% wo/DA)	35.3% all SLE (15% w/DA, 65% wo/DA)	ACPA and RF frequency significantly lower in SLE compared with RA
Amezcua-Guerra et al. [34]	11 (45.4% EA)	27.3% all SLE (60% EA, 0% non-EA)	45.4% all SLE (60% EA, 33% non-EA)	Significant higher CRP values in EA compared with non-EA
Qing et al. [92]	267 (4.4% EA)	27.3% all SLE (42.1% EA, 5.6% non-EA)	45.3% all SLE (44.7% EA, 46.3% non-EA)	Higher ACPA titer in EA than in non-EA
Zhao et al. [93]	138	13.8% all SLE (20% A-SLE, 7.4% nonA-SLE)	26.8% all SLE (28.6% A-SLE, 25% nonA-SLE)	Higher ACPA median levels in A-SLE compared with nonA-SLE Association between ACPA and X-ray erosive damage
Kakumanu et al. [94]	329	16.7% all SLE	–	High ACPA (> 10 units) in 12% of SLE with deforming/erosive arthritis.
Taraborelli et al. [95]	198 (EA 4%)	7% all SLE (44% EA, 9% w/DA, 5% wo/DA)	19% all SLE (55% EA, 31% w/DA, 15% wo/DA)	No significant differences among 3 groups in terms of ACPA levels Association between EA and positivity for ACPA (OR = 6.87)
Skare et al. [96]	109	13.7% all SLE	18.2% all SLE	Only 1 ACPA+ pt (6.7%) showed radiographic erosive damage (right 5th MTP)

A-SLE, SLE with arthritis at the time of evaluation; EA, erosive arthritis; MTP, metatarsophalangeal; nonA-SLE, SLE without arthritis at the time of evaluation; w/DA, with deforming arthropathy; wo/DA, without deforming arthropathy.

* Evaluation on 66 SLE patients; $P = 0.005$.

Ceccarelli et al. Seminars in Arthritis and Rheumatism 47 (2017) 53–6454

Lupus (2014) 23, 1156–1163
http://lup.sagepub.com

PAPER

Anti-cyclic citrullinated peptide antibody as a marker of erosive arthritis in patients with systemic lupus erythematosus: a systematic review and meta-analysis

A Budhram[1], R Chu[2], S Rusta-Sallehy[3], G Ioannidis[4], JA Denburg[5], JD Adachi[4] and DA Haaland[4,5]
[1]Michael G. DeGroote School of Medicine, McMaster University, Hamilton, Ontario, Canada; [2]Mississauga Academy of Medicine, University of Toronto, Mississauga, Ontario, Canada; [3]Peters-Boyd Academy, University of Toronto, Toronto, Ontario, Canada; [4]Division of Rheumatology, McMaster University, Hamilton, Ontario, Canada; and [5]Division of Clinical Immunology & Allergy, McMaster University, Hamilton, Ontario, Canada

Objective: Anti-cyclic citrullinated peptide (CCP) antibody is an established marker in the diagnosis and prognostication of rheumatoid arthritis (RA). Infrequently, systemic lupus erythematosus (SLE) patients also develop a deforming erosive arthritis, similar to that of RA. Our objective was to determine whether anti-CCP antibody is a useful marker of erosive disease in SLE patients presenting with arthritis. **Methods:** Electronic databases EMBASE, MEDLINE and non-indexed MEDLINE citations were searched through April 11, 2014, using the outlined key terms. Studies meeting predefined inclusion and exclusion criteria were reviewed. Two reviewers independently assessed the quality of included articles using previously described criteria. The DerSimonian-Laird random effects model was used to calculate pooled sensitivity and specificity of anti-CCP antibody for erosive arthritis in SLE. **Results:** Seven articles met inclusion and exclusion criteria. A total of 609 SLE patients with arthritis were identified, 70 of whom had erosive disease. Pooled sensitivity and specificity of anti-CCP antibody for erosive arthritis was 47.8% (95% CI, 26.2%–70.2%) and 91.8%

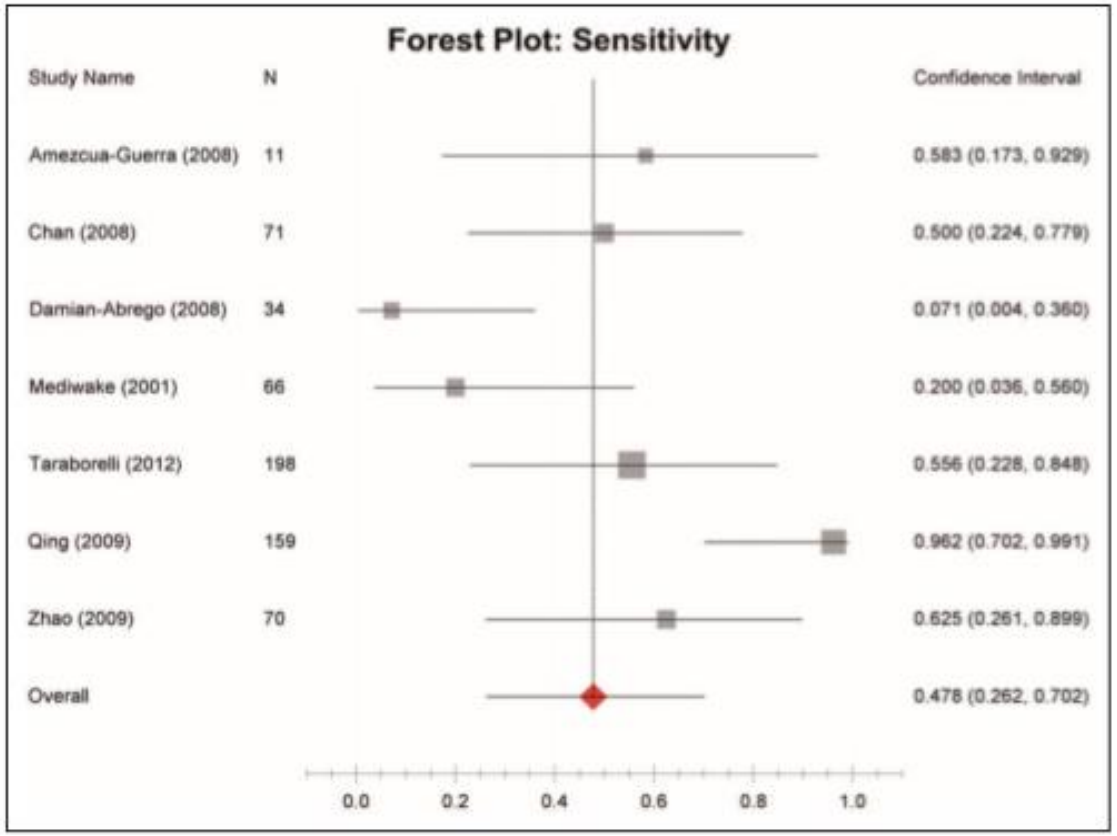


Figure 3 Pooled sensitivity of anti-CCP antibody in SLE erosive arthritis.
Anti-CCP: anti-cyclic citrullinated peptide; SLE: systemic lupus erythematosus.

Budhram et al. Lupus (2014) 23, 1156–1163.

