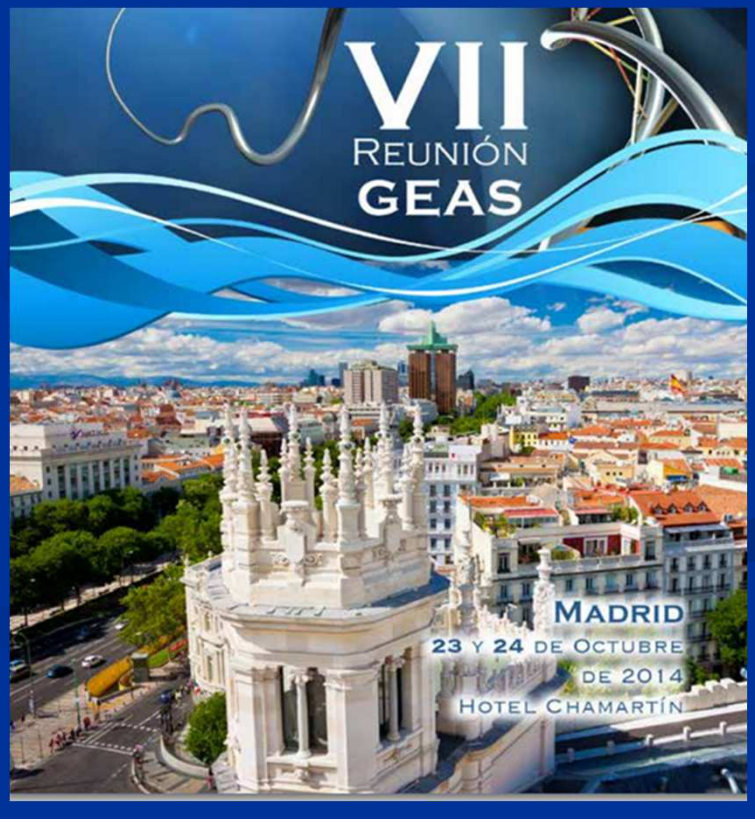
“Novedades en LES”

Los **GEAS** buscan a un hombre presuntamente ahogado en el **...**

madrid.netradio.es/__n828689_577_los-**geas**-buscan-a-un-hombre- presuntamente-ahogado-en-el-pantano-d.html ▾

NetRadio - **Madrid** - Emisión en directo ----- ... 22-07-**2014** ... El Grupo Especial de Actividades Subacuáticas (**GEAS**) de la Guardia Civil buscan a un hombre de ...



Juan Jiménez Alonso. Granada

PubMed.gov
US National Library of Medicine
National Institutes of Health

PubMed | systemic lupus erythematosus

RSS Save search Advanced

Show additional filters

Clear all

Article types clear
- ✓ Clinical Trial
- More ...

Text availability
- ✓ Abstract
- Free full text
- Full text

Publication dates clear
- 5 years
- 10 years
- ✓ From 2013/10/01 to 2014/11/31

Species
- Humans
- Other Animals

Clear all

Show additional filters

Display Settings: Summary, 20 per page, Sorted by Recently Added

Send to:

Results: 1 to 20 of 68

<< First < Prev Page 1 of 4 Next > Last >>

Filters activated: Clinical Trial, Abstract, Publication date from 2013/10/01 to 2014/11/31. Clear all to show 58075 items.

1. [Bosentan: a considerable increase in the survival of patients with pulmonary hypertension associated with **systemic** rheumatic diseases].
Volkov AV, Iudkina NN, Nikolaeva EV, Kurmukov IA, Glukhova SI, Nasonov EL.
Ter Arkh. 2014;86(5):32-9. Russian.
PMID: 25026800 [PubMed - indexed for MEDLINE]
Related citations

2. Utility and safety of rituximab in pediatric autoimmune and inflammatory CNS disease.
Dale RC, Brilot F, Duffy LV, Twilt M, Waldman AT, Narula S, Muscal E, Deiva K, Andersen E, Eyre MR, Eleftheriou D, Brogan PA, Kneen R, Alper G, Anlar B, Wassmer E, Heineman K, Hemingway C, Riney CJ, Kornberg A, Tardieu M, Stocco A, Banwell B, Gorman MP, Benseler SM, Lim M.
Neurology. 2014 Jul 8;83(2):142-50. doi: 10.1212/WNL.0000000000000570. Epub 2014 Jun 11.
PMID: 24920861 [PubMed - indexed for MEDLINE]
Related citations

3. IFN priming is necessary but not sufficient to turn on a migratory dendritic cell program in **lupus** monocytes.
Rodriguez-Pla A, Patel P, Maecker HT, Rossello-Urgell J, Baldwin N, Bennett L, Cantrell V, Baisch J,

Filters: Manage Filters

New feature

Try the new Display Settings option - **Sort by Relevance**

Results by year

Download CSV

Find related data

Database: Select

Find items

Search details

```
("lupus erythematosus,
systemic"[MeSH Terms] OR
("lupus"[All Fields]
AND "erythematosus"[All Fields]
AND "systemic"[All Fields])
```

Skywatchers awed by 'Blood Moon'

This shot of a "Blood Moon" was taken from Sydney, Australia, in August 2007

Temas...

- Clínica
  - Etiología-Índices-ACOs-TBC-Ca-aterosclerosis-costes
- Tratamiento
  - HCQ-abatacept-lupuzor-epratuzumab-vacunas zóster y papiloma-AAS
- Futuro/est.inmunológicos
  - Th17-Tregs-LT "doble –"
- EspañoLES por el mundo
- Otras publicaciones

Arthritis Care Res (Hoboken). 2014 Jul;66(7):1048-56. doi: 10.1002/acr.22282.

Modifying effect of N-acetyltransferase 2 genotype on the association between systemic lupus erythematosus and consumption of alcohol and caffeine-rich beverages.

Kiyohara C[1], Washio M, Horiuchi T, Asami T, Ide S, Atsumi T, Kobashi G, Takahashi H, Tada Y; Kyushu Sapporo SLE (KYSS) Study Group.

Collaborators (35)

Author information

Abstract

OBJECTIVE: N-acetyltransferase 2 (NAT2) is involved in the metabolism of various environmental substances, both with and without carcinogenic potential. Alcoholic and nonalcoholic caffeine-rich beverages may be associated with markers of inflammation. Systemic lupus erythematosus (SLE) is a chronic, multifaceted inflammatory disease. We investigated the effects of alcoholic and nonalcoholic caffeine-rich beverages on risk of SLE and determined whether the effects were modified by NAT2 status.

METHODS: The NAT2 polymorphism was genotyped in 152 SLE cases and 427 healthy controls, all women and Japanese. We assessed effect modification by testing an interaction term for the NAT2 polymorphism and consumption of beverages.

RESULTS: Consumption of black tea (odds ratio [OR] 1.88, 95% confidence interval [95% CI] 1.03-3.41) and coffee (OR 1.57, 95% CI 0.95-2.61), but not green tea, was associated with an increased risk of SLE, while alcohol use (OR 0.33, 95% CI 0.20-0.55) was associated with a decreased risk of SLE. There were significant interactions between the NAT2 polymorphism and either alcohol use (Pinteraction = 0.026) or consumption of black tea (Pinteraction = 0.048).

CONCLUSION: The NAT2 polymorphism significantly modified the effects of alcohol use and black tea consumption on SLE, emphasizing the importance of incorporating genetic and metabolic information in studies on management of SLE. Additional studies are warranted to confirm the findings suggested in this study.

Arthritis Rheumatol. 2014 Jun;66(6):1559-67. doi: 10.1002/art.38429.

The risk of systemic lupus erythematosus associated with vaccines: an international case-control study.

Grimaldi-Bensouda L[1], Le Guern V, Kone-Paut I, Aubrun E, Fain O, Ruel M, Machet L, Viallard JF, Magy-Bertrand N, Daugas E, Rossignol M, Abenhaim L, Costedoat-Chalumeau N; PGRx Lupus Study Group.

Author information

Abstract

OBJECTIVE: Studies have suggested that systemic lupus erythematosus (SLE) may be triggered by vaccinations. We undertook this study to investigate the relationship between vaccination and onset of SLE.

METHODS: This international case-control study was conducted between April 2008 and June 2012 in 36 specialist referral centers (34 in France and 2 in Quebec, Canada) and recruited patients ≤60 years old recently diagnosed as having either definite SLE (meeting ≥4 American College of Rheumatology [ACR] criteria including at least 1 immunologic criterion) or probable SLE (meeting 3 ACR criteria including at least 1 immunologic criterion). Controls were recruited from general practice settings through a closely monitored protocol and matched to patients by age, sex, region of residence, and date of recruitment. Vaccinations and other potential risk factors for SLE were assessed using a standardized telephone interview. We compared proportions of patients and controls who were vaccinated 12 and 24 months before the index date (date of first clinical symptom presented by the patient) using odds ratios (ORs) from conditional logistic regression.

RESULTS: We assessed 105 patients (89 with definite SLE and 16 with probable SLE) and 712 controls. Twenty-two of the 105 patients (21.0%) and 181 of the 712 controls (25.4%) had received at least 1 vaccination within 24 months before the index date (adjusted OR 0.9 [95% confidence interval 0.5-1.5]). The proportions of patients and controls vaccinated within the previous 12 months were also similar.

CONCLUSION: Our study showed no association between exposure to vaccination and risk of developing SLE.

Filters activated: Clinical Trial, Publication date from 2013/09/01 to 2014/07/31. Clear all

Rheumatology (Oxford). 2013 Dec;52(12):2187-95. doi: 10.1093/rheumatology/ket283. Epub 2013 Aug 22.

Supervised physical exercise improves endothelial function in patients with systemic lupus erythematosus.

dos Reis-Neto ET[1], da Silva AE, Monteiro CM, de Camargo LM, Sato EI.

Author information

[1]Rheumatology Division, Department of Medicine, Universidade Federal de São Paulo, Rua Botucatu, 720, CEP 04023 900 São Paulo, SP, Brazil. eisato@unifesp.br.

Ejercicio: 1 hora/3 veces por semana/16 semanas

Abstract

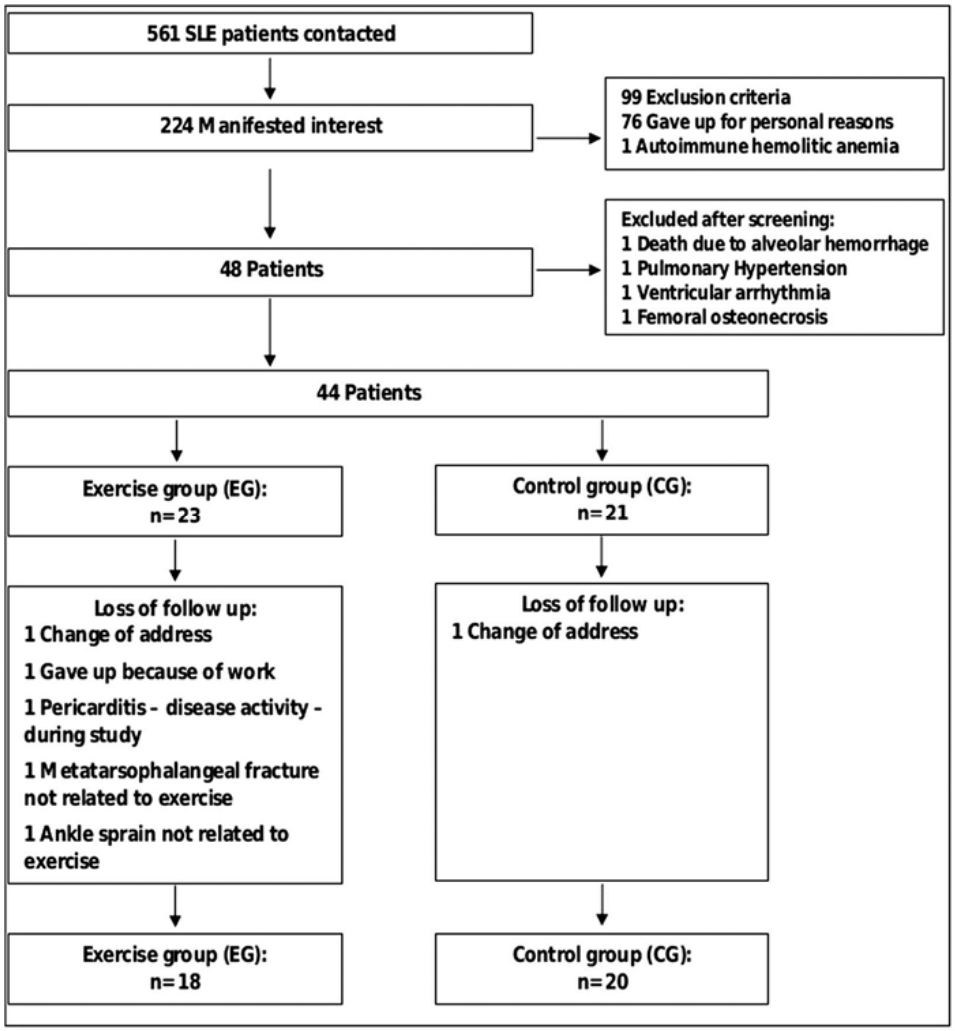
OBJECTIVE: The objective of this study was to evaluate the effect of supervised physical exercise on endothelial function, ergospirometric test variables and disease activity in SLE patients.

METHODS: We conducted a prospective study in which women with SLE who were available to perform physical exercise were allocated to the exercise group (EG) to practise supervised physical exercise for 1 h three times per week for 16 weeks. Those who were not available for this activity were allocated to the control group (CG). Intervention consisted of walking at a heart rate corresponding to the ventilatory 1 threshold obtained from ergospirometry and monitored by a frequency meter. At baseline (T0) and after 16 weeks (T16), patients were assessed for endothelial function by brachial artery (flow-mediated dilation), ergospirometry and disease activity (SLEDAI). Statistical analysis was performed through normality tests, Student's t-test and non-parametric tests for data with non-normal distribution. $P < 0.05$ was considered significant.

RESULTS: Eighteen patients were allocated in the EG and 20 in the CG. After 16 weeks there was an increase in FMD in the EG [6.3 (6.7)% vs 14.1 (9.1)%, P = 0.006] without a change in the CG [8.4 (8.2)% vs 9.4 (5.7)%, P = 0.598]. Regarding the ergospirometric test, we found improvement in exercise tolerance [12.3 (2.4) vs 13.4 (2.6) min, P = 0.027], maximum speed [7.7 (1.0) vs 8.3 (1.2) km/h, P = 0.027] and threshold speed [5.6 (0.7) vs 6.1 (0.9) km/h, P = 0.005] in the EG without a difference in the CG. There was no difference in the SLEDAI score in both groups.

CONCLUSION: Physical exercise is a useful strategy to improve endothelial function and aerobic capacity without worsening disease activity in SLE patients. TRIAL REGISTRATION; ClinicalTrials.gov (http://www.clinicaltrials.gov), NCT01712529.

Enrolment of SLE patients for the study.



Reis-Neto E T d et al. Rheumatology 2013;52:2187-2195

RHEUMATOLOGY

Supervised physical exercise improves endothelial function in patients with systemic lupus erythematosus

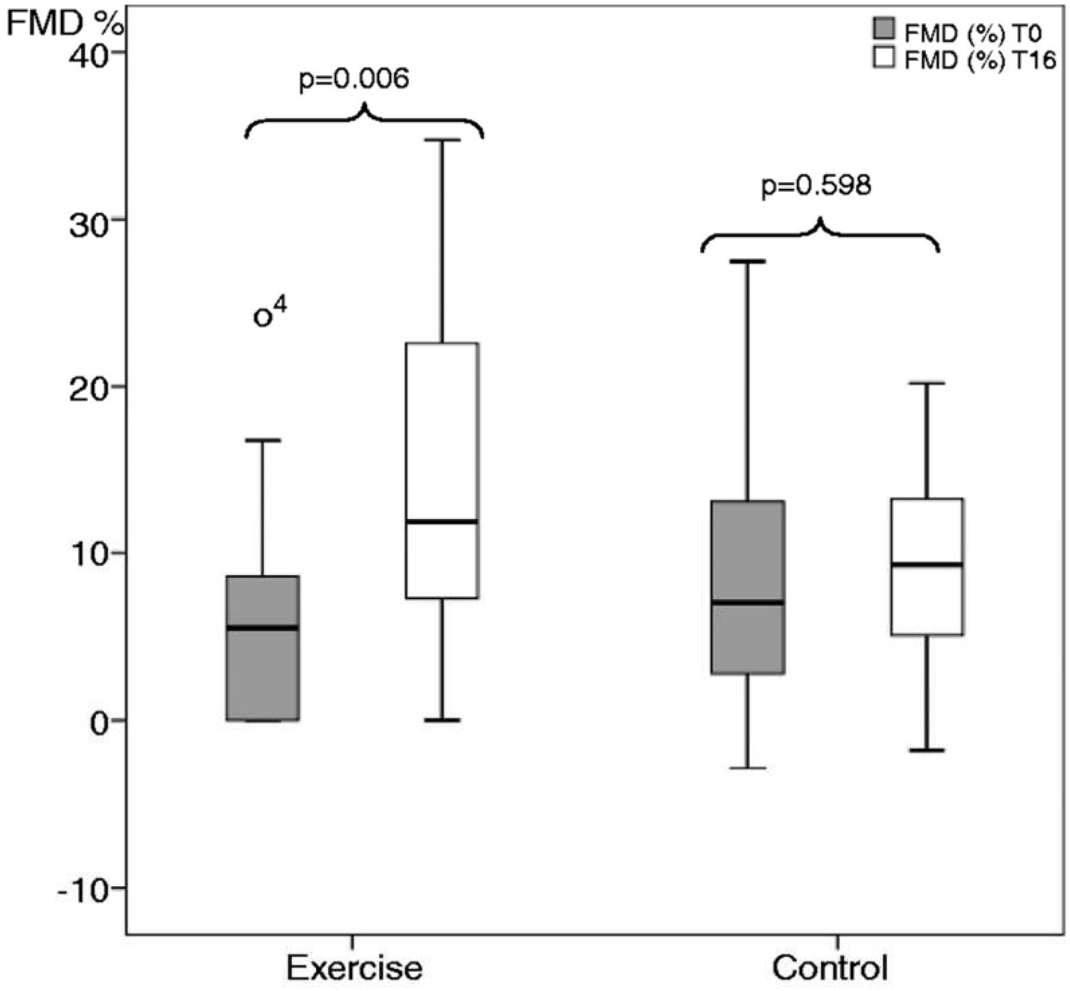
TABLE 2

CV risk factors in SLE patients in the EG and CG at baseline

	EG (n = 18)	CG (n = 20)	P
BMI, kg/m^2[a]	26.9 (4.7)	25.7 (4.0)	0.609
SBP, mmHg[a]	122.1 (14.4)	115.8 (13.0)	0.169
DBP, mmHg[a]	80.3 (7.4)	74.0 (9.3)	0.048
Abdominal circumference, cm[a]	87.2 (9.9)	86.1 (10.0)	0.751
Waist:hip ratio[a]	0.81 (0.06)	0.79 (0.06))	0.526
Fasting glucose, mg/dl[a]	84.6 (4.9)	81.3 (6.1)	0.076
Total cholesterol, mg/dl[a]	161.4 (32.9)	164.1 (38.0)	0.816
HDL, mg/dl[a]	50.8 (16.0)	49.4 (12.3)	0.953
LDL, mg/dl[a]	88.3 (22.9)	95.1 (31.9)	0.590
Triglycerides, mg/dl[a]	109.9 (48.3)	97.2 (35.8)	0.262
CAD family history, n (%)	4 (22.2)	3 (15.0)	0.687
Hypertension, n (%)	4 (22.2)	1 (5.0)	0.170
Dyslipidaemia, n (%)	4 (22.2)	5 (25.0)	1.0

[a]Mean (S.D.) unless stated otherwise. SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL: high density lipoprotein; LDL: low density lipoprotein; CAD: coronary artery disease.