LES & Artritis refractaria

Lupus (2014) 23, 1156–1163
http://lup.sagepub.com

PAPER

Anti-cyclic citrullinated peptide antibody as a marker of erosive arthritis in patients with systemic lupus erythematosus: a systematic review and meta-analysis

A Budhram[1], R Chu[2], S Rusta-Sallehy[3], G Ioannidis[4], JA Denburg[5], JD Adachi[4] and DA Haaland[4,5]
[1]Michael G. DeGroote School of Medicine, McMaster University, Hamilton, Ontario, Canada; [2]Mississauga Academy of Medicine, University of Toronto, Mississauga, Ontario, Canada; [3]Peters-Boyd Academy, University of Toronto, Toronto, Ontario, Canada; [4]Division of Rheumatology, McMaster University, Hamilton, Ontario, Canada; and [5]Division of Clinical Immunology & Allergy, McMaster University, Hamilton, Ontario, Canada

Objective: Anti-cyclic citrullinated peptide (CCP) antibody is an established marker in the diagnosis and prognostication of rheumatoid arthritis (RA). Infrequently, systemic lupus erythematosus (SLE) patients also develop a deforming erosive arthritis, similar to that of RA. Our objective was to determine whether anti-CCP antibody is a useful marker of erosive disease in SLE patients presenting with arthritis. **Methods:** Electronic databases EMBASE, MEDLINE and non-indexed MEDLINE citations were searched through April 11, 2014, using the outlined key terms. Studies meeting predefined inclusion and exclusion criteria were reviewed. Two reviewers independently assessed the quality of included articles using previously described criteria. The DerSimonian-Laird random effects model was used to calculate pooled sensitivity and specificity of anti-CCP antibody for erosive arthritis in SLE. **Results:** Seven articles met inclusion and exclusion criteria. A total of 609 SLE patients with arthritis were identified, 70 of whom had erosive disease. Pooled sensitivity and specificity of anti-CCP antibody for erosive arthritis was 47.8% (95% CI, 26.2%–70.2%) and 91.8%

- La sensibilidad y especificidad agrupadas de los Ac anti-CCP en artropatía erosiva LES fue menor que la previamente descrita en AR

  (91.8% vs 95% and 47.8% vs 67%, respectivamente)

- Al analizar pacientes que cumplían también criterios ACR para AR ("rhupus") la sensibilidad y especificidad para detectar erosiones aumenta

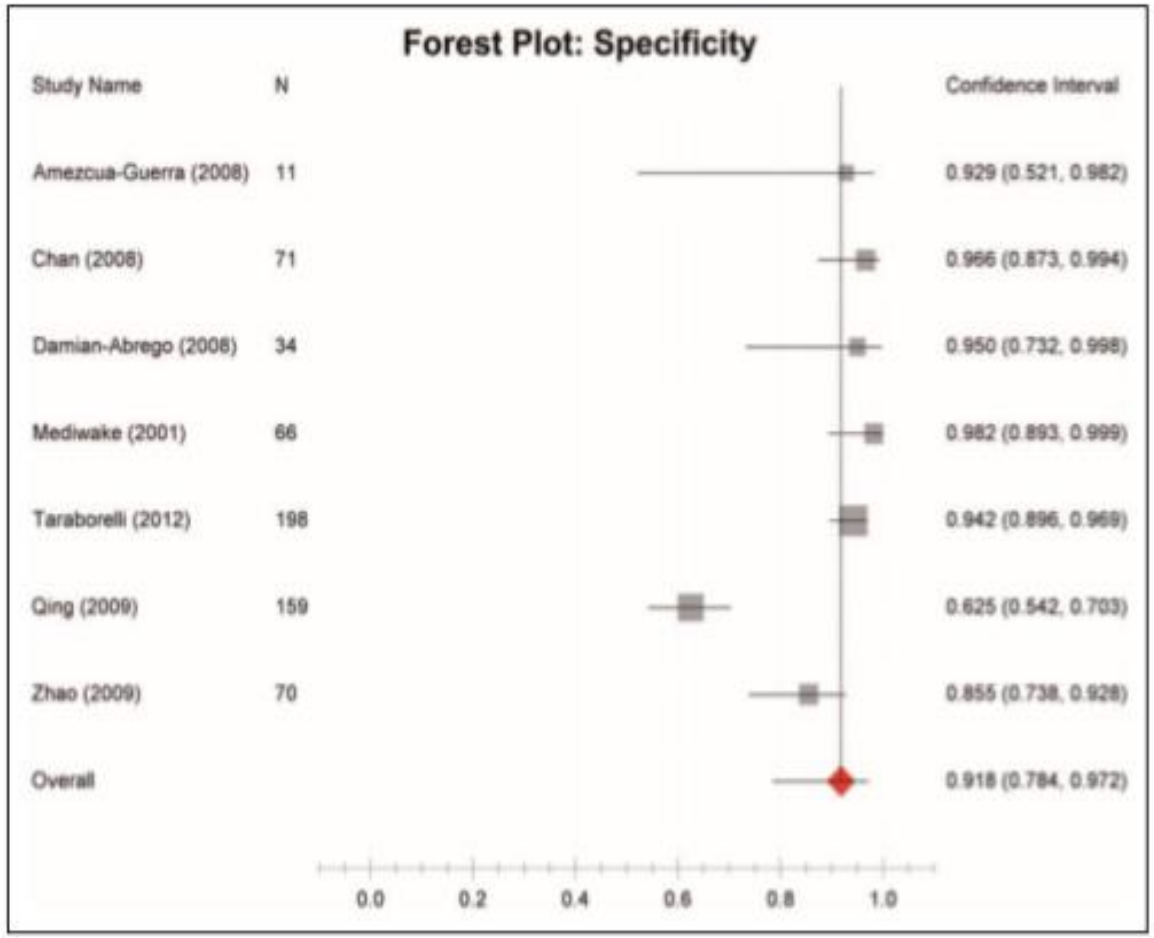


Figure 4 Pooled specificity of anti-CCP antibody in SLE erosive arthritis.
Anti-CCP: anti-cyclic citrullinated peptide; SLE: systemic lupus erythematosus.

Budhram et al. Lupus (2014) 23, 1156–1163.

LES & Artritis refractaria

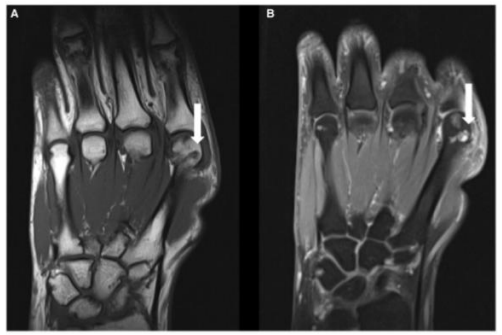
- FR y ACPA: Su papel en la esfera articular de LES está por concretar.

- Varios estudios han analizado el potencial de ACPA para predecir un subgrupo de pacientes con artritis erosiva en LES con resultados variables*

- Anticuerpos Anti-RA33 contra el antígeno nuclear hnRNP-A2 presentes en un 20%-25% de pacientes con LES.** Su relevancia en LES está poco estudiada:
  - No correlación con hallazgos clínicos
  - Correlación con afectación renal y actividad sistémica
  - Asociación significativa con artritis erosiva en un subgrupo de pacientes con rhupus

*Budhram et al. Lupus (2014) 23, 1156–1163.
**Hassfeld et al. Arthritis Rheum 1995;38:777-85.

Fig. 1 Coronal MRI MCP joint images of an SLE patient



RHEUMATOLOGY

Rheumatology 2014;53:1835–1843
doi:10.1093/rheumatology/keu215
Advance Access publication 20 May 2014

Original article

A study of erosive phenotypes in lupus arthritis using magnetic resonance imaging and anti-citrullinated protein antibody, anti-RA33 and RF autoantibody status

Elisabeth M. A. Ball[1,6], Ai Lyn Tan[2], Eiji Fukuba[3], Dennis McGonagle[2], Arthur Grey[4], Günter Steiner[5], Aubrey L. Bell[6] and Madeleine R. Rooney[1]

Abstract

Objectives. The aims of this study were to investigate the extent of MRI-determined joint disease (erosion and synovitis) in SLE and to link this to autoantibody profiles known to be relevant to SLE, including ACPA, RF and anti-RA33 antibodies.