Assessment of endothelial function in SLE patients in the EG and CG.



CONCLUSION: Physical exercise is a useful strategy to improve endothelial function and aerobic capacity without worsening disease activity in SLE patients. TRIAL REGISTRATION; ClinicalTrials.gov (http://www.clinicaltrials.gov), NCT01712529.

Ann Rheum Dis. 2014 Jan;73(1):154-60. doi: 10.1136/annrheumdis-2012-202443. Epub 2012 Dec 21.

Annual direct medical cost of active systemic lupus erythematosus in five European countries.

Doria A[1], Amoura Z, Cervera R, Khamastha MA, Schneider M, Richter J, Guillemin F, Kobelt G, Maurel F, Garofano A, Perna A, Murray M, Schmitt C, Boucot I.

Author information

Abstract

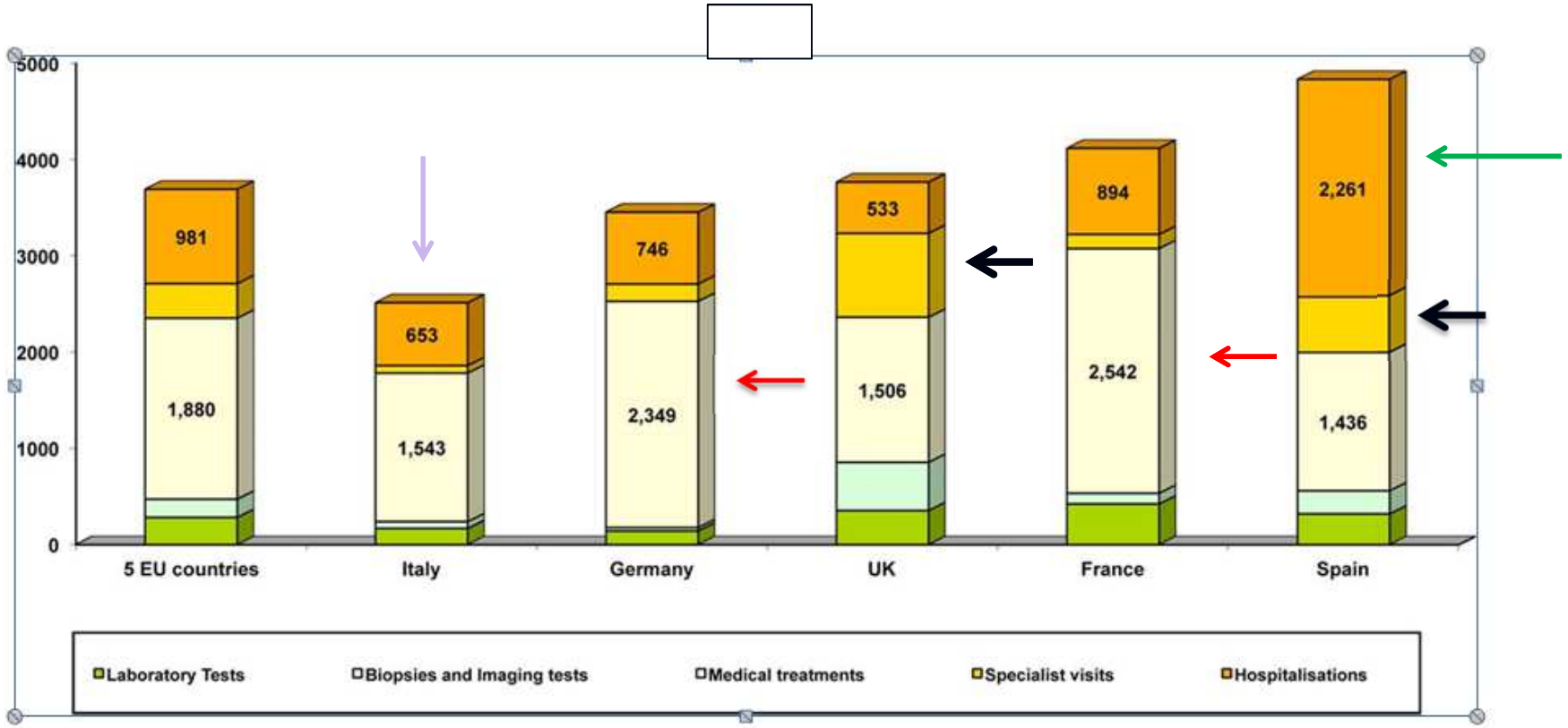
OBJECTIVES: To evaluate the annual direct medical cost of managing adult systemic lupus erythematosus (SLE) patients with active autoantibody positive disease in Europe.

METHODS: A 2-year, retrospective, multicentre, observational study was conducted in five countries (France, Germany, Italy, Spain and the UK). Data included patients' characteristics, disease activity and severity, flare assessments and health resource use (eg, laboratory tests, medications, specialist visits and hospitalisations). Costs were assessed from the public payers' perspective. Cost predictors were estimated by multivariate regression models.

RESULTS: Thirty-one centres enrolled 427 consecutive eligible patients stratified equally by disease severity. At baseline, mean (SD) age was 44.5 (13.8) years, 90.5% were women and mean (SD) SLE duration was 10.7 (8.0) years. The SELENA-SLEDAI (11.2 vs 5.3) and SLICC/ACR index (1.0 vs 0.7) scores were higher in severe patients. Over the study period, patients experienced on average 1.02 (0.71) flares/year. The mean annual direct medical cost was higher in severe compared to non-severe patients (€4748 vs €2650, p<0.001). Medication costs were €2518 in severe versus €1251 in non-severe patients (p<0.001). Medications represented 53% and 47% of the total cost for severe and non-severe patients, respectively, primarily due to immunosuppressants and biologics. Flares, especially severe flares, were identified as the major cost predictor, with each flare increasing the annual total cost by about €1002 (p<0.001).

CONCLUSIONS: The annual direct medical cost of SLE patients in Europe is related to disease severity and flares. Medical treatments were the main cost drivers. Severe flares and major organ involvement were identified as important cost predictors.

Cost of each category of health resource use (in €), globally and in the five countries.



Doria A et al. Ann Rheum Dis 2014;73:154-160

ARD

ELSEVIER DOYMA

Revista Clínica Española

www.elsevier.es/rce

ARTÍCULO ESPECIAL

Seguimiento de los pacientes con lupus eritematoso sistémico: lo que no está en las guías

J. Jiménez-Alonso[a,d,*], J.A. Vargas-Hitos[a], N. Navarrete-Navarrete[a], M. Zamora-Pasadas[a], S. Aguilar-Huergo[b], L. Jáimez[c] y J.M. Sabio[a]

[a] *Unidad de Enfermedades Autoinmunes Sistémicas, Servicio de Medicina Interna, Hospital Universitario «Virgen de las Nieves»,*

el seguimiento de 112 enfermos consecutivos, y el 71,4% tenían una sintomatología no explicable por el lupus, y solamente al 8,9% los derivamos a otros especialistas, probablemente, por nuestra capacitación general como internistas. Sugerimos que conocer la opinión de los

Filters activated: Clinical Trial, Abstract, Publication date from 2013/10/01 to 2014/10/31, Humans. Clear all

Ann Rheum Dis. 2014 Jan;73(1):183-90. doi: 10.1136/annrheumdis-2012-202760. Epub 2013 Jan 12.

Efficacy and safety of epratuzumab in patients with moderate/severe active systemic lupus erythematosus: results from EMBLEM, a phase IIb, randomised, double-blind, placebo-controlled, multicentre study.

Wallace DJ[1], Kalunian K, Petri MA, Strand V, Houssiau FA, Pike M, Kilgallen B, Bongardt S, Barry A, Kelley L, Gordon C.

Author information

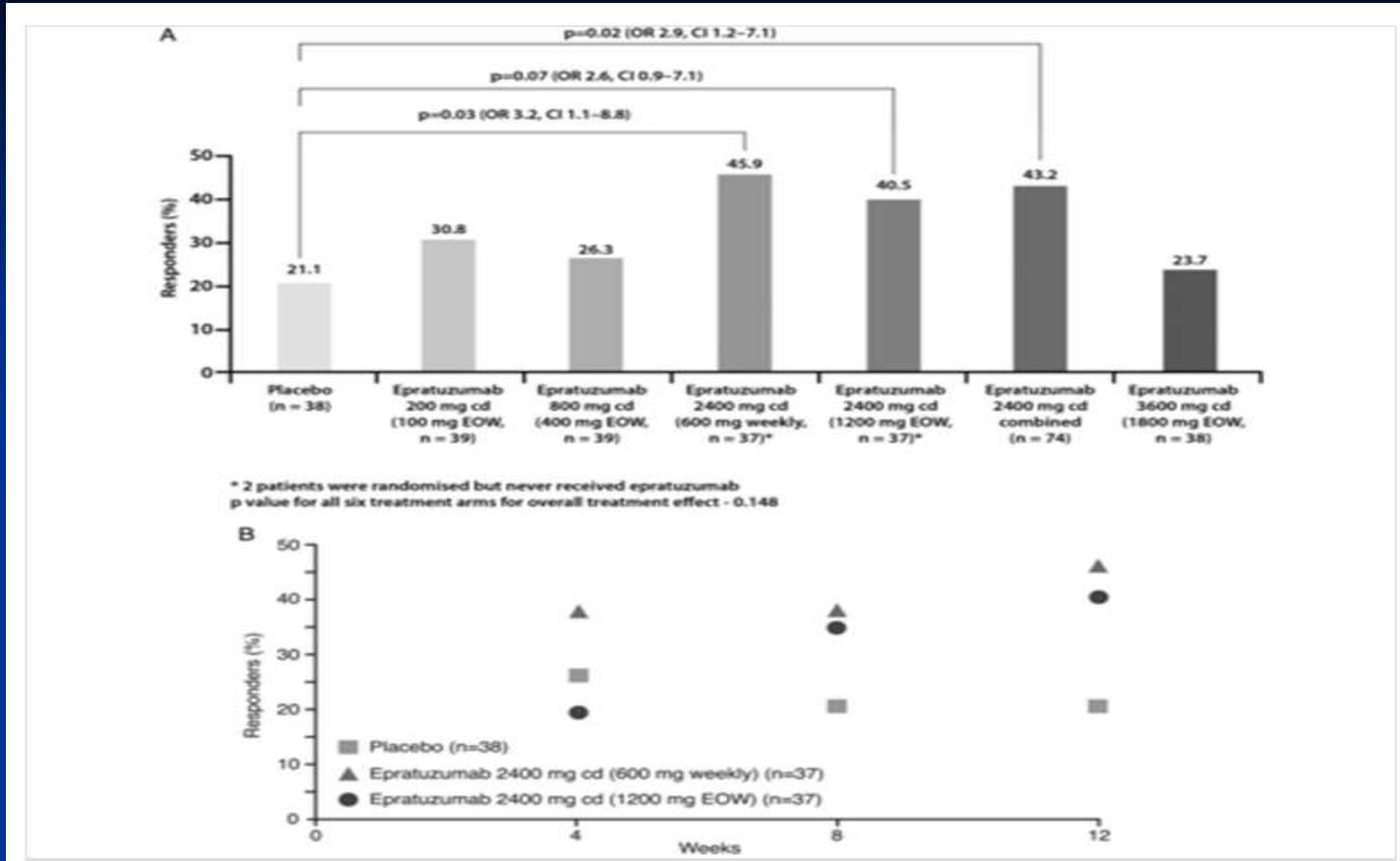
Abstract

OBJECTIVE: To identify a suitable dosing regimen of the CD22-targeted monoclonal antibody epratuzumab in adults with moderately to severely active systemic lupus erythematosus (SLE).

METHODS: A phase IIb, multicentre, randomised controlled study (NCT00624351) was conducted with 227 patients (37-39 per arm) receiving either: placebo, epratuzumab 200 mg cumulative dose (cd) (100 mg every other week (EOW)), 800 mg cd (400 mg EOW), 2400 mg cd (600 mg weekly), 2400 mg cd (1200 mg EOW), or 3600 mg cd (1800 mg EOW). The primary endpoint (not powered for significance) was the week 12 responder rate measured using a novel composite endpoint, the British Isles Lupus Assessment Group (BILAG)-based Combined Lupus Assessment (BICLA).

RESULTS: Proportion of responders was higher in all epratuzumab groups than with placebo (overall treatment effect test p=0.148). Exploratory pairwise analysis demonstrated clinical improvement in patients receiving a cd of 2400 mg epratuzumab (OR for 600 mg weekly vs placebo: 3.2 (95% CI 1.1 to 8.8), nominal p=0.03; OR for 1200 mg EOW vs placebo: 2.6 (0.9 to 7.1), nominal p=0.07). Post-hoc comparison of all 2400 mg cd patients versus placebo found an overall treatment effect (OR=2.9 (1.2 to 7.1), nominal p=0.02). Incidence of adverse events (AEs), serious AEs and infusion reactions was similar between epratuzumab and placebo groups, without decreases in immunoglobulin levels and only partial reduction in B-cell levels.

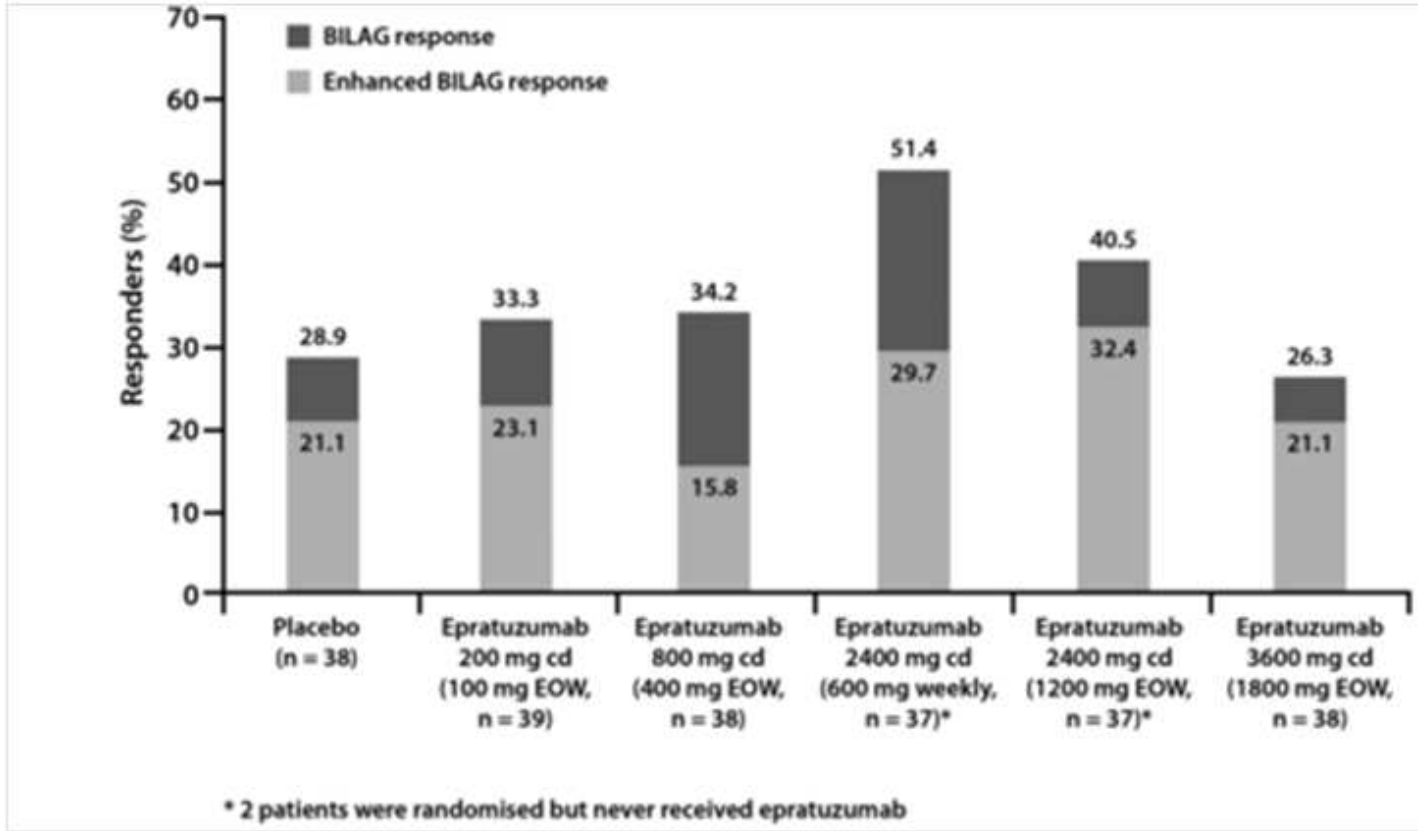
CONCLUSIONS: Treatment with epratuzumab 2400 mg cd was well tolerated in patients with moderately to severely active SLE, and associated with improvements in disease activity. Phase III studies are ongoing.



View larger version: In a new window Download as PowerPoint Slide

Figure 2

BILAG-based Combined Lupus Assessment response rate (A) at week 12 (intention-to-treat analysis) for all patient groups (B) over weeks 1–12 for the 2400 mg combined dose arms compared with the placebo group.

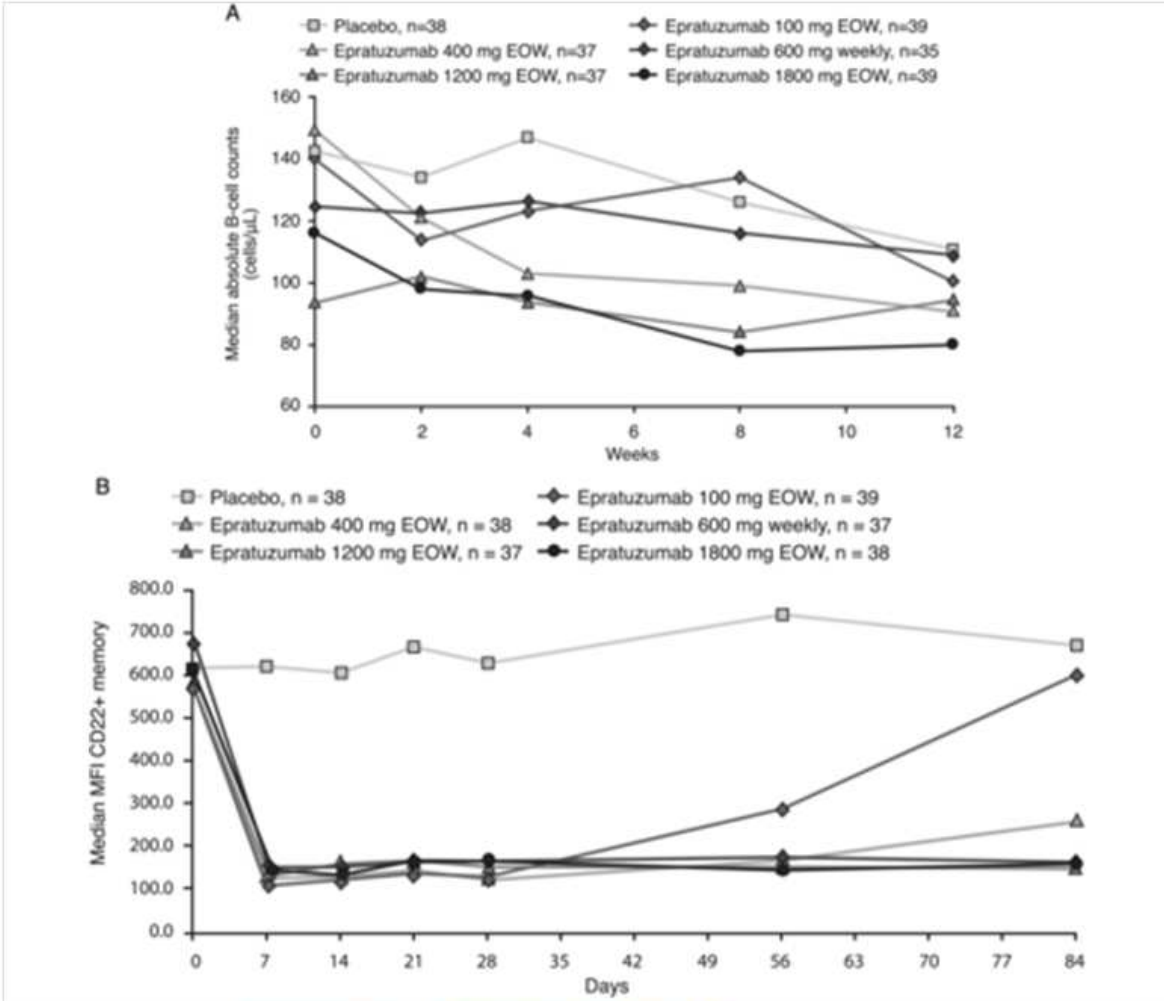


* 2 patients were randomised but never received epratuzumab

View larger version: In a new window Download as PowerPoint Slide

Figure 3

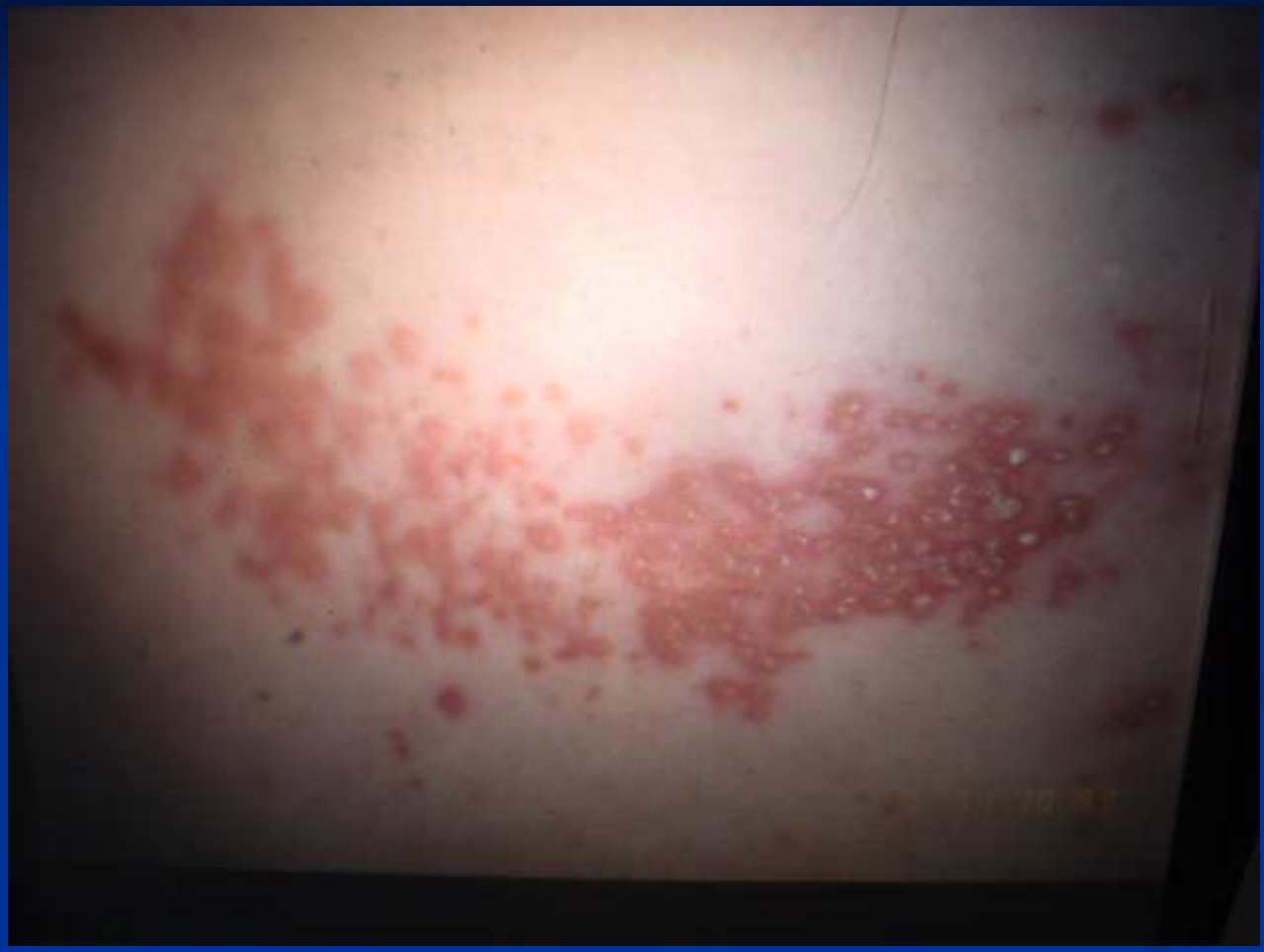
Percentage of patients meeting criteria for BILAG improvement and enhanced BILAG improvement at week 12.



View larger version: In a new window Download as PowerPoint Slide

Figure 4

Changes from baseline in B-cell and CD22 levels. (A) Changes in absolute B-cell counts (cells/µl) (B) Changes in mean fluorescent intensity of CD22+ memory B cells.



Filters activated: Clinical Trial, Publication date from 2013/09/01 to 2014/07/31. Clear all

J Rheumatol. 2013 Nov;40(11):1875-80. doi: 10.3899/jrheum.130170. Epub 2013 Sep 15.

Herpes zoster vaccination in SLE: a pilot study of immunogenicity.

Guthridge JM[1], Cogman A, Merrill JT, Macwana S, Bean KM, Powe T, Roberts V, James JA, Chakravarty EF.

Author information

Abstract

OBJECTIVE: Patients with systemic lupus erythematosus (SLE) are at increased risk of herpes zoster (HZ). Although a vaccine for HZ has been approved by the US Food and Drug Administration, its use in immunocompromised individuals remains controversial because it is a live-attenuated virus vaccine. We performed a pilot study of the immunogenicity of the HZ vaccine (Zostavax) in patients with SLE.

METHODS: Ten patients with SLE and 10 control subjects ≥ age 50 years participated in this open-label vaccination study. All were seropositive for varicella zoster virus (VZV). Patients with SLE were excluded for SLE Disease Activity Index (SLEDAI) > 4, or use of mycophenolate mofetil, cyclophosphamide, biologics, or > 10 mg prednisone daily. Followup visits occurred at 2, 6, and 12 weeks. Clinical outcomes included the development of adverse events, particularly HZ or vesicular lesions, and SLE flare. Immunogenicity was assessed with VZV-specific interferon-γ-producing enzyme-linked immunospot (ELISPOT) assays and with antibody concentrations.

RESULTS: All subjects were women. Patients with SLE were slightly older than controls (60.5 vs 55.3 yrs, $p < 0.05$). Median baseline SLEDAI was 0 (range 0-2) for patients with SLE. No episodes of HZ, vesicular rash, serious adverse events, or SLE flares occurred. Three injection site reactions occurred in each group: mild erythema or tenderness. The proportion of subjects with a > 50% increase in ELISPOT results following vaccination was comparable between both groups, although absolute SLE responses were lower than controls. Antibody titers increased only among controls following vaccination ($p < 0.05$).

CONCLUSION: The HZ vaccination yielded a measurable immune response in this cohort of patients with mild SLE taking mild-moderate immunosuppressive medications. No herpetiform lesions or SLE flares were seen in this small cohort of patients. ClinicalTrials.gov ID:NCT01474720.

Arthritis Care Res (Hoboken). 2014 Feb;66(2):285-92. doi: 10.1002/acr.22169.

Suboptimal inhibition of platelet cyclooxygenase 1 by aspirin in systemic lupus erythematosus: association with metabolic syndrome.

Kawai VK[1], Avalos I, Oeser A, Oates JA, Milne GL, Solus JF, Chung CP, Stein CM.

Author information

Abstract

OBJECTIVE: Low-dose aspirin prevents platelet aggregation by suppressing thromboxane A2 (TXA2) synthesis. However, in some individuals TXA2 suppression by aspirin is impaired, indicating suboptimal inhibition of platelet cyclooxygenase 1 (COX-1) by aspirin. Because patients with systemic lupus erythematosus (SLE) have increased risk of thrombotic events, many receive aspirin; however, the efficacy of aspirin in SLE has not been determined. We examined the hypothesis that aspirin response is impaired in SLE.

METHODS: We assessed the effect of aspirin by measuring concentrations of the stable metabolite of TXA2 , serum thromboxane B2 (sTXB2), before and after treatment with daily aspirin (81 mg) for 7 days in 34 patients with SLE and 36 control subjects. The inability to suppress sTXB2 synthesis to <10 ng/ml represents suboptimal inhibition of platelet COX-1 by aspirin.

RESULTS: Aspirin almost completely suppressed sTXB2 in control subjects to median 1.5 ng/ml (interquartile range [IQR] 0.8-2.7) but had less effect in patients with SLE (median 3.1 ng/ml [IQR 2.2-5.3]) (P = 0.002). A suboptimal effect of aspirin was present in 15% (5 of 34) of the patients with SLE but not in control subjects (0 of 36) (P = 0.023). Incomplete responders were more likely to have metabolic syndrome (P = 0.048), obesity (P = 0.048), and higher concentrations of C-reactive protein (CRP) (P = 0.018).

CONCLUSION: The pharmacologic effect of aspirin is suboptimal in 15% of patients with SLE but in none of the control subjects, and the suboptimal response was associated with metabolic syndrome, obesity, and higher CRP concentrations.

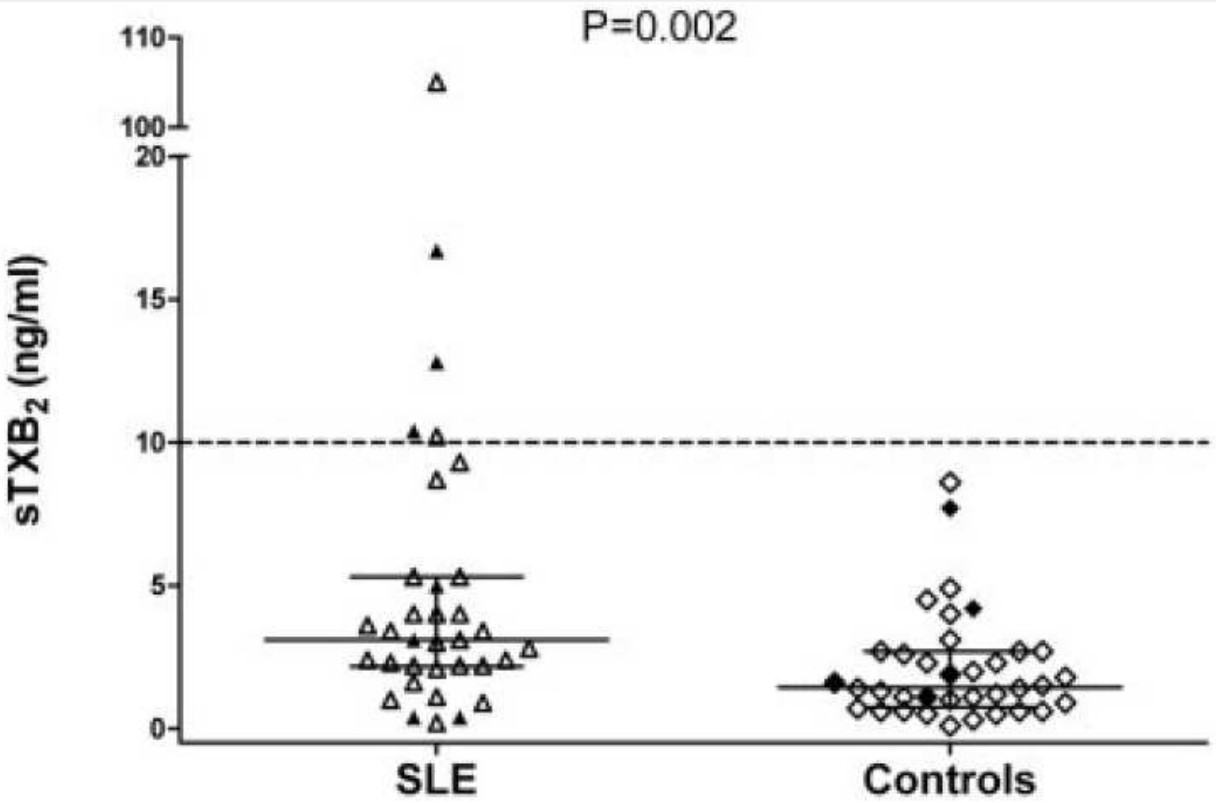


Figure 1. Distribution of serum thromboxane B_2 ($sTXB_2$) after 1 week of 81 mg/day of immediate-release aspirin. Broken line represents the threshold for suboptimal response to aspirin. Solid shapes represent individuals with metabolic syndrome. SLE = systemic lupus erythematosus.

EspañoLES por el Mundo

Estudios prospectivos, clínicos *

No casos aislados, ni series de casos

…no sólo de miembros del GEAS

bMed | systemic lupus erythematosus and Spain

RSS Save search Advanced

Display Settings: Summary, 20 per page, Sorted by Recently Added Send to:

Results: 1 to 20 of 83

<< First < Prev Page 1 of 5 Next > Last >>

Filters activated: Publication date from 2013/10/01 to 2014/10/31. Clear all to show 879 items.

1. Intestinal dysbiosis associated with **systemic lupus erythematosus**.
Hevia A, Milani C, López P, Cuervo A, Arboleya S, Duranti S, Turroni F, González S, Suárez A, Gueimonde M, Ventura M, Sánchez B, Margolles A.
MBio. 2014 Sep 30;5(5):e01548-14. doi: 10.1128/mBio.01548-14.
PMID: 25271284 [PubMed - in process] **Free Article**
Related citations

2. Association between low 25-hydroxyvitamin D, insulin resistance and arterial stiffness in nondiabetic women with **systemic lupus erythematosus**.
Sabio J, Vargas-Hitos J, Martinez-Bordonado J, Navarrete-Navarrete N, Díaz-Chamorro A, Olvera-Porcel C, Zamora M, Jiménez-Alonso J.
Lupus. 2014 Sep 12. pii: 0961203314551811. [Epub ahead of print]
PMID: 25216653 [PubMed - as supplied by publisher]
Related citations

3. Sex disparities in **systemic lupus erythematosus** in Northwestern **Spain** are not due to ethnic diversity.
González-Gay MA, Alonso MD, Martínez-Vázquez F, Llorca J.
Rheumatol Int. 2014 Sep 12. [Epub ahead of print] No abstract available.

Internet | Mod

Scand J Rheumatol. 2014;43(1):54-8. doi: 10.3109/03009742.2013.803150. Epub 2013 Sep 19.

Increased arterial stiffness is independently associated with metabolic syndrome and damage index in systemic lupus erythematosus patients.

Valero-Gonzalez S[1], Castejon R, Jimenez-Ortiz C, Rosado S, Tutor-Ureta P, Vargas JA, Yebra-Bango M.

Author information

Abstract

OBJECTIVES: We evaluated whether traditional or non-traditional cardiovascular (CV) risk factors and systemic lupus erythematosus (SLE)-related risk factors were associated with pathological arterial stiffness measured by pulse wave velocity (PWV) adjusted for patients' age and blood pressure.

METHOD: CV risk factors were measured in the 46 SLE female patients studied. Activity and organ damage were assessed by the SLE Disease Activity Index (SLEDAI) and the Systemic Lupus International Collaborative Clinics/American College of Rheumatology (SLICC/ACR) Damage Index, respectively. Other lupus-related parameters and information concerning treatment were recorded. Subclinical atherosclerosis was assessed by PWV calculated from pulse wave recording by Doppler, a non-invasive method to measure arterial stiffness. Multivariate logistic regression analysis was used to identify independent determinants of increased PWV.

RESULTS: PWV was categorized as normal or pathological arterial stiffness following the reference values adjusted by age and blood pressure recently published by the European Society of Cardiology. Pathological PWV was associated with CV risk factors including homocysteine ($p = 0.01$), high-sensitivity C-reactive protein (hs-CRP; $p = 0.03$), uric acid ($p = 0.01$), and metabolic syndrome ($p = 0.007$). With regard to SLE-specific risk factors, a significant association was found between PWV and SLICC/ACR score ($p = 0.006$). Multivariate analysis showed that increased PWV was independently associated with metabolic syndrome [odds ratio (OR) 6.6, 95% confidence interval (CI) 1.2-38, $p = 0.03$] and SLICC/ACR score (OR 1.5, 95% CI 1-2.32, $p = 0.05$).

CONCLUSIONS: We have found a close link between metabolic syndrome and SLICC/ACR score with increased aortic stiffness. These variables might be an indicator of subclinical atherosclerosis in SLE women without clinical evidence of atherosclerotic cardiovascular disease (CVD).

Rheumatology (Oxford). 2014 Apr;53(4):631-8. doi: 10.1093/rheumatology/ket367. Epub 2013 Nov 22.

Decreased circulating endothelial progenitor cells as an early risk factor of subclinical atherosclerosis in systemic lupus erythematosus.

Castejon R[1], Jimenez-Ortiz C, Valero-Gonzalez S, Rosado S, Mellor S, Yebra-Bango M.

Author information

Abstract

OBJECTIVE: Endothelial progenitor cells (EPCs) play an important role in vascular damage repair and it has been suggested that a decreased number of these cells is associated with increased subclinical atherosclerosis. Our study aim was to evaluate whether the number of circulating EPCs in patients with SLE is associated with subclinical atherosclerosis, the presence of cardiovascular (CV) risk factors and SLE-specific factors.

METHODS: Forty-six female SLE patients were included. At the time of each patient's appointment, CV risk factors, SLE-specific factors and EPCs were assessed in peripheral blood by flow cytometry. Simultaneously, atherosclerosis was assessed by measuring the carotid-femoral pulse wave velocity (PWV) by Doppler velocimetry, intima media thickness (IMT) and carotid plaque by B-mode US scanning.

RESULTS: Patients were classificated according to PWV following the reference values adjusted by age and blood pressure published by the European Society of Cardiology. Patients with pathological values of PWV showed a significant decrease of circulating EPC percentage compared with normal PWV patients. Decreased EPC counts were also associated with certain risk factors, including hypertension, tobacco use, impaired glucose metabolism, and metabolic syndrome, and correlate with high levels of high-sensitivity CRP (hsCRP) or fibrinogen. The presence of carotid plaque and IMT measurement were unrelated with EPC quantification.

CONCLUSION: Patients with a reduced percentage of EPCs showed pathological arterial stiffness and association with certain CV risk factors, suggesting that the measurement of circulating EPCs can be used as a biological marker to determine subclinical atherosclerosis in SLE.

KEYWORDS: arterial stiffness; endothelial progenitor cells; subclinical atherosclerosis; systemic lupus erythematosus

Relationship between homocysteine levels and hypertension in systemic lupus erythematosus.