Methods. Contrast-enhanced MRI of the hand and wrist was performed in 34 symptomatic SLE patients and in 15 RA patients with similar disease duration. Images were scored by two observers using the OMERACT rheumatoid arthritis MRI scoring (RAMRIS) system. Findings were correlated with clinical examination and autoantibody status.

Results. Erosions were present at the wrist in 93% of SLE patients and at the MCP joints in 61% of SLE patients. Despite the high prevalence of MRI-determined erosion, only 8.8% of SLE patients were ACPA positive, although these patients had a higher burden of erosive disease. There was no positive correlation with anti-RA33 titres and erosion scores in the SLE patients, but there was a negative correlation with anti-RA33 titres and total bone oedema scores in the SLE patients. Ninety-three per cent of SLE patients had at least grade 1 synovitis at one or more MCP joints, and wrist joint synovitis was present in all the SLE

Ball et al. Rheumatology. 2014; 53:1835–43

TABLE 4 MRI characteristics of SLE patients who were ACPA or RF positive or with highest RA33 titres

Patient number	ACPA	RF	Anti-RA33 titre, μg/l	Total MCP erosion score on MRI (range 0–50)	Total wrist erosion score on MRI (range 0–100)	Total MCP bone oedema (range 0–12)
89	+	–	10.2	24	7	0
45	+	–	8.4	0	1	0
59	+	–	9.5	22	10	6
3	–	+	3.2	33	7	19
6	–	–	28	0	1	0
16	–	–	52	2	5	0
33	–	–	82	3	1	0
37	–	–	316	2	8	0
39	–	–	96.2	0	4	0
67	–	–	40	14	12	0

+: positive antibody test; –: negative antibody test.

Ball et al. Rheumatology. 2014; 53:1835–43

TABLE 4 MRI characteristics of SLE patients who were ACPA or RF positive or with highest RA33 titres

Patient number	ACPA	RF	Anti-RA33 titre, μg/l	Total MCP erosion score on MRI (range 0–[illegible])	Total wrist erosion score on MRI (range 0–100)	Total MCP bone oedema (range 0–12)
89	+	–	10.2	24	7	0
45	+	–	8.4	0	1	0
59	+	–	9.5	22	10	6
3	–	+	3.2	33	7	19
6	–	–	28	0	1	0
16	–	–	52	2	5	0
33	–	–	82	3	1	0
37	–	–	316	2	8	0
39	–	–	96.2	0	4	0
67	–	–	40	14	12	0

+: positive antibody test; –: negative antibody test.

Ball et al. Rheumatology. 2014; 53:1835–43

TABLE 4 MRI characteristics of SLE patients who were ACPA or RF positive or with highest RA33 titres

Patient number	ACPA	RF	Anti-RA33 titre, μg/l	Total MCP erosion score on MRI (range 0–50)	Total wrist erosion score on MRI (range 0–100)	Total MCP bone oedema (range 0–12)
89	+	–	10.2	24	7	0
45	+	–	8.4	0	1	0
59	+	–	9.5	22	10	6
3	–	+	3.2	33	7	13
6	–	–	28	0	1	0
16	–	–	52	2	5	0
33	–	–	82	3	1	0
37	–	–	316	2	8	0
39	–	–	96.2	0	4	0
67	–	–	40	14	12	0

+: positive antibody test; –: negative antibody test.

Ball et al. Rheumatology. 2014; 53:1835–43

TABLE 4 MRI characteristics of SLE patients who were ACPA or RF positive or with highest RA33 titres

Patient number	ACPA	RF	Anti-RA33 titre, μg/l	Total MCP erosion score on MRI (range 0–[illegible])	Total wrist erosion score on MRI (range 0–100)	Total MCP bone oedema (range 0–12)
89	+	–	10.2	24	7	0
45	+	–	8.4	0	1	0
59	+	–	9.5	22	10	6
3	–	+	3.2	33	7	[illegible]
6	–	–	28	0	1	0
16	–	–	52	2	5	0
33	–	–	82	3	1	0
37	–	–	316	2	8	0
39	–	–	96.2	0	4	0
67	–	–	40	14	12	0

+: positive antibody test; –: negative antibody test.

Ball et al. Rheumatology. 2014; 53:1835–43

LES & Artritis refractaria

- La sinovitis (incluyendo grados leves) fue muy frecuente en LES y ofrece una potencial explicación para la aparición frecuente de artralgias en LES.

- La artritis erosiva en el LES con afectación articular crónica es frecuente y es independiente de ACPA.

- El edema óseo observado por RMN es expresión de una osteitis activa secundaria a sinovitis.

- En este estudio se observó una asociación inversa entre edema óseo y anti-RA33 en LES.

Ball et al. Rheumatology. 2014; 53:1835–43

LES & Artritis refractaria

- Desarrollo de definición de consenso de "Artritis refractaria"
- Potenciar la correlación entre hallazgos ecográficos / RMN y parámetros clínico-analíticos
- Estudio de nuevos biomarcadores en este subgrupo de pacientes de LES
- Tratamiento: ⇨ Más allá de FAME (Hidroxicloroquina / MTX / LFN)

Seminars in Arthritis and Rheumatism 44 (2015) 672–679

Contents lists available at ScienceDirect

Seminars in Arthritis and Rheumatism

journal homepage: www.elsevier.com/locate/semarthrit

Etanercept in refractory lupus arthritis: An observational study

Josefina Cortés-Hernández, Natalia Egri, Miquel Vilardell-Tarrés, Josep Ordi-Ros*

Systemic Autoimmune Diseases Unit, Internal Medicine Department, Universitari Vall d'Hebron Hospital, Institut de Recerca (VHIR), Universitat Autònoma de Barcelona, Passeig Vall- d'Hebron 119-129, Barcelona 08035, Spain

ARTICLE INFO

Keywords:
Refractory arthritis
Systemic lupus erythematosus
Etanercept

ABSTRACT

Objective: To investigate the long-term safety and preliminary efficacy of etanercept in patients with refractory lupus arthritis.
Methods: We evaluated 43 patients in this observational cohort study. All received etanercept (50 mg/week) in addition to concomitant immunosuppressive agents. Patient and disease characteristics were collected. Incidence of adverse events and the effect on autoantibody levels were evaluated. Clinical efficacy was measured by the 28-joint count and the SLEDAI-2K scores. Remission of lupus arthritis was defined by a 28-joint score = 0. Clinically inactive systemic disease was defined by a SLEDAI-2K score <4.
Results: The total follow-up time was 93 patient-years (median: 2.3 years per patient; range: 0.4–6.8 years). Most side effects were minor and related to local reactions. Only 2 significant adverse events occurred (8%), both were of infectious nature. The rate of autoantibody production was low (18%). A mild increase in titres of ANA (2), IgG anti-dsDNA (3) and IgM anticardiolipin (aCL) (2) antibodies was observed. All anti-dsDNA antibody increments were transient and coincided with systemic flares. No vascular events occurred. In general, disease activity declined during therapy. Most patients (83%) with lupus arthritis achieved clinical remission by week 12. All patients with simultaneous serositis experienced clinical and radiological resolution of this condition. Relapses were frequent (23%), mostly mild and related to etanercept reduction. A total of 24 patients discontinued treatment, 12 of them due to clinical remission.
Conclusions: Long-term therapy with etanercept was relatively safe and had remarkable long-term efficacy for refractory lupus arthritis. In view of these results, further controlled trials are warranted.