1. **Sabio JM**, Vargas-Hitos JA, Martinez-Bordonado J, Navarrete-Navarrete N, Díaz-Chamorro A, Olvera-Porcel C, Zamora-Pasadas M, Jiménez-Alonso J.
Arthritis Care Res (Hoboken). 2014 Apr 1. doi: 10.1002/acr.22340. [Epub ahead of print]

SIGNIFICANCE AND INNOVATIONS

- Homocysteine levels were independently associated with HT in SLE
- Homocysteine might play a role in the physiopathology of HT in SLE.
- SLE patients might be more vulnerable to the toxic effect of homocysteine on vasculature than general population

Lupus. 2014 Sep 12. pii: 0961203314551811. [Epub ahead of print]

Association between low 25-hydroxyvitamin D, insulin resistance and arterial stiffness in nondiabetic women with systemic lupus erythematosus.

Sabio J[1], Vargas-Hitos J[2], Martinez-Bordonado J[2], Navarrete-Navarrete N[2], Díaz-Chamorro A[2], Olvera-Porcel C[3], Zamora M[2], Jiménez-Alonso J[2].

Author information

Abstract

OBJECTIVE: The objective of this paper is to examine if there is an association between low levels of 25-hydroxyvitamin D (25(OH)D) and insulin resistance (IR) in nondiabetic women with systemic lupus erythematosus (SLE) and to evaluate its impact on arterial stiffness.

PATIENTS AND METHODS: In this cross-sectional study 25(OH)D, insulin, insulin resistance measured by the homeostatic model assessment (HOMA-IR), homocysteine, fibrinogen, characteristics of SLE, medications and pulse-wave velocity (PWV) were measured in 106 nondiabetic women with SLE and 101 matched controls.

RESULTS: Women with SLE tended to have lower 25(OH)D levels ($p = 0.078$) and a higher frequency of 25(OH)D deficiency (defined as <10 ng/ml) than controls ($p = 0.058$). Patients from the lowest quartile of the 25(OH)D range had higher PWV ($p = 0.043$), fasting glucose ($p = 0.035$), insulinemia ($p \leq 0.001$), HOMA-IR ($p = 0.006$), C4 ($p = 0.012$), as well as more frequent IR ($p = 0.002$) and metabolic syndrome ($p = 0.052$) than those in the upper quartile, and no differences were found in age, body mass index (BMI), blood pressure, lipid levels and renal function. In women with SLE, 25(OH)D inversely correlated with insulin ($p = 0.006$), HOMA-IR ($p = 0.008$) and C4 ($p = 0.048$) and tended to correlate with fibrinogen ($p = 0.060$) after adjustment for BMI, age, SLEDAI, prednisone dose, renal function, inflammation markers and seasonal variation, but not with PWV. In controls, 25(OH)D correlated only with homocysteine after the same adjustment, and the correlation with PWV tended to be significant after adjustment for BMI and age ($r = -0.190$, $p = 0.10$).

CONCLUSION: Low 25(OH)D levels were found to be associated with increased IR in nondiabetic women with SLE independently of BMI. Low 25(OH)D levels, but not IR, could be associated with increased arterial stiffness in these patients.

Clin Rheumatol. 2014 Apr;33(4):567-73. doi: 10.1007/s10067-013-2395-z. Epub 2013 Oct 6.

Health-related Internet use by lupus patients in southern Spain.

Callejas-Rubio JL[1], Ríos-Fernández R, Barnosi-Marín AC, García-Hernández FJ, Vargas-Hitos JA, Camps-García MT, González-Nieto JA, Sánchez-Román J, Jiménez-Alonso J, de Ramón Garrido E, Ortego-Centeno N.

Author information

Erratum in

Clin Rheumatol. 2014 Apr;33(4):575. Otego-Centeno, Norberto [corrected to Ortego-Centeno, Norberto].

Abstract

Internet has become a widely used tool by patients seeking information on different diseases. The information regarding lupus patients' Internet use is scarce. This study aims to explore the attitudes and practices of lupus patients in southern Spain, regarding Internet use to find health-related information. A survey was carried out including 150 patients from six Andalusian Hospitals. To search for information, 67.3 % of the patients used Internet. The proportion of female Internet users was higher (69.3 vs 46.2 %), particularly those belonging to a patients' association (81.8 vs 32.7 %), and are regular users of Internet (80.2 vs 44.4 %); 37.5 % thought the information found in the Internet was of little use or not useful at all, and 58 % of the respondents stated that the information found caused them concern while for 27 %, it was a relief. Most patients preferred the information given by their physicians (63.6 %); 33.9 % considered that the information from both sources was complementary, and 2.5 % preferred the information obtained from the Internet. A percentage of 85.3 of the patients would like their physicians to provide them with information on high-quality sites regarding their illness. Lupus patients make frequent use of the Internet to look for information on their disease. Considering this, and because better-informed patients follow more precisely the indications given by the physician, medical staff should collaborate in the development of high-quality sites for the patient to have additional sources of information.

Biomed Res Int. 2014;2014:291031. doi: 10.1155/2014/291031. Epub 2014 May 28.

Diagnosis of latent tuberculosis in patients with systemic lupus erythematosus: T.SPOT.TB versus tuberculin skin test.

Arenas Miras Mdel M[1], Hidalgo-Tenorio C[2], Jimenez-Gamiz P[3], Jiménez-Alonso J[1].

Author information

Abstract

Early studies in patients with systemic lupus erythematosus (SLE) reported increased incidence of tuberculosis. The tuberculin skin test (TST) is the technique of choice to detect latent tuberculosis infection (LTBI) but has several limitations.

OBJECTIVES: We compared TST and the newer T.SPOT.TB test to diagnose LTBI in SLE patients.

METHODS: In this observational cohort study conducted between August 2009 and February 2012, we recruited 92 patients from those attending the SLE clinic of our university hospital. Data recorded were epidemiological and sociodemographic characteristics. Laboratory analyses included TST and T.SPOT.TB tests.

RESULTS: Of the patients studied, 92% were women with an average age of 42.7 years. Overall, the degree of correlation between the two tests was low (Kappa index = 0.324) but was better in patients not receiving corticosteroids (CTC)/immunosuppressive (IS) therapy (Kappa = 0.436) and in those receiving hydroxychloroquine (Kappa = 0.473). While TST results were adversely affected by those receiving CTC and/or IS drugs (P = 0.021), the T.SPOT.TB results were not.

CONCLUSION: Although the TST test remains a useful tool for diagnosing LTBI in SLE patients, the T.SPOT.TB test is perhaps better employed when the patient is receiving CTC and/or IS drugs.

MBio. 2014 Sep 30;5(5):e01548-14. doi: 10.1128/mBio.01548-14.

Intestinal dysbiosis associated with systemic lupus erythematosus.

Hevia A[1], Milani C[2], López P[3], Cuervo A[4], Arboleya S[1], Duranti S[2], Turroni F[2], González S[4], Suárez A[3], Gueimonde M[1], Ventura M[2], Sánchez B[5], Margolles A[5].

Author information

Abstract

Systemic lupus erythematosus (SLE) is the prototypical systemic autoimmune disease in humans and is characterized by the presence of hyperactive immune cells and aberrant antibody responses to nuclear and cytoplasmic antigens, including characteristic anti-double-stranded DNA antibodies. We performed a cross-sectional study in order to determine if an SLE-associated gut dysbiosis exists in patients without active disease. A group of 20 SLE patients in remission, for which there was strict inclusion and exclusion criteria, was recruited, and we used an optimized Ion Torrent 16S rRNA gene-based analysis protocol to decipher the fecal microbial profiles of these patients and compare them with those of 20 age- and sex-matched healthy control subjects. We found diversity to be comparable based on Shannon's index. However, we saw a significantly lower Firmicutes/Bacteroidetes ratio in SLE individuals (median ratio, 1.97) than in healthy subjects (median ratio, 4.86; $P < 0.002$). A lower Firmicutes/Bacteroidetes ratio in SLE individuals was corroborated by quantitative PCR analysis. Notably, a decrease of some Firmicutes families was also detected. This dysbiosis is reflected, based on in silico functional inference, in an overrepresentation of oxidative phosphorylation and glycan utilization pathways in SLE patient microbiota.

IMPORTANCE: Growing evidence suggests that the gut microbiota might impact symptoms and progression of some autoimmune diseases. However, how and why this microbial community influences SLE remains to be elucidated. This is the first report describing an SLE-associated intestinal dysbiosis, and it contributes to the understanding of the interplay between the intestinal microbiota and the host in autoimmune disorders.

Lupus. 2014 Aug 8. pii: 0961203314546020. [Epub ahead of print]

Anti-ribosomal P antibodies are associated with elevated circulating IFNα and IL-10 levels in systemic lupus erythematosus patients.

Mozo L[1], López P[2], Caminal-Montero L[3], Rodríguez-Carrio J[2], Suárez A[2].

Author information

Abstract

OBJECTIVE: The objective of this paper is to analyze the relationship of anti-protein ribosomal P (RibP) antibodies with circulating levels of IFNα, TNFα, IFNγ, IL-17 and IL-10 in SLE. Disease activity and other systemic lupus erythematosus (SLE) features were also analyzed.

METHODS: Anti-RibP and other SLE-related antinuclear antibodies (ANA) were determined by fluoro-enzyme immunoassay in the sera of 107 SLE patients. Circulating cytokines were quantified by flow cytometry (IFNα, IL-10 and IL-17) or ELISA (TNFα and IFNγ).

RESULTS: Anti-RibP-positive patients (14.9%) displayed significantly higher serum levels of IFNα ($p = 0.023$) and IL-10 ($p = 0.016$) than their negative counterparts. This cytokine upregulation was independent of the presence of other ANA even though, in our patient cohort, anti-dsDNA was found to be associated with anti-RibP (OR, CI 95%: 6.03, 1.32 -27.93, $p = 0.021$) and to correlate with IL-10 levels ($r = 0.204$, $p = 0.036$). In fact, patients positive for anti-RibP but negative for anti-dsDNA exhibited the highest amounts of both IL-10 and IFN-α that were not related to disease activity since these patients showed lower SLEDAI than patients also positive for anti-dsDNA ($p = 0.018$). Anti-RibP positivity was also associated with early diagnosis, hypocomplementemia and leukopenia.

CONCLUSIONS: Presence of anti-RibP was found to be related to increased serum IFNα and IL-10 levels independently of both antibody status and disease activity.

Nephrol Dial Transplant. 2014 Sep;29(9):1740-9. doi: 10.1093/ndt/gfu062. Epub 2014 Apr 7.

Neutrophil gelatinase-associated lipocalin as a biomarker for lupus nephritis.

Torres-Salido MT, Cortés-Hernández J, Vidal X, Pedrosa A, Vilardell-Tarrés M, Ordi-Ros J.

Author information

Abstract

BACKGROUND: One of the challenges of treating patients with lupus nephritis (LN) is to accurately assess disease activity and predict its outcome. Since renal-biopsy cannot be performed routinely, new surrogate biomarkers are needed.

METHODS: We evaluated neutrophil gelatinase-associated lipocalin (NGAL), to predict renal outcome in LN. Serum and urinary NGAL levels, measured by the enzyme-linked immunosorbent assay, and the fractional excretion (FE) of NGAL relative to the FE of proteins (FE NGAL/FE protein ratio) were determined in a cross-sectional (n = 199) and longitudinal (n = 45) cohort of systemic lupus erythematosus (SLE) patients. Global and renal disease activity was assessed by the SLE disease activity indices, SLEDAI and rSLEDAI, respectively. Correlations between traditional biomarkers were established. Sensitivity, specificity and predictive values of NGAL for renal flare, response to therapy and progression to chronic kidney disease were calculated.

RESULTS: The FE NGAL/FE protein ratio exhibited the best sensitivity and specificity to discriminate patients with active LN from those with non-renal flare and inactive SLE. In the prospective study, this biomarker was found to be the best candidate to predict proteinuric flares with an 87% sensitivity and 62% specificity for ratios >14.56 and complete response with a 61% sensitivity and 78% specificity for ratios >26.54 in the presence of a simultaneous worsening or improving rSLEDAIs, respectively. In both conditions, the FE NGAL/FE protein ratio outperformed the anti-dsDNA antibody titres and C3 predictive value. Progression to chronic kidney disease was best predicted by estimated glomerular filtration rate levels, but persistently high levels of serum NGAL (>444.4 ng/mL, P = 0.0001 by Kaplan-Meier) predicted a faster progression.

CONCLUSIONS: The FE NGAL/FE protein ratio is a reliable marker of disease activity in patients with SLE and could be used as an indicator of response to therapy, although further studies are required to confirm these results.

Clin Exp Rheumatol. 2014 Jan-Feb;32(1):113-6. Epub 2013 Nov 15.

Clinical and serological findings associated with the expression of ITGAL, PRF1, and CD70 in systemic lupus erythematosus.

Balada E[1], Castro-Marrero J, Felip L, Ordi-Ros J, Vilardell-Tarrés M.

Author information

Abstract

We determined the expression of Integrin alpha L chain (ITGAL), Perforin 1 (PRF1), and CD70 and studied the associations with laboratory and clinical parameters. CD4+ T cells were isolated from 35 SLE patients and 30 healthy controls. The transcript levels of ITGAL, PRF1, and CD70 were quantified by real-time reverse-transcription polymerase chain reaction (RT-PCR). The SLE patients had significantly elevated transcript levels of ITGAL (18.61±22.17 vs. 7.33±9.17, p=0.042), PRF1 (21.67±26.34 vs. 10.67±11.65, p=0.039), and CD70 (1.45±1.63 vs. 0.67± 0.28, p=0.011). Patients with anti-microsomal and/or anti-thyroglobulin antibodies showed high levels of ITGAL (33.41±30.14 vs. 13.58±16.43, p=0.044; and 34.01±27.66 vs. 11.90±16.17, p=0.007, respectively). No association was seen either for the typical antibodies of SLE or for the disease activity. Although ITGAL, PRF1, and CD70 are overexpressed in SLE CD4+ T cells, their expression is not linked to the typical clinical and serological parameters associated with the disease. The role that ITGAL may play in autoimmune thyroiditis deserves further investigation.

Lupus. 2014 Sep;23(10):1014-22. doi: 10.1177/0961203314534909. Epub 2014 May 15.

The effects of rituximab on the lipid profile of patients with active systemic lupus erythematosus: results from a nationwide cohort in Spain (LESIMAB).

Fernández-Nebro A[1], Marenco JL[2], López-Longo F[3], Galindo M[4], Hernández-Cruz BE[5], Narváez J[6], Rúa-Figueroa I[7], Raya-Alvarez E[8], Zea A[9], Freire M[10], Sánchez-Atrio AI[11], García-Vicuña R[12], Pego-Reigosa JM[13], Manrique-Arija S[14], Nieves-Martín L[1], Carreño L[3]; LESIMAB GROUP.

⊕ Collaborators (31)

⊕ Author information

Abstract

INTRODUCTION: Patients with systemic lupus erythematosus (SLE) have increased cardiovascular risk related to lipid changes induced by inflammatory activity, proteinuria and treatments. Our objective was to analyse lipid changes in a cohort of patients with SLE resistant to standard treatments who were treated with rituximab.

METHODS: The study population comprised a retrospective multicentre, national cohort of patients with SLE resistant to standard treatments who were treated with rituximab. The basic lipid profile, concomitant treatment and disease activity were analysed at the start of the treatment, 24 weeks later, and at the end of the follow-up period. The effects of the main lupus variables and therapy on the lipid changes were analysed.

RESULTS: Seventy-nine patients with active lupus treated with rituximab were assessed during 149.3 patient-years. Prior to the treatment, 69% had dyslipidaemia. The most frequent abnormalities were a low-density lipoprotein (LDL) level of ≥100 mg/dl (34%) and a high-density lipoprotein (HDL) level of <50 mg/dl (27%). Baseline total cholesterol (TC) and LDL levels correlated with the degree of proteinuria, while the concentration of triglycerides (TGs) correlated with the SLE Disease Activity Index (SLEDAI). TGs were reduced at short- and long-term follow-up after rituximab treatment. A multiple linear regression analysis identified that the reduction of the lupus inflammatory activity, particularly changes in proteinuria, was the only independent variable that was positively associated with the reduction in TGs after 24 weeks ($p=0.001$) and with TC ($p=0.005$) and TGs ($p<0.001$) at the end of the follow-up period.

CONCLUSION: Our results suggest that rituximab may improve the long-term lipid profile of patients with SLE refractory to standard treatment, mainly by reducing inflammatory activity.

J Rheumatol. 2014 Sep;41(9):1801-7. doi: 10.3899/jrheum.131470. Epub 2014 Aug 1.

Clinical and immunogenetic factors associated with pneumonia in patients with systemic lupus erythematosus: a case-control study.

Rúa-Figueroa I[1], Nóvoa J[2], García-Laorden MI[2], Erausquin C[2], García-Bello M[2], Rodríguez de Castro F[2], Herrera-Ramos E[2], Ojeda S[2], Quevedo JC[2], Francisco F[2], Naranjo A[2], Rodríguez-Lozano C[2], Rodríguez-Gallego C[2].

Author information

Abstract

OBJECTIVE: To determine the incidence of pneumonia and associated factors in a single-center systemic lupus erythematosus (SLE) cohort.

METHODS: We included all our SLE patients [1997 American College of Rheumatology (ACR) criteria] with ≥ 1 pneumonia event, and 196 age and sex-matched SLE controls with no pneumonia events. Cumulative clinical data, weighted Systemic Lupus International Collaborating Clinics/ACR damage index (wSLICC/ACR-DI), comorbidities, and risk factors for pneumonia were retrospectively collected. The standardized incidence ratio (SIR) of pneumonia was estimated. Polymorphisms at genes coding for mannose binding lectin (MBL), MBL-associated serine protease 2, Fc-gamma receptors, and surfactant proteins A1, A2, and D were determined, and their potential association with pneumonia was analyzed. Patients with and without pneumonia were compared using a multivariate logistic regression model for adjustment of pneumonia-associated factors.

RESULTS: Thirty-six of 232 patients with SLE had experienced ≥ 1 pneumonia event. SIR for pneumonia was 5.1 (95% CI 3.5-7.4; $p < 0.0001$). Excluding patients receiving immunosuppressive therapy at the time of pneumonia (13%), associations were found for Katz Severity Index (KSI) ($p = 0.016$), wSLICC/ACR-DI ($p = 0.044$), number of SLE criteria ($p = 0.005$), hospital admissions ($p < 0.001$), FCGR2A HH genotype ($p = 0.03$), previous use of immunosuppressive therapy ($p = 0.049$), cutaneous ulcers ($p < 0.001$), and vasculitis ($p = 0.008$) in bivariate analyses. In the multivariate analysis adjusted to previous immunosuppressive treatment, only KSI and FCGR2A HH genotype remained statistically significant ($p = 0.05$ and $p = 0.03$, respectively).

CONCLUSION: The incidence of pneumonia in patients with SLE is higher than that in the general population, and particularly high in severe SLE, regardless of immunosuppressive therapy. The HH genetic variant of FCGR2A appears to predispose patients with SLE to pneumonia.

Biomed Res Int. 2014;2014:746192. doi: 10.1155/2014/746192. Epub 2014 Jun 11.

Renal transplantation in systemic lupus erythematosus: outcome and prognostic factors in 50 cases from a single centre.

Cairoli E[1], Sanchez-Marcos C[2], Espinosa G[2], Glucksmann C[3], Ercilla G[4], Oppenheimer F[3], Cervera R[2].

Author information

Abstract

BACKGROUND: End-stage renal disease (ESRD) is an important cause of morbidity and mortality in patients with systemic lupus erythematosus (SLE).

OBJECTIVES: To analyze the outcome and prognostic factors of renal transplantation in patients with ESRD due to SLE from January 1986 to December 2013 in a single center.

RESULTS: Fifty renal transplantations were performed in 40 SLE patients (32 female (80%), mean age at transplantation 36±10.4 years). The most frequent lupus nephropathy was type IV (72.2%). Graft failure occurred in a total of 15 (30%) transplantations and the causes of graft failure were chronic allograft nephropathy (n=12), acute rejection (n=2), and chronic humoral rejection (1). The death-censored graft survival rates were 93.9% at 1 year, 81.5% at 5 years, and 67.6% at the end of study. The presence of deceased donor allograft (P=0.007) and positive anti-HCV antibodies (P=0.001) negatively influence the survival of the renal transplant. The patient survival rate was 91.4% at the end of the study. Recurrence of lupus nephritis in renal allograft was observed in one patient.

CONCLUSION: Renal transplantation is a good alternative for renal replacement therapy in patients with SLE. In our cohort, the presence of anti-HCV antibodies and the type of donor source were related to the development of graft failure.

Rheumatology (Oxford). 2014 Aug;53(8):1470-6. doi: 10.1093/rheumatology/keu148. Epub 2014 Mar 27.

Glucocorticoids and irreversible damage in patients with systemic lupus erythematosus.

Ruiz-Arruza I[1], Ugarte A[1], Cabezas-Rodriguez I[1], Medina JA[1], Moran MA[1], Ruiz-Irastorza G[2].

Author information

Abstract

OBJECTIVE: The aim of this study was to analyse the relationship between glucocorticoids and damage accrual in SLE.

METHODS: We report an observational cohort study including 230 patients with SLE enrolled at diagnosis with 5 years of follow-up. Damage was calculated using the SLICC damage index. Glucocorticoid-related damage was defined as avascular osteonecrosis, osteoporotic fractures, diabetes mellitus or cataracts. Prednisone doses were calculated at the end of the fourth year of follow-up (prednisone-4). A categorical prednisone-4 variable was constructed: no prednisone, ≤7.5 mg/day (low dose), >7.5 mg/day (medium-high dose). The relationship between methylprednisolone pulses and damage was also tested.

RESULTS: By the fifth year, 188 patients (82%) had been treated with prednisone. Eighty-seven patients (37.8%) had accrued damage at 5 years. Patients with damage at year 5 had received a higher mean daily prednisone-4 dose (10.4 vs 6 mg/day, P < 0.001). The mean daily prednisone-4 dose was higher in patients accruing glucocorticoid-attributable damage (11 vs 7 mg/day, P = 0.04). Patients taking medium-high doses of prednisone-4 had a higher risk of accruing damage than those taking no prednisone [adjusted odds ratio (OR) 5.39, 95% CI 1.59, 18.27]. Patients taking medium-high doses of prednisone-4 were more likely to develop glucocorticoid-related damage than those on no prednisone (adjusted OR 9.9, 95% CI 1.1, 84). No differences were seen between patients on low doses and those on no prednisone. The cumulative dose of i.v. methylprednisolone-4 was not associated with global or glucocorticoid-related damage.

CONCLUSION: Prednisone causes damage in SLE. Doses <7.5 mg/day and methylprednisolone pulses are not associated with damage accrual.

Autoimmun Rev. 2014 Feb;13(2):206-14. doi: 10.1016/j.autrev.2013.10.013. Epub 2013 Nov 2.

Prednisone in lupus nephritis: how much is enough?

Ruiz-Irastorza G[1], Danza A, Perales I, Villar I, Garcia M, Delgado S, Khamashta M.

Author information

Abstract

OBJECTIVE: To assess the effectiveness and safety of a protocol using medium doses of prednisone to treat lupus nephritis.

METHODS: Patients receiving the 'Cruces-protocol cohort' (CPC) were paired 1:2 with patients from the 'historic cohort' (HC). The CPC received medium doses of prednisone combined with methyl-prednisolone pulses, hydroxychloroquine and immunosuppressive drugs, usually cyclophosphamide. The HC received cyclophosphamide and high-dose prednisone. Partial and complete remission rates and glucocorticoid-related toxicity were assessed.

RESULTS: 15 CPC and 30 HC patients were analysed. The mean (SD) initial dose of prednisone was 22 (8) mg/d in the CPC vs. 49 (19) mg/d in the HC ($p<0.001$). The 6-month mean (SD) cumulative dose of prednisone was 1.7 (0.5) g (average daily dose 9mg) vs. 4.5 (2.1) g (average daily dose 25mg), respectively ($p<0.001$). The median cumulative dose of cyclophosphamide at six months was 3 (0-4.5) g in the CPC vs. 5 (0-16.8) in the HC ($p<0.001$). 15/15 (100%) vs. 10/30 (33%) patients were treated with hydroxychloroquine ($p<0.001$). At six months, 12/15 (80%) patients in the CPC achieved partial or complete remission vs. 14/30 (47%) in the HC ($p=0.015$). At 12months, 13/15 (87%) vs. 19/30 (63%) patients, respectively, were in complete or partial remission ($p=0.055$). Toxicity attributable to glucocorticoids was observed in 1/15 (7%) vs. 20/30 (67%) patients, respectively ($p<0.0001$).

CONCLUSION: A combination of medium-dose prednisone, methylprednisolone pulses, cyclophosphamide and hydroxychloroquine is at least as effective in achieving remission of lupus nephritis as regimes containing high-dose prednisone and causes less toxicity.

J Rheumatol. 2014 Feb;41(2):310-7. doi: 10.3899/jrheum.130817. Epub 2014 Jan 15.

Peripheral arterial disease in systemic lupus erythematosus: prevalence and risk factors.

Erdozain JG[1], Villar I, Nieto J, Ruiz-Irastorza G.

Author information

Abstract

OBJECTIVE: To analyze the prevalence of peripheral arterial disease (PAD) and cardiovascular (CV) risk factors in a cohort of patients with systemic lupus erythematosus (SLE) and to identify variables potentially related to PAD.

METHODS: The study included 216 patients with SLE from the Lupus-Cruces prospective observational cohort. The ankle brachial index (ABI) was determined in each patient, with values < 0.9 considered diagnostic of PAD. Demographic and clinical variables, presence of traditional risk factors and CV events, cardiovascular risk calculated by Systematic Coronary Risk Evaluation (SCORE), and treatments received by each patient were analyzed.

RESULTS: Ninety-two percent of patients were women. The mean age (SD) was 49 years (15), with a mean followup (SD) of 12 years (9). The prevalence of low ABI was 21%. CV risk factors were frequent: smoking, 30% of patients; high blood pressure, 32.7%; diabetes mellitus, 3.2%; hypercholesterolemia, 34.1%; and metabolic syndrome, 9.7%. The following variables were associated with low ABI in the univariate analysis: age ($p < 0.001$), hypertension ($p = 0.002$), diabetes ($p = 0.018$), hypercholesterolemia ($p = 0.018$), CV events ($p < 0.001$), SCORE ($p = 0.004$), cumulative dose of cyclophosphamide ($p = 0.03$), and fibrinogen levels ($p = 0.002$). In the multivariate analysis, the only independent variable in the final model was age (OR 1.04, 95% CI 1.02-1.07, $p < 0.001$), with a tendency for the presence of any vascular risk factor (diabetes, hypertension, hypercholesterolemia, or current smoking; OR 2.3, 95% CI 0.99-5.1, $p = 0.053$).

CONCLUSION: The prevalence of low ABI in patients with SLE is higher than expected. While the association with CV risk factors and vascular disease in other territories was strong, we could not identify SLE-specific variables independently associated with PAD.

KEYWORDS: ATHEROSCLEROSIS; CARDIOVASCULAR RISK FACTORS; HYPERCHOLESTEROLEMIA; HYPERTENSION; SYSTEMIC LUPUS ERYTHEMATOSUS; VASCULAR DISEASE

Ann Rheum Dis. 2014 May 16. pii: annrheumdis-2013-205171. doi: 10.1136/annrheumdis-2013-205171. [Epub ahead of print]

Factors associated with damage accrual in patients with systemic lupus erythematosus: results from the Systemic Lupus International Collaborating Clinics (SLICC) Inception Cohort.

Bruce IN[1], O'Keeffe AG[2], Farewell V[3], Hanly JG[4], Manzi S[5], Su L[3], Gladman DD[6], Bae SC[7], Sanchez-Guerrero J[6], Romero-Diaz J[8], Gordon C[9], Wallace DJ[10], Clarke AE[11], Bernatsky S[12], Ginzler EM[13], Isenberg DA[14], Rahman A[14], Merrill JT[15], Alarcón GS[16], Fessler BJ[16], Fortin PR[17], Petri M[18], Steinsson K[19], Dooley MA[20], Khamashta MA[21], Ramsey-Goldman R[22], Zoma AA[23], Sturfelt GK[24], Nived O[24], Aranow C[25], Mackay M[25], Ramos-Casals M[26], van Vollenhoven RF[27], Kalunian KC[28], Ruiz-Irastorza G[29], Lim S[30], Kamen DL[31], Peschken CA[32], Inanc M[33], Urowitz MB[6].

⊕ Author information

Abstract

BACKGROUND AND AIMS: We studied damage accrual and factors determining development and progression of damage in an international cohort of systemic lupus erythematosus (SLE) patients.

METHODS: The Systemic Lupus International Collaborating Clinics (SLICC) Inception Cohort recruited patients within 15 months of developing four or more 1997 American College of Rheumatology (ACR) criteria for SLE; the SLICC/ACR damage index (SDI) was measured annually. We assessed relative rates of transition using maximum likelihood estimation in a multistate model. The Kaplan-Meier method estimated the probabilities for time to first increase in SDI score and Cox regression analysis was used to assess mortality.

RESULTS: We recruited 1722 patients; mean (SD) age 35.0 (13.4) years at cohort entry. Patients with damage at enrolment were more likely to have further worsening of SDI (SDI 0 vs ≥1; p<0.001). Age, USA African race/ethnicity, SLEDAI-2K score, steroid use and hypertension were associated with transition from no damage to damage, and increase(s) in pre-existing damage. Male gender (relative transition rates (95% CI) 1.48 (1.06 to 2.08)) and USA Caucasian race/ethnicity (1.63 (1.08 to 2.47)) were associated with SDI 0 to ≥1 transitions; Asian race/ethnicity patients had lower rates of new damage (0.60 (0.39 to 0.93)). Antimalarial use was associated with lower rates of increases in pre-existing damage (0.63 (0.44 to 0.89)). Damage was associated with future mortality (HR (95% CI) 1.46 (1.18 to 1.81) per SDI point).

CONCLUSIONS: Damage in SLE predicts future damage accrual and mortality. We identified several potentially modifiable risk factors for damage accrual; an integrated strategy to address these may improve long-term outcomes.

Ann Rheum Dis. 2014 Mar 21. doi: 10.1136/annrheumdis-2013-204351. [Epub ahead of print]

Atherosclerosis and cardiovascular disease in systemic lupus erythematosus: effects of in vivo statin treatment.

Ruiz-Limon P[1], Barbarroja N, Perez-Sanchez C, Aguirre MA, Bertolaccini ML, Khamashta MA, Rodriguez-Ariza A, Almadén Y, Segui P, Khraiwesh H, Gonzalez-Reyes JA, Villalba JM, Collantes-Estevez E, Cuadrado MJ, Lopez-Pedrera C.

Author information

Abstract

OBJECTIVE: Statins may have beneficial vascular effects in systemic lupus erythematosus (SLE) beyond their cholesterol-lowering action, although the mechanisms involved are not completely understood. We investigated potential mechanisms involved in the efficacy of fluvastatin in preventing atherothrombosis in SLE.

METHODS: Eighty-five patients with SLE and 62 healthy donors were included in the study. Selected patients (n=27) received 20 mg/day fluvastatin for 1 month. Blood samples were obtained before the start and at the end of treatment. Monocytes from five patients were treated in vitro with fluvastatin.

RESULTS: Increased prothrombotic and inflammatory variables were found in patients with SLE. SLE monocytes displayed altered mitochondrial membrane potential and increased oxidative stress. Correlation and association analyses demonstrated a complex interplay among autoimmunity, oxidative stress, inflammation and increased risk of atherothrombosis in SLE. Fluvastatin treatment of patients for 1 month reduced the SLE Disease Activity Index and lipid levels, oxidative status and vascular inflammation. Array studies on monocytes demonstrated differential expression in 799 genes after fluvastatin treatment. Novel target genes and pathways modulated by fluvastatin were uncovered, including gene networks involved in cholesterol and lipid metabolism, inflammation, oxidative stress and mitochondrial activity. Electron microscopy analysis showed increased density volume of mitochondria in monocytes from fluvastatin-treated patients, who also displayed higher expression of genes involved in mitochondrial biogenesis. In vitro treatment of SLE monocytes confirmed the results obtained in the in vivo study.

CONCLUSIONS: Our overall data suggest that fluvastatin improves the impairment of a redox-sensitive pathway involved in processes that collectively orchestrate the pathophysiology of atherothrombosis in SLE.

Lupus. 2014 Apr;23(4):353-9. doi: 10.1177/0961203314522335. Epub 2014 Feb 7.

Differential expression pattern of microRNAs in CD4+ and CD19+ cells from asymptomatic patients with systemic lupus erythematosus.

Martínez-Ramos R[1], García-Lozano JR, Lucena JM, Castillo-Palma MJ, García-Hernández F, Rodríguez MC, Núñez-Roldán A, González-Escribano MF.

Author information

Abstract

OBJECTIVE: The aim of this study was to investigate the pattern of microRNA (miRNA) expression in CD19+ and CD4+ cells from asymptomatic patients with systemic lupus erythematosus (SLE).

METHODS: A screening of the expression of 377 miRNAs was performed in human CD4+ and CD19+ cells isolated from the peripheral blood by using a TaqMan Human MicroRNA Array. Validation of differential expression pattern of those was performed using TaqMan assays in these cell populations obtained from a larger cohort of patients and controls.

RESULTS: According to the screening assays, three miRNAs were differentially expressed (p value <0.1) in cell populations from both patients and controls: hsa-miR-143, hsa-miR-224 and hsa-miR-576-5p for CD4+ cells, and hsa-miR-10a, hsa-miR-31 and hsa-miR-345 for CD19+ cells. After validation, significant differences (p value <0.05) were confirmed only for hsa-miR-143 and hsa-miR-224 in CD4+ cells and for hsa-miR-10a and hsa-miR-345 in CD19+ cells. In all cases, the miRNAs were over expressed in SLE patients compared with healthy donors.

CONCLUSIONS: Our results support a different pattern of miRNA expression in SLE patients.

Lupus. 2014 Apr;23(4):431-5. doi: 10.1177/0961203313517015. Epub 2013 Dec 10.

Trends in systemic lupus erythematosus mortality in Spain from 1981 to 2010.

Ruiz E[1], Ramalle-Gómara E, Elena Á, Quiñones C, Alonso V, Posada M; Spain RDR Working group.

Author information

[1]1Department of Epidemiology, La Rioja Regional Authority, Logroño, Spain.

Abstract

BACKGROUND: Incidence and mortality of systemic lupus erythematosus (SLE) seem to be increasing in the last few decades, in contrast to the survival rate that has improved over time. The objective of this study was to examine the trends in the SLE mortality in Spain over a 30-year period (1981-2010).

METHODS: Data on SLE deaths were drawn from the National Statistics Institute of Spain. Crude and overall age-standardized SLE mortality rates were calculated and joinpoint regression models were used to describe trend changes. Mean age of deaths by SLE each year was also assessed.

RESULTS: The overall age-standardized SLE mortality rate was 1.82 per million in 1981 and 2.24 in 2010. It was higher in women, 1.39 vs 0.43 in 1981 and 1.96 vs 0.28 in 2010. There was a statistically significant change in 1999. The overall age-standardized mortality rate increased from 1981 to 1999 and stabilized from 2000 to 2010. Only male rates decreased from 2000 to 2010. The mean age at death increased with time, from 42 years in 1981 to 61 years in 2010.

CONCLUSIONS: In conclusion, a slight decrease in SLE mortality has been observed in Spain over the last decade and future studies would be needed to explain the factors contributing to the improvement in the mortality rates.

KEYWORDS: International Classification of Diseases; Systemic lupus erythematosus; mortality; registries; surveillance

J Rheumatol. 2014 Mar;41(3):453-7. doi: 10.3899/jrheum.130535. Epub 2014 Feb 1.

Influence of psychological stress on headache in patients with systemic lupus erythematosus.

Vargas-Hitos JA[1], Sabio JM, Martínez-Egea I, Jiménez-Jáimez E, Rodríguez-Guzmán M, Navarrete-Navarrete N, López-Lozano E, Romero-Alegría Á, de la Calle C, Jáimez-Gámiz L, Baños-Piñero P, Nebrera-Navarro F, Fidalgo A, Caminal L, de Ramón Garrido E, Ortego-Centeno N, Expósito M, Zamora-Pasadas M, Jiménez-Alonso J.

Author information

Abstract

OBJECTIVE: To compare the prevalence and disability of headache in patients with systemic lupus erythematosus (SLE) with the general population and to assess the role of chronic psychological stress (CPS) in headache development.

METHODS: One hundred seventy patients with SLE and 102 control subjects matched for age, sex, and level of education were included in this multicenter, cross-sectional study. CPS, headache-related disability, and chronic analgesic intake (CAI) were evaluated in all participants.

RESULTS: No statistical differences in the prevalence of headache between both groups were observed but headache disability was significantly higher in patients with SLE. In addition, a higher average score in the Cohen Perceived Stress Scale (CPSS) and a higher prevalence of patients with CAI were observed in patients with SLE. In multivariate analysis, CPSS score was positively (OR 1.09; 95% CI: 1.03-1.14; p = 0.001) and CAI negatively (OR 0.43; 95% CI: 0.19-0.99; p = 0.049) associated with headache in patients with SLE.

CONCLUSION: Despite the prevalence of headache in patients with SLE and the general population being similar, headache-related disability may be higher in patients with SLE. Moreover, CPS might play a role in the pathogenesis of SLE headache, whereas CAI might have a protective effect against it.

KEYWORDS: HEADACHE; PSYCHOLOGICAL STRESS; SYSTEMIC LUPUS ERYTHEMATOSUS

Granada, Málaga, Córdoba, Sevilla, Jaén, Madrid, Valencia
48 pacientes/GC – análisis datos…redacción artículo

Lupus Eritematoso sistémico y SAF en pacientes de etnia gitana.

Dra. MV. Manzano Gamero

Otras publicaciones de interés sobre LES en el último año

Lupus. 2013 Nov;22(13):1425-30. doi: 10.1177/0961203313500547. Epub 2013 Aug 13.

Association of Asian ethnicity with disease activity in SLE: an observational study from the Monash Lupus Clinic.

Golder V[1], Connelly K, Staples M, Morand E, Hoi A.

Author information

Abstract

OBJECTIVE: Systemic lupus erythematosus (SLE), an autoimmune condition with diverse clinical manifestations, is reported to have different expression in populations of different ancestry. Most previous studies compared patients of different ethnic groups from geographically distinct cohorts. In our study, we aimed to characterize disease manifestations in patients of different ethnic groups from a single centre, and studied patterns of disease activity over time.

METHODS: Demographics, baseline disease characteristics and autoantibody profiles, and disease activity (SLEDAI) measured at each visit, were captured from all consenting patients prospectively followed between 2007 and 2011 in an urban teaching hospital lupus clinic. Ethnicity was self-reported.

RESULTS: Asian ethnicity was significantly associated with more clinically severe SLE. Time-adjusted mean SLEDAI ($p = 0.01$) and maximum SLEDAI ($p = 0.0018$) were significantly higher in Asian patients. Asians were more likely to have renal disease (OR 2.9, 95% CI 1.4-5.98; $p = 0.004$) and persistently active disease (PAD) (OR 2.14, 95% CI 1.05-4.38, $p = 0.04$). Asian lupus patients also had a significantly higher proportion of autoantibody positivity to anti-dsDNA, anti-RNP, anti-Sm, anti-Ro and anti-La, as well as increased likelihood of hypocomplementaemia and immunosuppressant use.