- Etanercept
  - E. Observacional

N=43

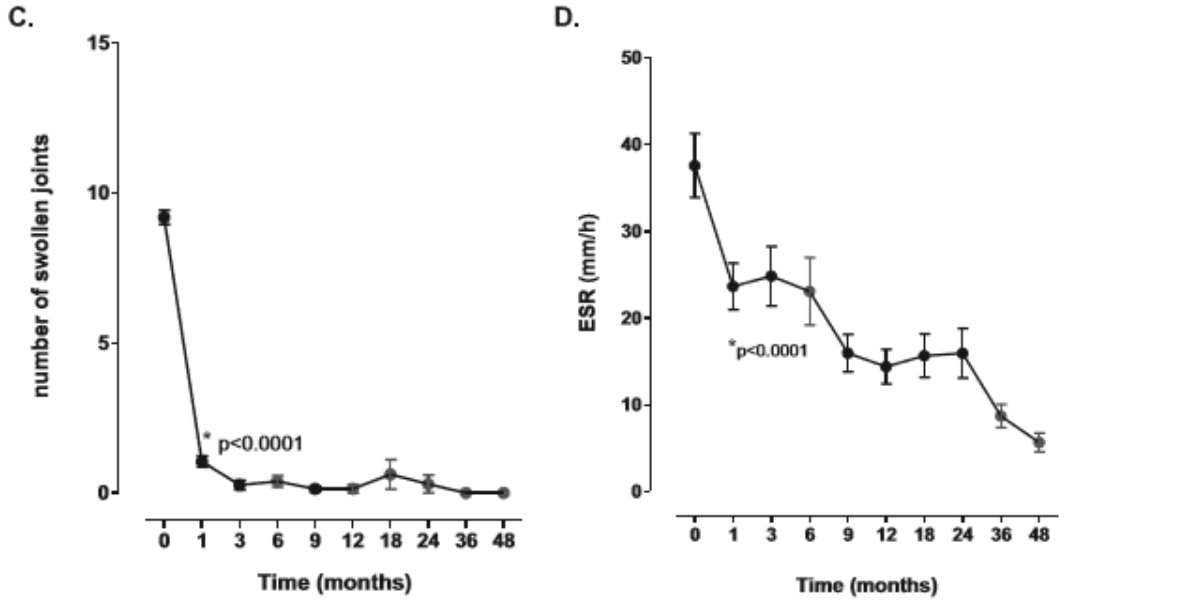


Fig. 2. Decrease in systemic disease activity as measured by the Systemic Lupus Erythematosus Disease activity Index (SLEDAI) (A), tender (B) and swollen joint counts (C) and ESR levels (D) following TNFα blocking therapy in patients with systemic lupus erythematosus with refractory arthritis. Results are shown by the mean ± SD. *$p < 0.05$ versus baseline by Mann–Whitney test.

Cortés-Hernández et al. Semin Arthritis Rheum.2015 (6):672–79.

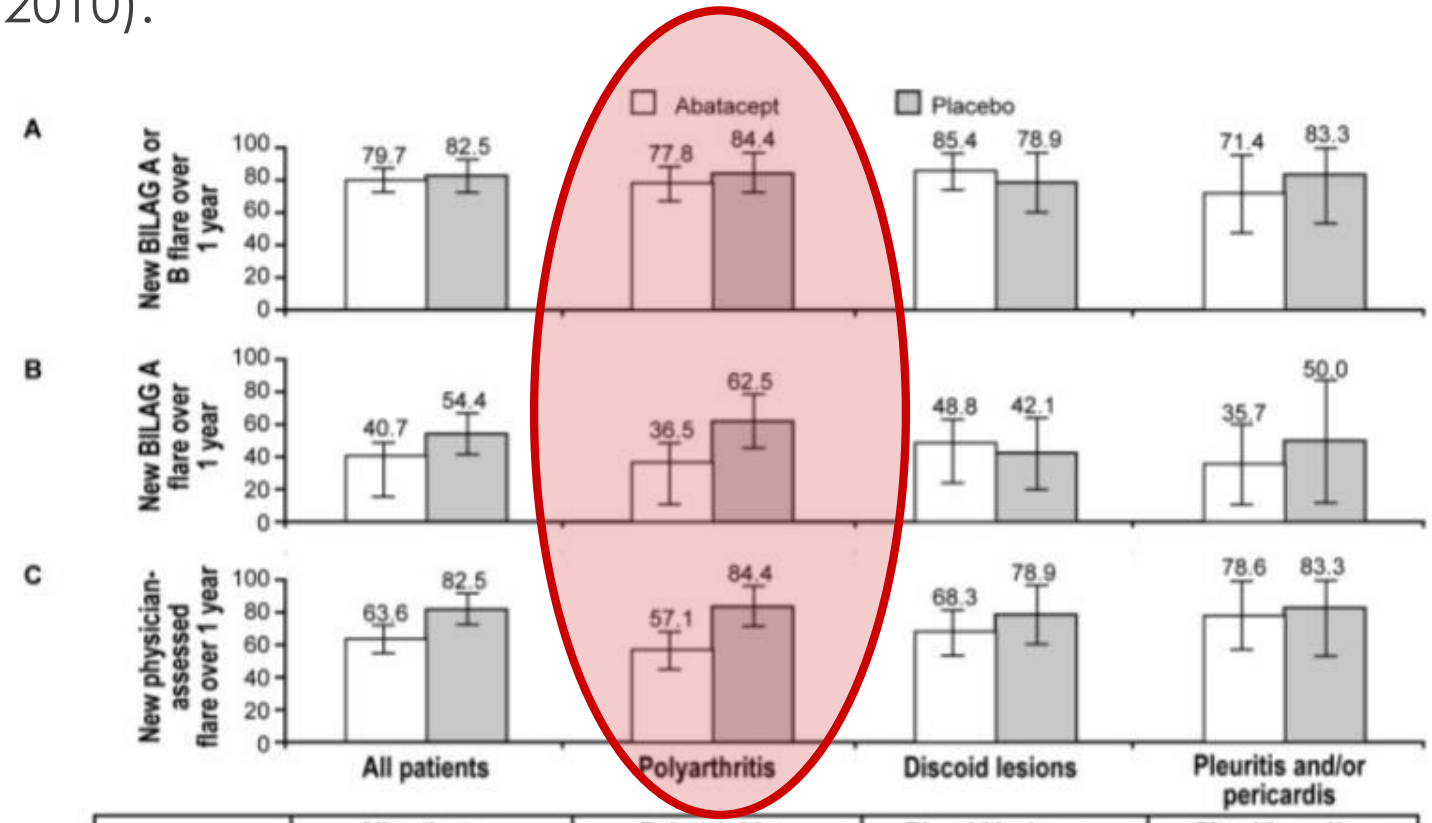
Tratamiento

MERRILL ET AL

- Abatacept vs Placebo (2010):

N=175

- EC Randomizado
- 12 meses



	All patients	Polyarthritis	Discoid lesions	Pleuritis and/or pericardis
Abatacept	118	63	41	14
Placebo	57	32	19	6

Merrill et al. Arthritis Rheum. 2010 (62):3077-87.

- Abatacept vs Placebo:

Table 2. Safety summary over 12 months

	No. (%) taking abatacept (n = 121)	No. (%) taking placebo (n = 59)
AEs	110 (90.9)	54 (91.5)
Treatment-related AEs	59 (48.8)	28 (47.5)
Discontinuations due to AEs*	10 (8.3)	3 (5.1)
SAEs	24 (19.8)	4 (6.8)
Treatment-related SAEs	7 (5.8)	2 (3.4)
Discontinuations due to SAEs*	7 (5.8)	1 (1.7)
Deaths	1 (0.8)	0

Merrill et al. Arthritis Rheum. 2010(62):3077-87.