CONCLUSION: In this single-cohort study, Asian ethnicity was found to be associated with increased SLE disease activity. This suggests significant inter-ethnic genetic contributions to the regulation of autoimmune responses and disease severity in SLE.

Filters activated: Clinical Trial, Publication date from 2013/09/01 to 2014/07/31. Clear all

Atherosclerosis. 2013 Nov;231(1):129-35. doi: 10.1016/j.atherosclerosis.2013.09.004. Epub 2013 Sep 11.

Perivascular adipose tissue of the descending thoracic aorta is associated with systemic lupus erythematosus and vascular calcification in women.

Shields KJ[1], Barinas-Mitchell E, Gingo MR, Tepper P, Goodpaster BH, Kao AH, Manzi S, Sutton-Tyrrell K.

Author information

[1]Lupus Center of Excellence, West Penn Allegheny Health System, 320 East North Avenue, Pittsburgh, PA 15212, USA. Electronic address: kshield1@wpahs.org.

Abstract

OBJECTIVE: Women with systemic lupus erythematosus (SLE) have an increased risk of cardiovascular disease (CVD). Traditional CVD and SLE-disease related risk factors do not fully account for this increased risk. Perivascular adipose tissue (PVAT) is a visceral adipose depot in close proximity to blood vessels possibly influencing CVD. We hypothesized that women with SLE have an increased volume of descending thoracic aortic PVAT (aPVAT) associated with increased vascular calcification.

METHODS: Using electron beam computed tomography, we quantified the aPVAT in clinically CVD-free SLE women (n = 135) and age-/race-matched healthy controls (HC, n = 152). Coronary artery calcification (CAC) and aortic calcification (AC) were quantified using Agatston scores and the aPVAT was quantified using standard Hounsfield Units (HU) for adipose tissue.

RESULTS: Women with SLE had greater median aPVAT (32.2 cm(3) vs HC aPVAT 28.6 cm(3), p = 0.0071) and greater median AC (26.0 vs HC AC 6.0, p = 0.0013) than the healthy control women. Total aPVAT (per 25 cm(3)) remained significantly associated with SLE after adjusting for CVD risk factors (Odds Ratio 1.74 [95% Confidence Interval: 1.04-2.9], p = 0.034), but was attenuated when adjusting for circulating inflammatory markers (p = 0.34). In a logistic regression analysis, SLE aPVAT (per 25 cm(3)) was associated with AC (6.78 [2.0-23], p = 0.0019), which remained significant after adjusting for circulating inflammatory markers (p = 0.0074), and CAC (2.66 [1.4-5.0], p = 0.0028).

CONCLUSIONS: Total aPVAT is greater in clinically CVD-free SLE women than in age-/race-matched controls and is associated with calcification in different vascular beds.

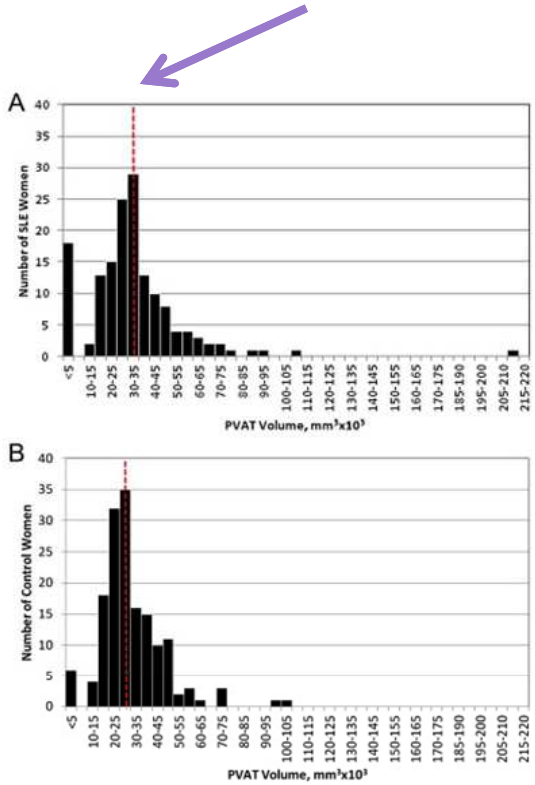


Fig. 1 Total aPVAT (mm 3 × 10 3) distribution for A) SLE Median (25%–75%): 32.2 (25–42) mm 3 × 10 3 ; B) controls, 28.6 (22–37) mm 3 × 10 3 . (p = 0.0071). Dash indicates median values.

Kelly J. Shields , Emma Barinas-Mitchell , Matthew R. Gingo , Ping Tepper , Bret H. Goodpaster , Amy H. Kao , Susa...

Perivascular adipose tissue of the descending thoracic aorta is associated with systemic lupus erythematosus and vascular calcification in women

Atherosclerosis, Volume 231, Issue 1, 2013, 129 - 135

http://dx.doi.org/10.1016/j.atherosclerosis.2013.09.004

Rheumatol Int. 2013 Nov;33(11):2789-96. doi: 10.1007/s00296-013-2811-3. Epub 2013 Jul 2.

Omega-3 in SLE: a double-blind, placebo-controlled randomized clinical trial of endothelial dysfunction and disease activity in systemic lupus erythematosus.

Bello KJ[1], Fang H, Fazeli P, Bolad W, Corretti M, Magder LS, Petri M.

Author information

[1]Division of Rheumatology, Johns Hopkins University School of Medicine, 1830 East Monument Street, Suite 7500, Baltimore, MD, 21205, USA, bellojibril@yahoo.co.uk.

Abstract

Accelerated atherosclerosis remains a major cause of death in late systemic lupus erythematosus (SLE). Omega-3 has been reported to have benefit for endothelial dysfunction, one of the earliest stages of atherosclerosis, and to reduce disease activity in SLE. We performed a randomized, double-blind placebo-controlled trial to examine the effect of Omega-3 on endothelial function, disease activity, inflammatory markers and lipids in SLE. SLE patients (n = 85, mean age 47, 55% Caucasian, 38% African-American, 94% female) were randomly assigned to 3 g of Omega-3 (Lovaza, GSK) versus placebo for 12 weeks. Endothelial function was measured at baseline and at 12 weeks using flow-mediated dilation, calculated using high-resolution B-mode ultrasound of the brachial artery diameter in response to vasoactive stimuli (hyperemia). Disease activity was measured using the physician global assessment and SELENA-SLEDAI score. Inflammatory markers (sICAM-1, sVCAM-1, IL-6) and fasting lipid profile were done at baseline and 12-week follow-up. There was no difference between the treatment groups with respect to changes in flow-mediated dilation parameters or disease activity. An average increase in LDL cholesterol of 3.11 mg/dL (±21.99) was found with Omega-3 versus a decrease of 1.87 mg/dL (±18.29) with placebo (p = 0.0266). In this trial, Omega-3 did not improve endothelial function, disease activity, nor reduce inflammatory markers in SLE. Longer trials might be required if there are delayed clinical effects. There was evidence that Omega-3 may increase LDL cholesterol, but not the LDL/HDL ratio.

Comment in

Omega-3: a double-edged sword for autoimmune diseases. [Rheumatol Int. 2014]

Oncology. 2013;85(4):235-40. doi: 10.1159/000350165. Epub 2013 Oct 2.

Non-lymphoma hematological malignancies in systemic lupus erythematosus.

Lu M[1], Bernatsky S, Ramsey-Goldman R, Petri M, Manzi S, Urowitz MB, Gladman D, Fortin PR, Ginzler EM, Yelin E, Bae SC, Wallace DJ, Jacobsen S, Dooley MA, Peschken CA, Alarcón GS, Nived O, Gottesman L, Criswell LA, Sturfelt G, Dreyer L, Lee JL, Clarke AE.

Author information

[1]Division of Clinical Epidemiology, McGill University Health Centre, Montreal, Que., Canada.

Abstract

OBJECTIVE: To describe non-lymphoma hematological malignancies in systemic lupus erythematosus (SLE).

METHODS: A large SLE cohort was linked to cancer registries. We examined the types of non-lymphoma hematological cancers.

RESULTS: In 16,409 patients, 115 hematological cancers [including myelodysplastic syndrome (MDS)] occurred. Among these, 33 were non-lymphoma. Of the 33 non-lymphoma cases, 13 were of lymphoid lineage: multiple myeloma (n = 5), plasmacytoma (n = 3), B cell chronic lymphocytic leukemia (B-CLL; n = 3), precursor cell lymphoblastic leukemia (n = 1) and unspecified lymphoid leukemia (n = 1). The remaining 20 cases were of myeloid lineage: MDS (n = 7), acute myeloid leukemia (AML; n = 7), chronic myeloid leukemia (CML; n = 2) and 4 unspecified leukemias. Most of these malignancies occurred in female Caucasians, except for plasma cell neoplasms (4/5 multiple myeloma and 1/3 plasmacytoma cases occurred in blacks).

CONCLUSIONS: In this large SLE cohort, the most common non-lymphoma hematological malignancies were myeloid types (MDS and AML). This is in contrast to the general population, where lymphoid types are 1.7 times more common than myeloid non-lymphoma hematological malignancies. Most (80%) multiple myeloma cases occurred in blacks; this requires further investigation.

Lupus. 2013 Nov;22(13):1341-8. doi: 10.1177/0961203313505689. Epub 2013 Sep 18.

The frequency of and associations with hospitalization secondary to lupus flares from the 1000 Faces of Lupus Canadian cohort.

Lee J[1], Peschken CA, Muangchan C, Silverman E, Pineau C, Smith CD, Arbillaga H, Zummer M, Clarke A, Bernatsky S, Hudson M, Hitchon C, Fortin PR, Pope JE.

Author information

Abstract

OBJECTIVES: Hospitalization is a major factor in health care costs and a surrogate for worse outcomes in chronic disease. The aim of this study was to determine the frequency of hospitalization secondary to lupus flare, the causes of hospitalization, and to determine risk factors for hospitalization in patients with systemic lupus erythematosus (SLE).

METHODS: Data were collected as part of the 1000 Canadian Faces of Lupus, a prospective cohort study, where annual major lupus flares including hospitalizations were recorded over a 3-year period.

RESULTS: Of 665 patients with available hospitalization histories, 68 reported hospitalization related to a SLE flare over 3 years of follow-up. The average annual hospitalization rate was 7.6% (range 6.6-8.9%). The most common reasons for hospitalization were: hematologic (22.1%), serositis (20.6%), musculoskeletal (MSK) (16.2%), and renal (14.7%). Univariate risk factors for lupus hospitalization included (OR [95% CI]; $p < 0.05$): juvenile-onset lupus (2.2 [1.1-4.7]), number of ACR SLE criteria (1.4 [1.1-1.7], baseline body mass index (BMI) (1.1 [1.0-1.1]), psychosis (3.4 [1.2-9.9]), aboriginal race (3.2 [1.5-6.7]), anti-Smith (2.6 [1.2-5.4]), erythrocyte sedimentation rate >25 mm/hr (1.9 [1.1-3.4]), proteinuria >0.5 g/d (4.2 [1.9-9.3], and SLAM-2 score (1.1 [1.0-1.2]). After multivariate regression only BMI, number of ACR criteria, and psychosis were associated with hospitalization for lupus flare.

CONCLUSIONS: The mean annual rate of hospitalization attributed to lupus was lower than expected. Hematologic, serositis, MSK and renal were the most common reasons. In a regression model elevated BMI, more ACR criteria and psychosis were associated with hospitalization.

Índices

Ann Rheum Dis. 2014 Feb;73(2):401-6. doi: 10.1136/annrheumdis-2012-202376. Epub 2013 Jan 23.

Validation of the systemic lupus erythematosus responder index for use in juvenile-onset systemic lupus erythematosus.

Mina R[1], Klein-Gitelman MS, Nelson S, Eberhard BA, Higgins G, Singer NG, Onel K, Tucker L, O'Neil KM, Punaro M, Levy DM, Haines K, Martini A, Ruperto N, Lovell D, Brunner HI.

Author information

Abstract

OBJECTIVES: This study tested the concurrent validity of the systemic lupus erythematosus responder index (SRI) in assessing improvement in juvenile-onset systemic lupus erythematosus (jSLE).

METHODS: The SRI considers changes in the SELENA-SLEDAI, BILAG and a 3-cm visual analogue scale of physician-rated disease activity (PGA) to determine patient improvement. Using prospectively collected data from 760 unique follow-up visit intervals of 274 jSLE patients, we assessed the sensitivity and specificity of the SRI using these external standards: physician-rated improvement (MD-change), patient/parent-rated major improvement of wellbeing (patient-change) and decrease in prescribed systemic corticosteroids (steroid-change). Modifications of the SRI that considered different thresholds for the SELENA-SLEDAI, BILAG and 10-cm PGA were explored and agreement with the American College of Rheumatology/PRINTO provisional criteria for improvement of jSLE (PCI) was examined.

RESULTS: The sensitivity/specificity in capturing major improvement by the MD-change were 78%/76% for the SRI and 83%/78% for the PCI, respectively. There was fair agreement between the SRI and PCI (kappa=0.35, 95% CI 0.02 to 0.73) in capturing major improvement by the MD-change. Select modified versions of the SRI had improved accuracy overall. All improvement criteria tested had lower sensitivity when considering patient-change and steroid-change as external standards compared to MD-change.

CONCLUSIONS: The SRI and its modified versions based on meaningful changes in jSLE have high specificity but at most modest sensitivity for capturing jSLE improvement. When used as an endpoint of clinical trials in jSLE, the SRI will provide a conservative estimate regarding the efficacy of the therapeutic agent under investigation.

Validation of the systemic lupus erythematosus responder index for use in juvenile-onset systemic lupus erythematosus

Table 4

Accuracy of the SRI and PCI when considering baseline disease activity*

Sensitivity/specificity (accuracy) of response criteria†	SELENA–SLEDAI low-moderate‡ (visit intervals 329)		SELENA–SLEDAI high§ (visit intervals 177)	
	Major improvement (N¶=7)	Any improvement (N=67)	Major improvement (N=29)	Any improvement (N=73)
SRI	57%/86% (0.49)	36%/90% (0.32)	83%/55% (0.46)	68%/62% (0.42)
PCI	100%/76% (0.76)	59%/83% (0.49)	83%/70% (0.58)	59%/76% (0.45)

*External standard is physician-rated change in juvenile-onset systemic lupus erythematosus, considering all visits in which SRI and PCI information is concurrently available.

†For details, please see tables 1 and 3.

‡SELENA–SLEDAI low: baseline SELENA–SLEDAI 4–7.

§SELENA–SLEDAI high: baseline SELENA–SLEDAI ≥8.

¶Number of events.

PCI, American College of Rheumatology/PRINTO provisional criteria for improvement of juvenile-onset systemic lupus erythematosus; SELENA–SLEDAI, safety of oestrogens in lupus erythematosus: national assessment version of the systemic lupus erythematosus disease activity index; SRI, systemic lupus erythematosus responder index.

Filters activated: Clinical Trial, Publication date from 2013/09/01 to 2014/07/31. Clear all

Obstet Gynecol. 2014 Jun;123(6):1213-20. doi: 10.1097/AOG.0000000000000279.

Receipt of prescription contraception by commercially insured women with chronic medical conditions.

DeNoble AE[1], Hall KS, Xu X, Zochowski MK, Piehl K, Dalton VK.

Author information

[1]Program on Women's Healthcare Effectiveness Research, Department of Obstetrics and Gynecology, the University of Michigan Medical School, Ann Arbor, Michigan; and the Department of Obstetrics, Gynecology and Reproductive Sciences, Yale University School of Medicine, New Haven, Connecticut.

Abstract

OBJECTIVE: To assess differences in receipt of prescription contraception among women with and without chronic medical conditions.

METHODS: This observational study used 3 years of administrative claims records for insured women aged 21-45 years who were enrolled in a commercial insurance company in Michigan between 2004 and 2009. Women were considered to have a chronic medical condition if they had at least two claims for one of the following conditions, in order of prevalence in our study population: hypertension, asthma, hypothyroidism, diabetes, obesity, rheumatoid arthritis, inflammatory bowel disease, or systemic lupus erythematosus. Our primary outcome was receipt of prescription contraception, defined by a pharmacy claim or diagnostic or procedural code. We used multivariable logistic regression to estimate the association of chronic condition status with the odds of receiving prescription contraception within 3 years adjusting for age, community-level socioeconomic status, total outpatient visits, and cervical cancer screening.

RESULTS: Of 11,649 women studied, 16.0% (n=1,862) had at least one of the chronic conditions we considered. Of those with a chronic condition, 33.5% (n=623) received prescription contraception during the 3-year study period compared with 41.1% (n=4,018) of those without a chronic condition (P<.001). After adjusting for covariates, women with a chronic condition remained less likely than women without a chronic condition to have received prescription contraception (adjusted odds ratio 0.85, 95% confidence interval 0.76-0.96, P=.010).

CONCLUSION: Despite a greater risk for adverse outcomes with an unplanned pregnancy, women with these chronic conditions were less likely to receive prescription contraception.

LEVEL OF EVIDENCE: III.

Filters activated: Clinical Trial. Clear all

Lupus. 2013 Nov;22(13):1416-24. doi: 10.1177/0961203313499956. Epub 2013 Aug 8.

The clinical manifestations and survival of systemic lupus erythematosus patients in Turkey: report from two centers.

Pamuk ON[1], Akbay FG, Dönmez S, Yilmaz N, Calayir GB, Yavuz S.

Author information

Abstract

BACKGROUND: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease with a variety of clinical features. Survival has become longer as a result of better treatment modalities and better supportive care. There is no information on survival of SLE patients in Turkey. We evaluated clinical features and survival in SLE patients in two rheumatology departments.

METHODS: All SLE patients being followed up by the Department of Rheumatology, Trakya University Medical Faculty, and the Department of Rheumatology, Marmara University Medical Faculty, over the 1996-2012 period were included. Patients were diagnosed with SLE if they fulfilled at least four American College of Rheumatology (ACR) criteria. The clinical and laboratory features, mortality data were obtained from medical charts.

RESULTS: We had 428 SLE patients, and women (399 patients, 93.2%) far outnumbered men (29 patients, 6.8%). The mean age at the time of SLE diagnosis was 40.3 ± 12.4 years. The most frequent clinical manifestations were arthritis (76.9%) and photosensitivity (70.1%). Renal disease was present in 32.9% of patients and neurological involvement in 12.9% of patients. After a median follow-up of 60 months, 19 patients died. The most frequent causes of death were ischemic heart disease, chronic renal failure and sepsis. The rate of five-year survival was 96%; 10-year survival, 92%; and 15-year survival, 88.8%. Multivariate Cox analysis showed that serositis at the time of diagnosis, SLE disease activity index (SLEDAI) score 6, and autoimmune hemolytic anemia were independent prognostic factors.

CONCLUSIONS: Data from two centers in Northwestern Turkey show that the mortality rate for SLE is similar to the rate in Western countries.

Arthritis Care Res (Hoboken). 2014 Jun;66(6):934-42. doi: 10.1002/acr.22237.

Discordance of global estimates by patients and their physicians in usual care of many rheumatic diseases: association with 5 scores on a Multidimensional Health Assessment Questionnaire (MDHAQ) that are not found on the Health Assessment Questionnaire (HAQ).

Castrejón I[1], Yazici Y, Samuels J, Luta G, Pincus T.