Seminars in Arthritis and Rheumatism 44 (2014) 175–185

Contents lists available at ScienceDirect

Seminars in Arthritis and Rheumatism

journal homepage: www.elsevier.com/locate/semarthrit

Efficacy and safety of rituximab in the treatment of non-renal systemic lupus erythematosus: A systematic review

Tatiana Cobo-Ibáñez, MD, PhD[a,*], Estíbaliz Loza-Santamaría, MD[b], José María Pego-Reigosa, MD, PhD[c], Alejandro Olivé Marqués, MD, PhD[d], Íñigo Rúa-Figueroa, MD[e], Antonio Fernández-Nebro, MD, PhD[f], Rafael Cáliz Cáliz, MD[g], Francisco Javier López Longo, MD, PhD[h], Santiago Muñoz-Fernández, MD, PhD[a]

[a] Rheumatology Department, Hospital Universitario Infanta Sofía, Paseo de Europa, 34, San Sebastián de los Reyes 28702, Madrid, Spain
[b] Institute for Musculoskeletal Health, Madrid, Spain
[c] Rheumatology Department, Vigo, Department, Instituto de Investigación Biomédica de Vigo (IBIV), Vigo, Spain
[d] Rheumatology Department, Hospital Universitario Germans Trías i Pujol, Badalona, Barcelona, Spain
[e] Rheumatology Department, Hospital Universitario Doctor Negrín, Las Palmas de Gran Canaria, Spain
[f] Rheumatology Department, Hospital Regional Universitario de Málaga, Universidad de Málaga, Instituto de Investigación biomédica de Málaga (IBIMA), Málaga, Spain
[g] Rheumatology Department, Hospital General Universitario Virgen de las Nieves, Granada, Spain
[h] Rheumatology Department, Hospital General Universitario Gregorio Marañón, Madrid, Spain

ARTICLE INFO

Keywords:
Systemic lupus erythematosus
Rituximab
Systematic review

ABSTRACT

Objective: To analyse the efficacy and safety of rituximab in the treatment of non-renal systemic lupus erythematosus (SLE).
Methods: We systematically searched MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials up to June 2013. The following were the selection criteria: (1) adult patients with SLE, (2) rituximab treatment, (3) placebo or active comparator, (4) outcome measures assessing efficacy and/or (5) safety. Meta-analysis, systematic literature reviews, randomised control trials (RCT), open clinical trials and cohort studies were included.

Independent extraction of articles by 2 authors using predefined data fields was performed. The quality of each study was graded using the Oxford Levels of Evidence and Jadad's scale.
Results: A total of 26 articles met our inclusion criteria: one RCT and its exploratory analysis, 2 open studies and 22 cohort studies, which analysed 1,231 patients. Overall, patients had active disease refractory to steroids and/or immunosuppressant drugs. Acceptable evidence suggested improvements in disease

- Rituximab:
- 7 cohortes*

*Definiciones de mejoría articular diferentes

- Respuesta parcial / completa:
  - 72% – 81,5 % a corto plazo (3- 6 meses)
  - 36,6% – 93% a largo plazo (≥12 meses)

Cobo-Ibáñez et al. Semin Arthritis Rheum.2014;(2):175–85.

Arthritis Care & Research
Vol. 69, No. 1, January 2017, pp 115–123
DOI 10.1002/acr.22971

ORIGINAL ARTICLE

Effects of Belimumab on Flare Rate and Expected Damage Progression in Patients With Active Systemic Lupus Erythematosus

LUCA IACCARINO,[1] SILVANO BETTIO,[1] ROSSELLA REGGIA,[2] MARGHERITA ZEN,[1] MICOL FRASSI,[2] LAURA ANDREOLI,[2] MARIELE GATTO,[1] SILVIA PIANTONI,[2] LINDA NALOTTO,[1] FRANCO FRANCESCHINI,[2] MADDALENA LAROSA,[1] MICAELA FREDI,[2] LEONARDO PUNZI,[1] ANGELA TINCANI,[2] AND ANDREA DORIA[1]

Objective. To investigate effectiveness and safety of belimumab in patients with active systemic lupus erythematosus (SLE) in a clinical practice setting.

Methods. Sixty-seven patients with active SLE, mean ± SD age 39.3 ± 10.2 years, from 2 Italian prospective cohorts were treated with belimumab (10 mg/kg on day 0, 14, 28, and then every 28 days) added to background therapy. The Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K), the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index, the Disease Activity Score in 28 joints (DAS28), 24-hour proteinuria, the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) activity score, anti–double-stranded DNA (anti-dsDNA), C3 and C4 levels, and prednisone daily dose were recorded at baseline, month 3, 6, 9, 12, 18, and 24. Arthritis was subdivided into "classical" (CLP) and "rheumatoid-like"; skin manifestations into acute (ACLE), subacute (SCLE), and chronic. SLE flares, defined according to the SLEDAI Flare Index, were calculated before and after belimumab initiation. Adverse events were carefully evaluated during treatment. Statistics were performed by the SPSS package (version 21.0)

- Belimumab:
- Estudio cohortes Prospectivo

N=67

Table 2. Clinical and serologic disease activity variables in 67 patients with active SLE treated with belimumab*

	Patients, no.	Baseline	3 months	6 months	9 months	12 months	18 months	24 months
SLEDAI-2K	67	8.7 ± 3.8	6.1 ± 4.1†	5.3 ± 3.3‡	5.6 ± 3.4†	5.1 ± 3.2†	5.2 ± 3.2‡	4.8 ± 2.5‡
Prednisone daily dose, mg/day	67	11.2 ± 6.6	8.8 ± 4.6	7.6 ± 3.7‡	7.0 ± 4.3‡	5.5 ± 2.5‡	4.5 ± 2.4‡	5.1 ± 5.3‡
DAS28 score	30	4.03 ± 1.09	2.59 ± 0.75‡	2.62 ± 1.19‡	2.40 ± 1.13‡	2.19 ± 0.61‡	1.72 ± 0.24‡	2.29 ± 1.25†
CLASI activity score, median (range)§	19	5 (1–14)	2 (0–12)†	2 (0–12)¶	1.5 (0–12)¶	1 (0–6)†	2 (0–8)¶	0.5 (0–6)¶
C3, gm/liter	67	0.68 ± 0.17	0.75 ± 0.19	0.76 ± 0.18	0.77 ± 0.17	0.79 ± 0.19	0.76 ± 0.18	0.76 ± 0.19
C4, gm/liter	67	0.11 ± 0.05	0.13 ± 0.06	0.17 ± 0.21	0.18 ± 0.22	0.15 ± 0.07	0.18 ± 0.13	0.14 ± 0.05
Anti-dsDNA (ELISA; KIU/liter)	41	587 ± 1,111‡	231 ± 291.5‡	197.3 ± 263‡	194.6 ± 235¶	196.6 ± 239†	168.9 ± 226†	124.1 ± 143
Anti-dsDNA (Farr; UI/ml)	26	102.4 ± 201.0	53.1 ± 69.0	40.6 ± 45.0	32.0 ± 30.2	25.6 ± 31.8	33.1 ± 41.1	29.9 ± 26.1
24-hour proteinuria, gm/die	16	1.27 ± 0.68	1.08 ± 0.99	0.88 ± 0.65¶	0.72 ± 0.63¶	0.69 ± 0.53¶	0.69 ± 0.71†	0.70 ± 0.77
Creatinine, mmoles/liter	16	67.83 ± 24.80	74.63 ± 17.48	75.01 ± 24.24	71.00 ± 14.42	71.90 ± 20.28	62.62 ± 9.70	65.86 ± 18.18
White blood cells, mm^3	16	2,588 ± 910	3,840 ± 1,741†	3,701 ± 1,808†	4,162 ± 1,083¶	4,500 ± 1,534¶	3,667 ± 1,192†	4,485 ± 21.2

* Values are the mean ± SD unless indicated otherwise. SLE = systemic lupus erythematosus; SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index 2000; DAS28 = Disease Activity Score in 28 joints; CLASI = Cutaneous Lupus Erythematosus Area and Severity Index; dsDNA = double-stranded DNA; ELISA = enzyme-linked immunosorbent assay.
† $P < 0.01$ by *t*-test (vs. baseline).
‡ $P < 0.001$ by *t*-test (vs. baseline).
§ Due to nonparametric distribution of data, the CLASI score is expressed as median (range).
¶ $P < 0.05$ by *t*-test (vs. baseline).

Iaccarino et al. Arthritis Care Res (Hoboken). 2017;69(1):115-123

Arthritis Care & Research
Vol. 69, No. 1, January 2017, pp 115–123
DOI 10.1002/acr.22971

ORIGINAL ARTICLE

Effects of Belimumab on Flare Rate and Expected Damage Progression in Patients With Active Systemic Lupus Erythematosus

LUCA IACCARINO,[1] SILVANO BETTIO,[1] ROSSELLA REGGIA,[2] MARGHERITA ZEN,[1] MICOL FRASSI,[2] LAURA ANDREOLI,[2] MARIELE GATTO,[1] SILVIA PIANTONI,[2] LINDA NALOTTO,[1] FRANCO FRANCESCHINI,[2] MADDALENA LAROSA,[1] MICAELA FREDI,[2] LEONARDO PUNZI,[1] ANGELA TINCANI,[2] AND ANDREA DORIA[1]

Objective. To investigate effectiveness and safety of belimumab in patients with active systemic lupus erythematosus (SLE) in a clinical practice setting.

Methods. Sixty-seven patients with active SLE, mean ± SD age 39.3 ± 10.2 years, from 2 Italian prospective cohorts were treated with belimumab (10 mg/kg on day 0, 14, 28, and then every 28 days) added to background therapy. The Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K), the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index, the Disease Activity Score in 28 joints (DAS28), 24-hour proteinuria, the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) activity score, anti–double-stranded DNA (anti-dsDNA), C3 and C4 levels, and prednisone daily dose were recorded at baseline, month 3, 6, 9, 12, 18, and 24. Arthritis was subdivided into "classical" (CLP) and "rheumatoid-like"; skin manifestations into acute (ACLE), subacute (SCLE), and chronic. SLE flares, defined according to the SLEDAI Flare Index, were calculated before and after belimumab initiation. Adverse events were carefully evaluated during treatment. Statistics were performed by the SPSS package (version 21.0)

- Belimumab:
- Estudio cohortes Prospectivo

N=67

Table 2. Clinical and serologic disease activity variables in 67 patients with active SLE treated with belimumab*

	Patients, no.	Baseline	3 months	6 months	9 months	12 months	18 months	24 months
SLEDAI-2K	67	8.7 ± 3.8	6.1 ± 4.1†	5.3 ± 3.3‡	5.6 ± 3.4†	5.1 ± 3.2†	5.2 ± 3.2‡	4.8 ± 2.5‡
Prednisone daily dose, mg/day	67	11.2 ± 6.6	8.8 ± 4.6	7.6 ± 3.7‡	7.0 ± 4.3‡	5.5 ± 2.5‡	4.5 ± 2.4‡	5.1 ± 5.3‡
DAS28 score	30	4.03 ± 1.09	2.59 ± 0.75‡	2.62 ± 1.19‡	2.40 ± 1.13‡	2.19 ± 0.61‡	1.72 ± 0.24‡	2.29 ± 1.25†
CLASI activity score, median (range)§	15	5 (1–14)	2 (0–12)†	2 (0–12)¶	1.5 (0–12)¶	1 (0–6)†	2 (0–6)¶	0.5 (0–6)¶
C3, gm/liter	67	0.68 ± 0.17	0.75 ± 0.19	0.76 ± 0.18	0.77 ± 0.17	0.79 ± 0.19	0.76 ± 0.18	0.76 ± 0.19
C4, gm/liter	67	0.11 ± 0.05	0.13 ± 0.06	0.17 ± 0.21	0.18 ± 0.22	0.15 ± 0.07	0.18 ± 0.13	0.14 ± 0.05
Anti-dsDNA (ELISA; KIU/liter)	41	587 ± 1,111‡	231 ± 291.5‡	197.3 ± 263‡	194.6 ± 235¶	196.6 ± 239†	168.9 ± 226†	124.1 ± 143
Anti-dsDNA (Farr; UI/ml)	26	102.4 ± 201.0	53.1 ± 69.0	40.6 ± 45.0	32.0 ± 30.2	25.6 ± 31.8	33.1 ± 41.1	29.9 ± 26.1
24-hour proteinuria, gm/die	16	1.27 ± 0.68	1.08 ± 0.99	0.88 ± 0.65¶	0.72 ± 0.63¶	0.69 ± 0.53¶	0.69 ± 0.71†	0.70 ± 0.77
Creatinine, mmoles/liter	16	67.83 ± 24.80	74.63 ± 17.48	75.01 ± 24.24	71.00 ± 14.42	71.90 ± 20.28	62.62 ± 9.70	65.86 ± 18.18
White blood cells, mm^3	16	2,588 ± 910	3,840 ± 1,741†	3,701 ± 1,808†	4,162 ± 1,083¶	4,500 ± 1,534¶	3,667 ± 1,192†	4,485 ± 21.2

* Values are the mean ± SD unless indicated otherwise. SLE = systemic lupus erythematosus; SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index 2000; DAS28 = Disease Activity Score in 28 joints; CLASI = Cutaneous Lupus Erythematosus Area and Severity Index; dsDNA = double-stranded DNA; ELISA = enzyme-linked immunosorbent assay.
† $P < 0.01$ by *t*-test (vs. baseline).
‡ $P < 0.001$ by *t*-test (vs. baseline).
§ Due to nonparametric distribution of data, the CLASI score is expressed as median (range).
¶ $P < 0.05$ by *t*-test (vs. baseline).

Iaccarino et al. Arthritis Care Res (Hoboken). 2017;69(1):115-123

Arthritis Care & Research
Vol. 69, No. 1, January 2017, pp 115–123
DOI 10.1002/acr.22971