Author information

Abstract

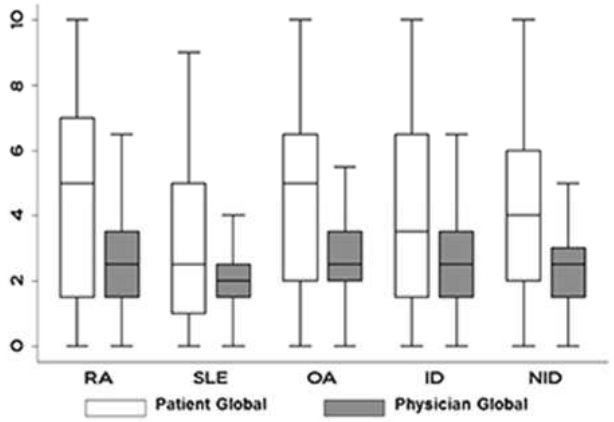
OBJECTIVE: To analyze discordance between global estimates by patients (PATGL) and their physicians (DOCGL) according to demographic and self-report variables on a Multidimensional Health Assessment Questionnaire (MDHAQ) in patients with many rheumatic diseases seen in usual care.

METHODS: Each patient completed an MDHAQ at each visit, which includes scores for physical function, pain, and PATGL, each found on the traditional Health Assessment Questionnaire (HAQ), and scores for sleep quality, anxiety, depression, self-report joint count, and fatigue, which are not found on the HAQ. A random visit of 980 patients with any rheumatic diagnosis was analyzed in 3 categories: PATGL=DOCGL (within 2 of 10 units), PATGL>DOCGL (by ≥2 of 10 units), and DOCGL>PATGL (by ≥2 of 10 units), using descriptive statistics and multinomial logistic regression models.

RESULTS: Patients included 145 with rheumatoid arthritis, 57 with systemic lupus erythematosus, 173 with osteoarthritis, 348 with other inflammatory diseases, and 257 with other noninflammatory diseases. Overall, PATGL=DOCGL in 509 (52%), PATGL>DOCGL in 371 (38%), and DOCGL>PATGL in 100 (10%). PATGL>DOCGL was associated significantly with older age, female sex, low formal education, Hispanic ethnicity, not working, high MDHAQ physical function and pain scores, and high scores for fatigue, poor sleep, anxiety, depression, and self-report joint count, which are not available on the HAQ. Pain and fatigue were significant in a final multinomial logistic regression; the other variables may raise awareness of discordance to clinicians.

CONCLUSION: Global estimates of patients indicated significantly poorer status than estimates of their physicians in 38% of 980 patients with rheumatic conditions, and were associated with demographic and MDHAQ scores, 5 of which are not available on the HAQ.

Discordance of Global Estimates by Patients and Their Physicians in Usual Care of Many Rheumatic Diseases: Association With 5 Scores on a Multidimensional Health Assessment Questionnaire (MDHAQ) That Are Not Found on the Health Assessment Questionnaire (HAQ)



RESULTS: Patients included 145 with rheumatoid arthritis, 57 with systemic lupus erythematosus, 173 with osteoarthritis, 348 with other inflammatory diseases, and 257 with other noninflammatory diseases. Overall, PATGL=DOCGL in 509 (52%), PATGL>DOCGL in 371 (38%), and DOCGL>PATGL in 100 (10%). PATGL>DOCGL was associated significantly with older age, female sex, low formal education, Hispanic ethnicity, not working, high MDHAQ physical function and pain scores, and high scores for fatigue, poor sleep, anxiety, depression, and self-report joint count, which are not available on the HAQ. Pain and fatigue were significant in a final multinomial logistic regression; the other variables may raise awareness of discordance to clinicians.

CONCLUSION: Global estimates of patients indicated significantly poorer status than estimates of their physicians in 38% of 980 patients with rheumatic conditions, and were associated with demographic and MDHAQ scores, 5 of which are not available on the HAQ.

Arthritis Care & Research
Volume 66, Issue 6, pages 934-942, 27 MAY 2014 DOI: 10.1002/acr.22237
http://onlinelibrary.wiley.com/doi/10.1002/acr.22237/full#acr22237-fig-0001

Box 1. Significance & Innovations

- Approximately 38% of patients had patient global estimates ≥2 units higher (on a 0–10 scale) than their physicians' global estimates, with similar patterns in rheumatoid arthritis, osteoarthritis, systemic lupus erythematosus, other inflammatory rheumatic diseases, and other noninflammatory rheumatic diseases.
- Patients with higher global estimates than their doctors were more likely to be older, female, of Hispanic ethnicity, and not working full time, and have lower formal education and poor status for 9 variables on a Multidimensional Health Assessment Questionnaire (MDHAQ), including 4 found on the HAQ, i.e., physical function, pain, patient global estimate (by definition), and Routine Assessment of Patient Index Data 3 (comprised of scores for function, pain, and patient global), and 5 variables not found on the HAQ: fatigue, sleep quality, anxiety, depression, and self-report painful joint count.
- In a final multinomial logistic regression model, the only independent explanatory variables for associations with discordance are pain and fatigue, although the other variables that are significant in bivariate analyses may be helpful to clinicians to recognize a likelihood of discordance between their global estimates and those of individual patients.
- The MDHAQ provides a simple questionnaire, on a single sheet of paper, that can be completed easily by most patients in 5–10 minutes in the waiting area and reviewed in ~10 seconds by a doctor, to facilitate awareness of many variables that may be associated with discordance in global estimates of physicians and patients.

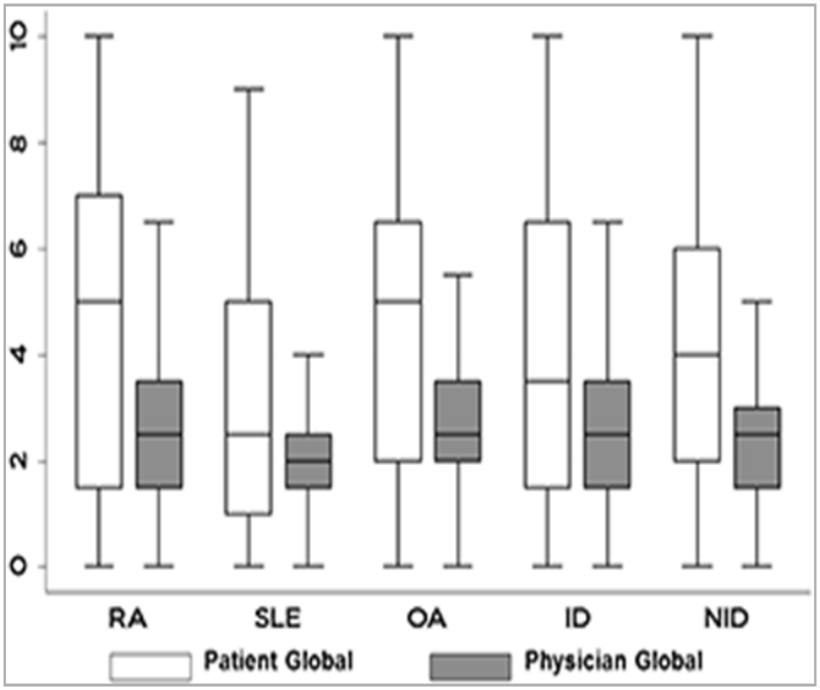


Figure 1.

Open in figure viewer

Box plot of patient and physician global estimates of status by diagnostic category: rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), osteoarthritis (OA), other inflammatory rheumatic diseases (ID), and other noninflammatory rheumatic diseases (NID).

Arthritis Rheum. 2013 Oct;65(10):2661-71. doi: 10.1002/art.38091.

Phase I, randomized, double-blind, placebo-controlled, multiple intravenous, dose-ascending study of sirukumab in cutaneous or systemic lupus erythematosus.

Szepietowski JC[1], Nilganuwong S, Wozniacka A, Kuhn A, Nyberg F, van Vollenhoven RF, Bengtsson AA, Reich A, de Vries DE, van Hartingsveldt B, Robinson DW Jr, Gordon R, Hsu B.

Author information

[1]Wroclaw Medical University, Wroclaw, Poland.

Abstract

OBJECTIVE: We undertook a 2-part, phase I, double-blind, placebo-controlled study to evaluate the safety and pharmacokinetics of multiple intravenous infusions of sirukumab, a human anti-interleukin-6 monoclonal antibody, in patients with cutaneous lupus erythematosus (CLE) or systemic lupus erythematosus (SLE).

METHODS: In part A, patients with histologically confirmed CLE were randomized to 4 infusions of placebo or 1, 4, or 10 mg/kg sirukumab every 2 weeks. In part B, SLE patients diagnosed according to American College of Rheumatology criteria with a score of 5-12 on the Safety of Estrogens in Lupus Erythematosus National Assessment version of the SLE Disease Activity Index were randomized to 4 infusions of placebo or 10 mg/kg sirukumab every 2 weeks.

RESULTS: We treated 31 CLE patients (23 with sirukumab, 8 with placebo) and 15 SLE patients (10 with sirukumab, 5 with placebo). Adverse events (AEs) occurred more often with sirukumab than placebo in CLE patients (91% versus 63%) and in SLE patients (90% versus 80%). Sirukumab led to sustained, dose-independent decreases in white blood cell counts, absolute neutrophil counts (neutropenia), and platelet counts (thrombocytopenia) and to minor elevations in total cholesterol levels. The majority of infections were mild respiratory infections. which were reported similarly across CLE cohorts but more often in sirukumab-treated than in placebo-treated SLE patients. Two serious AEs of infection occurred (pneumonia in the 10 mg/kg-treated group and iatrogenic wound infection in the 4 mg/kg-treated group). Sirukumab showed linear pharmacokinetics in CLE patients. Systemic exposure and half-life were comparable between CLE and SLE patients. No patient developed antibodies to sirukumab through 22 weeks. C-reactive protein and serum amyloid A mean concentrations were suppressed with sirukumab from week 1 to week 14.

CONCLUSION: Treatment with intravenous sirukumab infusions was generally well tolerated in both CLE and SLE patients with mild, stable, active disease. Sirukumab demonstrated linear pharmacokinetics over the dose range studied and comparable systemic exposure and half-life in CLE and SLE patients.

Clin Pharmacokinet. 2013 Nov;52(11):1017-27. doi: 10.1007/s40262-013-0085-2.

Population pharmacokinetics of sifalimumab, an investigational anti-interferon-α monoclonal antibody, in systemic lupus erythematosus.

Narwal R[1], Roskos LK, Robbie GJ.

Author information

Abstract

BACKGROUND AND OBJECTIVES: Sifalimumab is a fully human immunoglobulin G1κ monoclonal antibody that binds to and neutralizes a majority of the subtypes of human interferon-α. Sifalimumab is being evaluated as a treatment for systemic lupus erythematosus (SLE). The primary objectives of this analysis were (a) to develop a population pharmacokinetic model for sifalimumab in SLE; (b) to identify and quantitate the impact of patient/disease characteristics on pharmacokinetic variability; and (c) to evaluate fixed versus body weight (WT)-based dosing regimens.

METHODS: Sifalimumab serum concentration-time data were collected from a phase Ib study (MI-CP152) designed to evaluate the safety and tolerability of sifalimumab in adult patients with SLE. Sifalimumab was administered every 14 days as a 30- to 60-minute intravenous infusion with escalating doses of 0.3, 1.0, 3.0, and 10 mg/kg and serum concentrations were collected over 350 days. A total of 120 patients provided evaluable pharmacokinetic data with a total of 2,370 serum concentrations. Sifalimumab serum concentrations were determined using a validated colorimetric enzyme-linked immunosorbent assay (ELISA) with a lower limit of quantitation of 1.25 µg/mL. Population pharmacokinetic modeling of sifalimumab was performed using a non-linear mixed effects modeling approach with NONMEM VII software. Impact of patient demographics, clinical indices, and biomarkers on pharmacokinetic parameters were explored using a stepwise forward selection and backward elimination approach. The appropriateness of the final model was tested using visual predictive check (VPC). The impact of body WT-based and fixed dosing of sifalimumab was evaluated using a simulation approach. The final population model was utilized for phase IIb dosing projections.

RESULTS: Sifalimumab pharmacokinetics were best described using a two-compartment linear model with first order elimination. Following intravenous dosing, the typical clearance (CL) and central volume of distribution (V 1) were estimated to be 176 mL/day and 2.9 L, respectively. The estimates (coefficient of variation) of between-subject variability for CL and V 1 were 28 and 31 %, respectively. Patient baseline body WT, interferon gene signature from 21 genes, steroid use, and sifalimumab dose were identified as significant covariates for CL, whereas only baseline body WT was a significant covariate for V 1 and peripheral volume of distribution (V 2). Although the above-mentioned covariates were statistically significant, they did not explain variability in pharmacokinetic parameters to any relevant extent (<7 %). Thus, no dosing adjustments are necessary. VPC confirmed good predictability of the final population pharmacokinetic model. Simulation results demonstrate that both fixed and body WT-based dosing regimens yield similar median steady state concentrations and overall variability. Fixed sifalimumab doses of 200, 600, and 1,200 mg monthly (with a loading dose at Day 14) were selected for a phase IIb clinical trial.

CONCLUSION: A two-compartment population pharmacokinetic model adequately described sifalimumab pharmacokinetics. The estimated typical pharmacokinetic parameters were similar to other monoclonal antibodies without target mediated elimination. Although the population pharmacokinetic analysis identified some statistically significant covariates, they explained <7 % between-subject variability in pharmacokinetic parameters indicating that these covariates are not clinically relevant. The population pharmacokinetic analysis also demonstrated the feasibility of switching to fixed doses in phase IIb clinical trials of sifalimumab.

Lupus. 2014 Oct 10. pii: 0961203314555352. [Epub ahead of print]

Hydroxychloroquine and pregnancy on lupus flares in Korean patients with systemic lupus erythematosus.

Koh JH[1], Ko HS[2], Kwok SK[1], Ju JH[1], Park SH[3].

Author information

Abstract

We investigated the clinical and laboratory characteristics of pregnancies with systemic lupus erythematosus (SLE) and identified lupus flare predictors during pregnancy. Additionally, we examined lupus activity and pregnancy outcomes in SLE patients who continued, discontinued or underwent no hydroxychloroquine (HCQ) treatment during pregnancy. We retrospectively analyzed 179 pregnancies in 128 SLE patients at Seoul St. Mary's Hospital, Korea, between 1998 and 2012 and then assessed the clinical profiles and maternal and fetal outcomes. Overall, 90.5% of pregnancies resulted in a successful delivery and were divided into two groups: those who experienced lupus flares (80 pregnancies, 44.7%) and those who did not (99 pregnancies, 55.3%). Increased preeclampsia, preterm births, low birth weight, intrauterine growth restriction (IUGR), and low 1-minute Apgar scores occurred in pregnancies with lupus flares compared to pregnancies in quiescent disease. Lupus flares were predicted by HCQ discontinuation, a history of lupus nephritis, high pre-pregnancy serum uric acid and low C4 levels. Our study indicates that achieving pre-pregnancy remission and continuing HCQ treatment during pregnancy are important for preventing lupus flares.

Arthritis Rheumatol. 2014 Feb;66(2):379-89. doi: 10.1002/art.38260.

Efficacy and safety of abatacept in lupus nephritis: a twelve-month, randomized, double-blind study.

Furie R[1], Nicholls K, Cheng TT, Houssiau F, Burgos-Vargas R, Chen SL, Hillson JL, Meadows-Shropshire S, Kinaszczuk M, Merrill JT.

Author information

Abstract

OBJECTIVE: To compare the efficacy and safety of intravenous (IV) abatacept, a selective T cell costimulation modulator, versus placebo for the treatment of active class III or IV lupus nephritis, when used on a background of mycophenolate mofetil and glucocorticoids.

METHODS: This was a 12-month, randomized, phase II/III, multicenter, international, double-blind study. A total of 298 patients were treated in 1 of 3 IV treatment arms: placebo, abatacept at the standard weight-tiered dose (approximating 10 mg/kg), or abatacept at 30 mg/kg for 3 months, followed by the standard weight-tiered dose (abatacept 30/10). The primary end point, time to confirmed complete response, was a composite measure that required maintenance of glomerular filtration rate, minimal proteinuria, and inactive urinary sediment over the 52-week treatment period.

RESULTS: There were no differences among treatment arms in the time to confirmed complete response or in the proportion of subjects with confirmed complete response following 52 weeks of treatment. Treatment with abatacept was associated with greater improvements from baseline in anti-double-stranded DNA antibody, C3, and C4 levels. Among 122 patients with nephrotic-range proteinuria, treatment with abatacept resulted in an ~20-30% greater reduction in mean urinary protein-to-creatinine ratio compared with placebo. Abatacept was well tolerated; rates of deaths, serious adverse events, and serious infections were similar across treatment arms. Gastroenteritis and herpes zoster occurred more frequently with abatacept treatment.

CONCLUSION: Although the primary end point was not met, abatacept showed evidence of biologic activity and was well tolerated in patients with active class III or IV lupus nephritis.

Rheumatology (Oxford). 2014 Mar;53(3):502-11. doi: 10.1093/rheumatology/ket378. Epub 2013 Nov 22.

Epratuzumab for patients with moderate to severe flaring SLE: health-related quality of life outcomes and corticosteroid use in the randomized controlled ALLEVIATE trials and extension study SL0006.

Strand V[1], Petri M, Kalunian K, Gordon C, Wallace DJ, Hobbs K, Kelley L, Kilgallen B, Wegener WA, Goldenberg DM.

Author information

Abstract

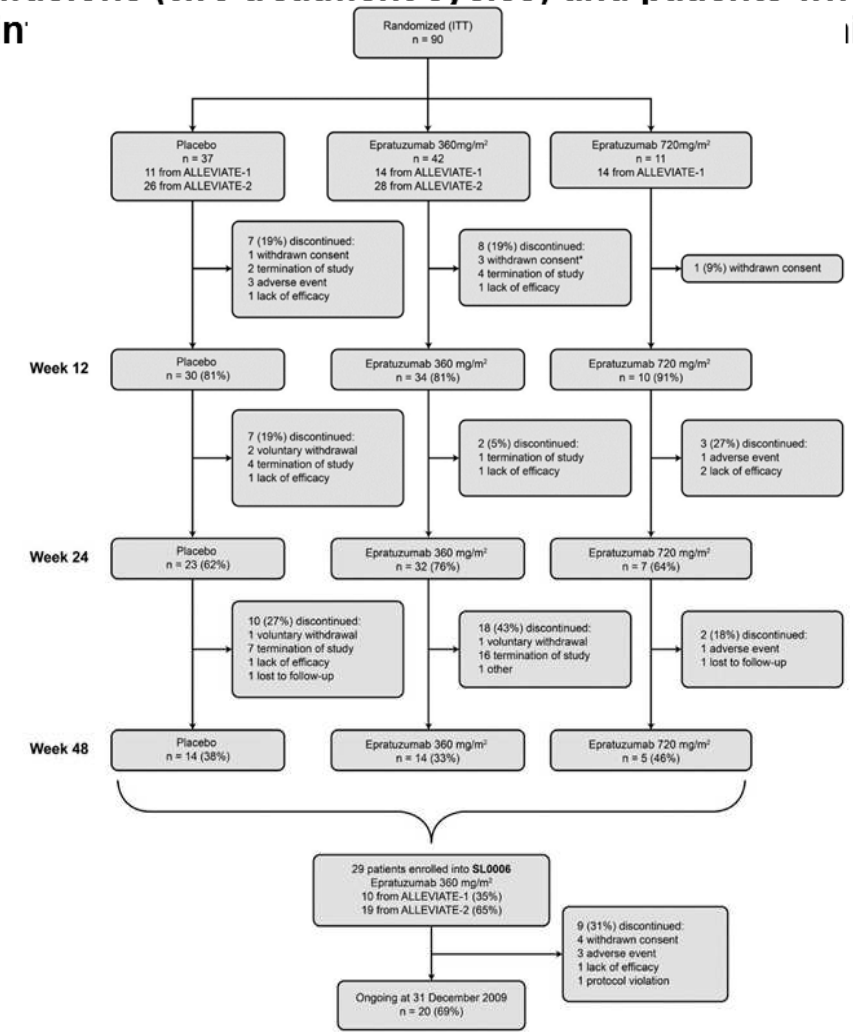
OBJECTIVE: To evaluate health-related quality of life (HRQOL) and corticosteroid use in patients with moderate to severely active SLE enrolled in two international, multicentre, randomized controlled trials of epratuzumab (ALLEVIATE-1 and -2) and a long-term extension study (SL0006).