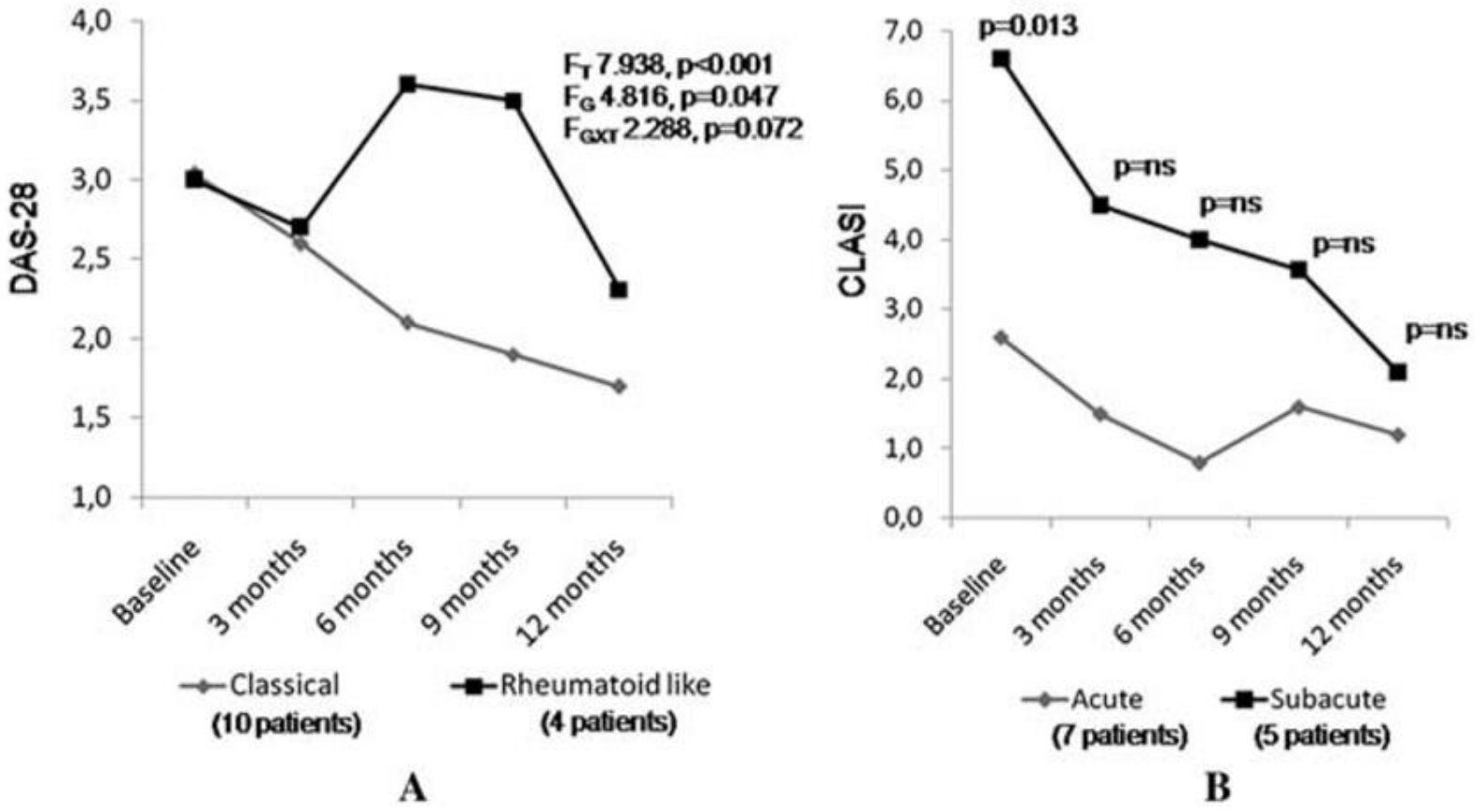
ORIGINAL ARTICLE

Effects of Belimumab on Flare Rate and E
Damage Progression in Patients With Acti
Systemic Lupus Erythematosus

LUCA IACCARINO,[1] SILVANO BETTIO,[1] ROSSELLA REGGIA,[2] MARGHERITA ZEN,[1]
LAURA ANDREOLI,[2] MARIELE GATTO,[1] SILVIA PIANTONI,[2] LINDA NALOTTO,[1]
FRANCO FRANCESCHINI,[2] MADDALENA LAROSA,[1] MICAELA FREDI,[2] LEONARDO
ANGELA TINCANI,[2] AND ANDREA DORIA[1]

Objective. To investigate effectiveness and safety of belimumab in patients with active systemic (SLE) in a clinical practice setting.
Methods. Sixty-seven patients with active SLE, mean ± SD age 39.3 ± 10.2 years, from 2 Italian pro treated with belimumab (10 mg/kg on day 0, 14, 28, and then every 28 days) added to background t Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K), the Systemic Lupus International American College of Rheumatology Damage Index, the Disease Activity Score in 28 joints (DAS28), 24 Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) activity score, anti-double dsDNA), C3 and C4 levels, and prednisone daily dose were recorded at baseline, month 3, 6, 9, 12, 18, subdivided into "classical" (CLP) and "rheumatoid-like"; skin manifestations into acute (ACLE), chronic. SLE flares, defined according to the SLEDAI Flare Index, were calculated before and after

N=67



Iaccarino et al. Arthritis Care Res (Hoboken). 2017;69(1):115-123

Arthritis Care & Research
Vol. 69, No. 1, January 2017, pp 115–123
DOI 10.1002/acr.22971

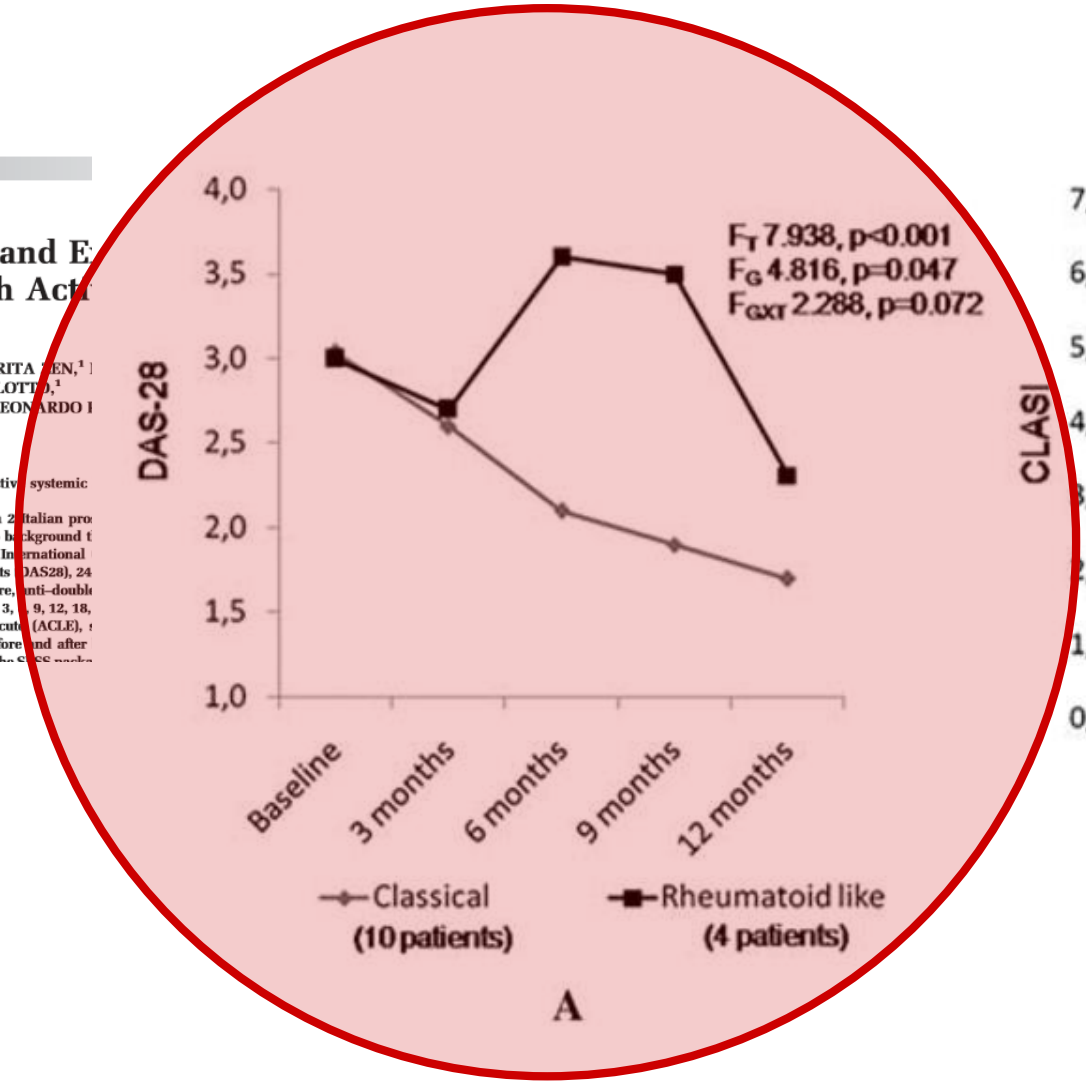
ORIGINAL ARTICLE

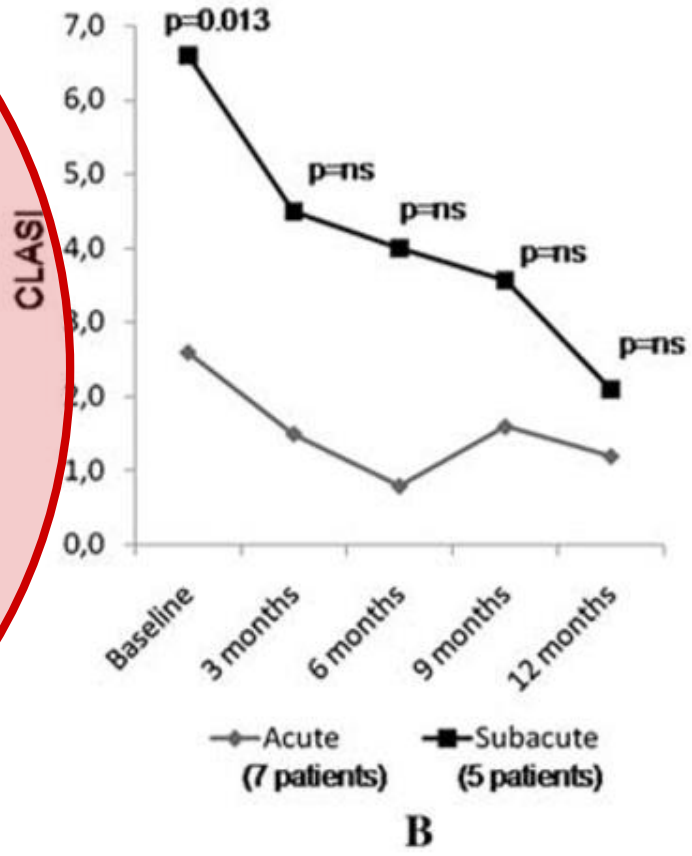
Effects of Belimumab on Flare Rate and E
Damage Progression in Patients With Acti
Systemic Lupus Erythematosus

LUCA IACCARINO,[1] SILVANO BETTIO,[1] ROSSELLA REGGIA,[2] MARGHERITA
LAURA ANDREOLI,[2] MARIELE GATTO,[1] SILVIA PIANTONI,[2] LINDA NALOTTO,[1]
FRANCO FRANCESCHINI,[2] MADDALENA LAROSA,[1] MICAELA FREDI,[2] LEONARDO
ANGELA TINCANI,[2] AND ANDREA DORIA[1]

Objective. To investigate effectiveness and safety of belimumab in patients with activ systemic (SLE) in a clinical practice setting.

Methods. Sixty-seven patients with active SLE, mean ± SD age 39.3 ± 10.2 years, from 2 Italian pro treated with belimumab (10 mg/kg on day 0, 14, 28, and then every 28 days) added to b kground t Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K), the Systemic Lupus In rnational American College of Rheumatology Damage Index, the Disease Activity Score in 28 joints DAS28), 24 Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) activity score, nti–doubl dsDNA), C3 and C4 levels, and prednisone daily dose were recorded at baseline, month 3, 9, 12, 18, subdivided into "classical" (CLP) and "rheumatoid-like"; skin manifestations into acut (ACLE), chronic. SLE flares, defined according to the SLEDAI Flare Index, were calculated before nd after

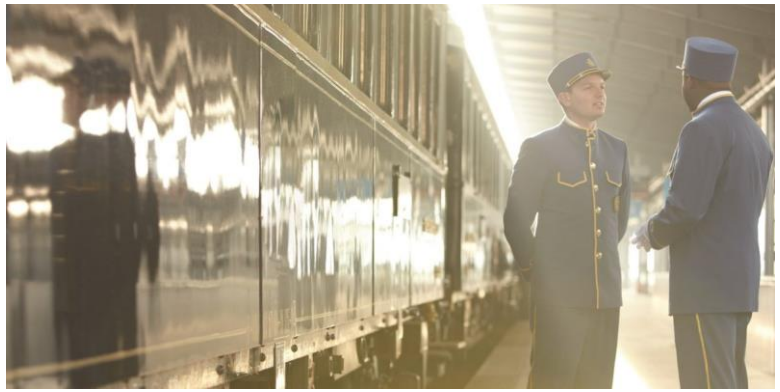




N=67

Iaccarino et al. Arthritis Care Res (Hoboken). 2017;69(1):115-123

Conclusiones



- Es necesario precisar definición de "Artritis refractaria"
- Potenciar el estudio y correlación entre hallazgos ecográficos / RMN y parámetros clínico-analíticos
- Subgrupo de pacientes con perfil "rhupus" es distinto al resto de LES
- El tratamiento de las manifestaciones articulares con Anti-TNF (ETN), Rituximab y Belimumab parece mostrarse razonablemente eficaz y seguro en estos pacientes *

Referencias

- Gormezano NW, Silva CA, Aikawa NE, Barros DL, et al. Chronic arthritis in systemic lupus erythematosus: distinct features in 336 paediatric and 1830 adult patients. Clin Rheumatol. 2016 Jan;35(1):227-31.
- Ceccarelli F, Perricone C, Cipriano E, Massaro L, et al. Joint involvement in systemic lupus erythematosus: From pathogenesis to clinical assessment. Semin Arthritis Rheum. 2017 Aug;47(1):53-64.
- Budhram A, Chu R, Rusta-Sallehy S, Ioannidis G, et al. Anti-cyclic citrullinated peptide antibody as a marker of erosive arthritis in patients with systemic lupus erythematosus: a systematic review and meta-analysis. Lupus. 2014 Oct;23(11):1156-63.
- Ball EM, Tan AL, Fukuba E, McGonagle D, et al. A study of erosive phenotypes in lupus arthritis using magnetic resonance imaging and anti-citrullinated protein antibody, anti-RA33 and RF autoantibody status. Rheumatology (Oxford). 2014 Oct;53(10):1835-43.
- Cortés-Hernández J, Egri N, Vilardell-Tarrés M, Ordi-Ros J. Etanercept in refractory lupus arthritis: An observational study. Semin Arthritis Rheum. 2015 Jun;44(6):672-9.
- Merrill JT, Burgos-Vargas R, Westhovens R, Chalmers A, et al. The efficacy and safety of abatacept in patients with non-life-threatening manifestations of systemic lupus erythematosus: results of a twelve-month, multicenter, exploratory, phase IIb, randomized, double-blind, placebo-controlled trial. Arthritis Rheum. 2010 Oct;62(10):3077-87.
- Cobo-Ibáñez T, Loza-Santamaría E, Pego-Reigosa JM, Marqués AO, et al. Efficacy and safety of rituximab in the treatment of non-renal systemic lupus erythematosus: a systematic review. Semin Arthritis Rheum. 2014 Oct;44(2):175-85.
- Iaccarino L, Bettio S, Reggia R, Zen M, et al. Effects of Belimumab on Flare Rate and Expected Damage Progression in Patients With Active Systemic Lupus Erythematosus. Arthritis Care Res (Hoboken). 2017 Jan;69(1):115-123
- Mathieu Artifoni, Xavier Puéchala. How to treat refractory arthritis in lupus?. Joint Bone Spine 79 (2012) 347–350
- Ana Campar , Fátima Farinha , Carlos Vasconcelos. Refractory disease in Systemic Lupus Erythematosus. Autoimmunity Reviews 10 (2011) 685–692

Conclusiones