METHODS: Ninety ALLEVIATE patients (43% BILAG A, mean BILAG score 13.2) were randomized to receive 360 mg/m(2) (n = 42) or 720 mg/m(2) (n = 11) epratuzumab or placebo (n = 37), plus standard of care, in 12-week cycles. Corticosteroid use, patient and physician global assessments of disease activity (PtGA and PGA) and 36-item Medical Outcomes Survey Short Form (SF-36) results were recorded at baseline and every 4 weeks. Both trials were prematurely discontinued due to a drug supply interruption; patients followed for ≥6 months were analysed. Twenty-nine patients continued in SL0006, with interim analysis at a median exposure of 120 (range 13-184) weeks.

RESULTS: At week 12, proportions of patients with a PGA ≥20% above baseline or with a PtGA improvement greater than or equal to the minimum clinically important difference were higher in the epratuzumab arms than the placebo arm. PGA and PtGA improvements were sustained but did not reach statistical significance. At week 24, mean cumulative corticosteroid doses with epratuzumab 360 and 720 mg/m(2) were 1051 and 1973 mg less than placebo (P = 0.034 and 0.081, respectively). At week 48, SF-36 scores approached or exceeded US age- and gender-matched norms in five domains with the 360 mg/m(2) treatment. Improvements were maintained in SL0006 over ~2 years.

CONCLUSION: Epratuzumab treatment produced clinically meaningful and sustained improvements in PGA, PtGA and HRQOL and reductions in corticosteroid doses.

Patient disposition (ITT population) through ALLEVIATE and SL0006.Patients who continued to week 12 received a total of 4 infusions (one treatment cycle), patients who continued to week 24 received a total of 8 infusions (two treatment cycles) and patients who continued to week 48 received a total of 12 in ized but did not receive



Strand V et al. Rheumatology 2014;53:502-511

RHEUMATOLOGY

Epratuzumab for patients with moderate to severe flaring SLE: health-related quality of life outcomes and corticosteroid use in the randomized controlled ALLEVIATE trials and extension study SL0006

TABLE 3
Corticosteroid use and reductions in ALLEVIATE (intention to treat population)

	Placebo (n = 37)	Epratuzumab 360 mg/m^2 (n = 42)	Epratuzumab 720 mg/m^2 (n = 11)
Baseline corticosteroid dose, median (range), mg/day	20.0 (15.0–60.0)	25.0 (10.0–60.0)	46.0 (10.0–80.0)
Baseline–week 24	n = 37	n = 40	n = 11
Corticosteroid dose, median (range), mg/day	9.64 (0–137.4)	10.55 (0–24.6)	13.51 (4.3–49.0)
Cumulative corticosteroid use, median (range), mg	2533 (595–16585)	2384 (1078–4985)	4668 (1240–6960)
Cumulative corticosteroid use, mean (S.D.), mg	3738 (3412)	2786 (1195)	4566 (1601)
Least-squares (LS) mean difference from placebo in cumulative corticosteroid use (95% CI), mg		−1051 (−2018, −83)	−1973 (−4203, 256)
P-value (LS mean *vs* placebo)		0.034*	0.081
Week 24–48	n = 31	n = 34	n = 9
Corticosteroid dose, median (range), mg/day	4.79 (−0.2 to 87.1)	4.85 (−0.2 to 56.0)	4.28 (−0.4 to 8.4)
Cumulative corticosteroid use, median (range), mg	1268 (45–11120)	1254 (55–6035)	1358 (458–5020)
Cumulative corticosteroid use, mean (S.D.), mg	2292 (2678)	1670 (1578)	1534 (1361)
LS mean difference from placebo in cumulative corticosteroid use (95% CI), mg		−675 (−1744, 395)	−652 (−2907, 1603)
P-value (LS mean *vs* placebo)		0.212	0.561
Patients who achieved corticosteroid-tapering criteria[a] at week 24			
Assessed	23	32	6
Yes, n (%)	13 (56.5)	24 (75)	6 (100)
No, n (%)	10 (43.5)	8 (25)	0 (0)
Difference in proportion		18.5	43.5
P-value		0.25	0.072

[a]Corticosteroid-tapering criteria: reduction in corticosteroids to ≤10 mg/day (ALLEVIATE-1) or ≤7.5 mg/day (ALLEVIATE-2) prednisone equivalents by week 24. *Statistically significant P-value from analysis of variance (ANOVA), adjusting for baseline factors.

Rheumatology key messages

- Epratuzumab treatment resulted in clinically meaningful improvements in health –related quality of life for patients with moderate to severe SLE.
- Epratuzumab treatment reduced corticosteroid doses by clinically meaningful amounts in patients with moderate to severe SLE.
- Epratuzumab treatment resulted in clinically meaningful improvements in physician global assessments in patients with moderate to severe SLE.

Ann Rheum Dis. 2013 Nov;72(11):1786-92. doi: 10.1136/annrheumdis-2012-202322. Epub 2012 Nov 10.

Hydroxychloroquine in systemic lupus erythematosus: results of a French multicentre controlled trial (PLUS Study).

Costedoat-Chalumeau N[1], Galicier L, Aumaître O, Francès C, Le Guern V, Lioté F, Smail A, Limal N, Perard L, Desmurs-Clavel H, Boutin du LT, Asli B, Kahn JE, Pourrat J, Sailler L, Ackermann F, Papo T, Sacré K, Fain O, Stirnemann J, Cacoub P, Jallouli M, Leroux G, Cohen-Bittan J, Tanguy ML, Hulot JS, Lechat P, Musset L, Amoura Z, Piette JC; Group PLUS.

Collaborators (83)

Author information

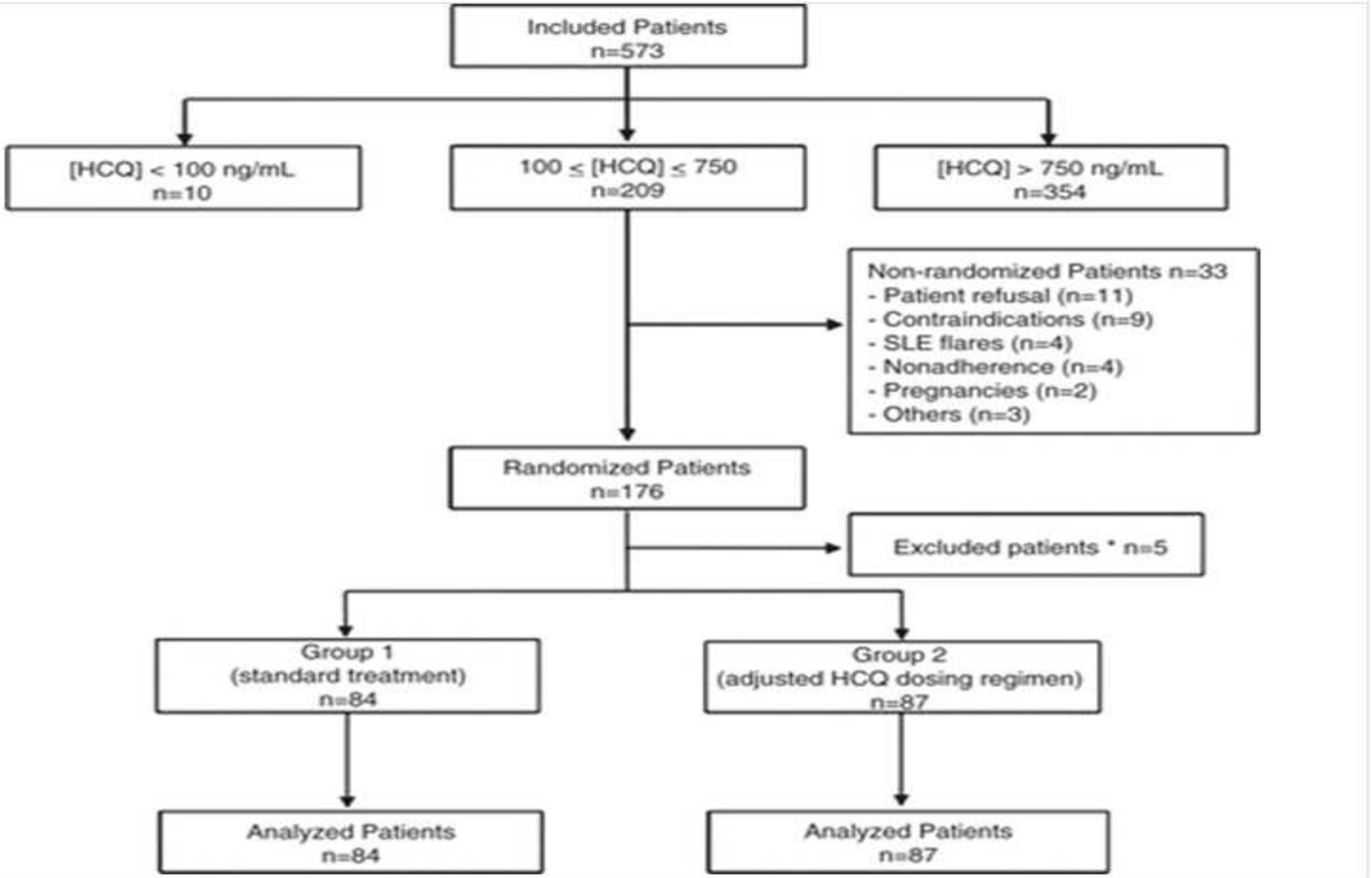
Abstract

INTRODUCTION: Hydroxychloroquine (HCQ) is an important medication for treating systemic lupus erythematosus (SLE). Its blood concentration ([HCQ]) varies widely between patients and is a marker and predictor of SLE flares. This prospective randomised, double-blind, placebo-controlled, multicentre study sought to compare standard and adjusted HCQ dosing schedules that target [HCQ] ≥1000 ng/ml to reduce SLE flares.

PATIENTS AND METHODS: [HCQ] was measured in 573 patients with SLE (stable disease and SELENA-SLEDAI≤12) treated with HCQ for at least 6 months. Patients with [HCQ] from 100 to 750 ng/ml were randomised to one of two treatment groups: no daily dose change (group 1) or increased HCQ dose to achieve the target [HCQ] (group 2). The primary end point was the number of patients with flares during 7 months of follow-up.

RESULTS: Overall, mean [HCQ] was 918±451 ng/ml. Active SLE was less prevalent in patients with higher [HCQ]. A total of 171 patients were randomised and followed for 7 months. SLE flare rates were similar in the two groups (25% in group 1 vs 27.6% in group 2; p=0.7), but a significant spontaneous increase in [HCQ] in both groups between inclusion and randomisation strongly suggested improved treatment adherence. Patients at the therapeutic target throughout follow-up tended to have fewer flares than those with low [HCQ] (20.5% vs 35.1%, p=0.12).

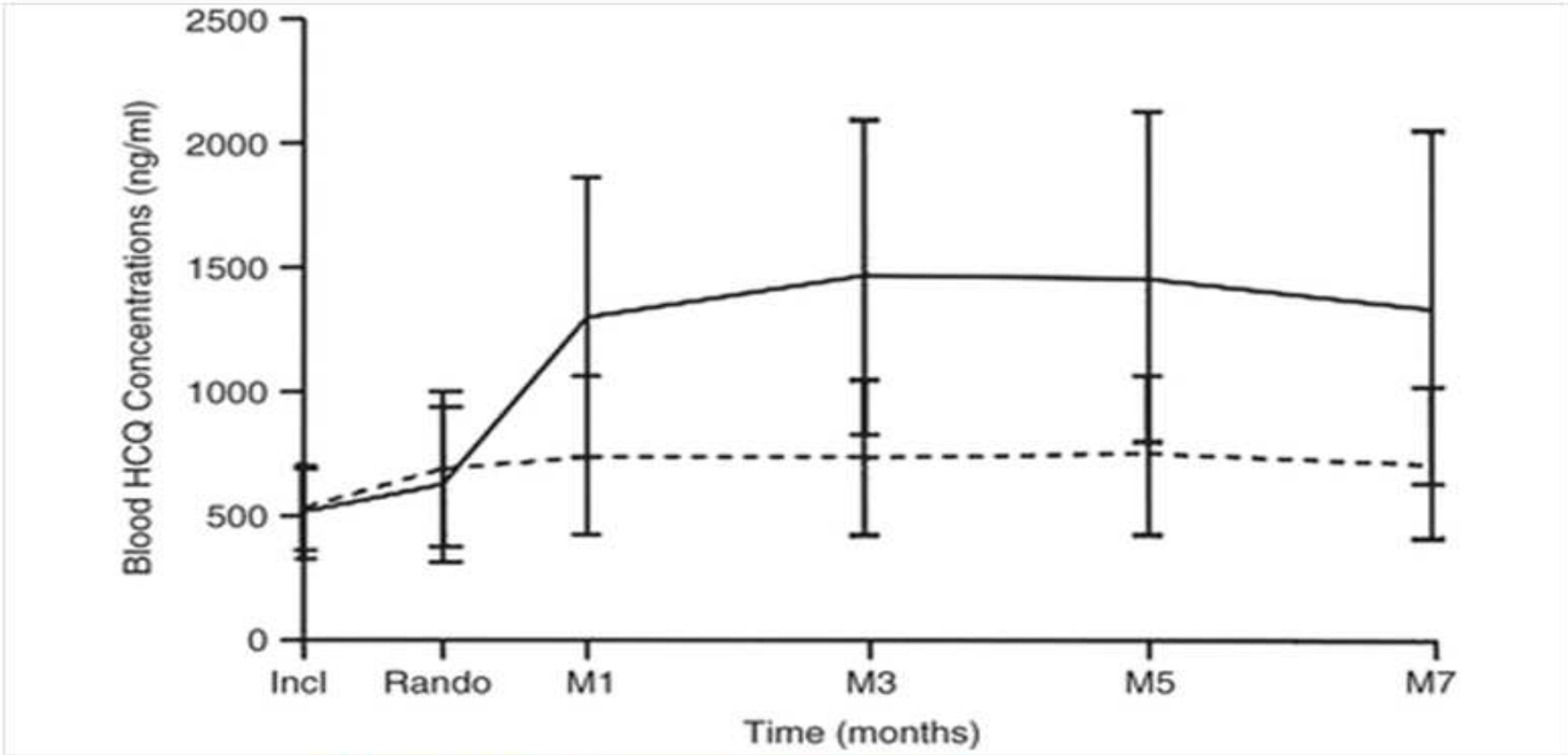
CONCLUSIONS: Although low [HCQ] is associated with higher SLE activity, adapting the HCQ dose did not reduce SLE flares over a 7-month follow-up.



View larger version: In a new window Download as PowerPoint Slide

Figure 1

Study flow chart. *Randomisation criteria were not met, and patients did not receive the study treatment. Group 1: standard treatment (no change in daily hydroxychloroquine (HCQ) dosage). Group 2: adjusted HCQ dosing regimen (to obtain a blood HCQ concentration of ≥1000 ng/ml).



View larger version: In a new window Download as PowerPoint Slide

Figure 2

Course of blood hydroxychloroquine concentrations (mean±SD) during the study in randomised patients. Incl, inclusion; Rando, randomisation; M1, month 1; M3, month 3; M5, month 5; M7, month 7; HCQ, hydroxychloroquine. The number of patients was 573 at inclusion and 171 patients at randomisation and after. Broken line, group 1 (standard treatment; n=84 patients); plain line, group 2 (adjusted HCQ dosing regimen to obtain a HCQ concentration of ≥1000 ng/ml; n=87 patients). Blood HCQ concentration increased significantly in both groups between inclusion and randomisation (before any therapeutic intervention). After randomisation, blood HCQ concentration was significantly higher in group 2.

Ann Rheum Dis. 2013 Nov;72(11):1830-5. doi: 10.1136/annrheumdis-2012-202460. Epub 2012 Nov 21.

Lupuzor/P140 peptide in patients with systemic lupus erythematosus: a randomised, double-blind, placebo-controlled phase IIb clinical trial.

Zimmer R[1], Scherbarth HR, Rillo OL, Gomez-Reino JJ, Muller S.

Author information

Abstract

OBJECTIVES: To evaluate treatment with the peptide-based agent, Lupuzor, in a double-blind, randomised, placebo-controlled study of patients with systemic lupus erythematosus.

METHODS: Patients who met ≥4 of the American College of Rheumatology criteria, had a score of ≥6 on the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) and did not have an A score on the British Isles Lupus Assessment Group (BILAG)-2004 scale were eligible. 149 intention-to-treat (ITT) patients were randomly assigned to receive Lupuzor (200 µg) subcutaneously every 4 weeks (n=49; group 1) or every 2 weeks (n=51; group 2) or placebo (n=49; group 3) in addition to standard of care (SOC). A target population (136 ITT patients) consisting of patients having a clinical SLEDAI score ≥6 at week 0 was considered. The clinical SLEDAI score is the SLEDAI-2K score obtained by omitting low complement and increased DNA binding components.

RESULTS: In the ITT overall population, 53.1% in group 1 (p=0.048), 45.1% in group 2 (p=0.18) and 36.2% in the placebo group achieved an SLE Responder Index (SRI) response at week 12. In the target population, the results were more impressive: 61.9% in group 1 (p=0.016), 48.0% in group 2 (p=0.18) and 38.6% in the placebo group achieved an SRI response at week 12. An interim analysis including 114 patients from the target population demonstrated an even better efficacy (according to SLEDAI score) in group 1 compared with placebo (67.6% vs 41.5% (p<0.025) at week 12 and 84.2% vs 45.8% (p<0.025) at week 24). The most common adverse event was a mild injection-site erythema.

CONCLUSIONS: Lupuzor/200 µg given three times at 4-week intervals during 12 weeks in addition to SOC is efficacious and generally well tolerated.

Ann Rheum Dis. 2014 Mar;73(3):557-66. doi: 10.1136/annrheumdis-2012-202315. Epub 2013 Feb 22.

Secondary analysis of APPLE study suggests atorvastatin may reduce atherosclerosis progression in pubertal lupus patients with higher C reactive protein.

Ardoin SP[1], Schanberg LE, Sandborg CI, Barnhart HX, Evans GW, Yow E, Mieszkalski KL, Ilowite NT, Eberhard A, Imundo LF, Kimura Y, Levy D, von Scheven E, Silverman E, Bowyer SL, Punaro L, Singer NG, Sherry DD, McCurdy DK, Klein-Gitelman M, Wallace C, Silver RM, Wagner-Weiner L, Higgins GC, Brunner HI, Jung L, Soep JB, Reed AM, Thompson SD; APPLE investigators.

Author information

Abstract

OBJECTIVE: Participants in the Atherosclerosis Prevention in Paediatric Lupus Erythematosus (APPLE) trial were randomised to placebo or atorvastatin for 36 months. The primary endpoint, reduced carotid intima medial thickness (CIMT) progression, was not met but atorvastatin-treated participants showed a trend of slower CIMT progression. Post-hoc analyses were performed to assess subgroup benefit from atorvastatin therapy.

METHODS: Subgroups were prespecified and defined by age (> or ≤15.5 years), systemic lupus erythematosus (SLE) duration (> or ≤24 months), pubertal status (Tanner score≥4 as post-pubertal or <4 as pre-pubertal), low density lipoprotein cholesterol (LDL) (≥ or <110 mg/dl) and high-sensitivity C reactive protein (hsCRP) (≥ or <1.5 mg/l). A combined subgroup (post-pubertal and hsCRP≥1.5 mg/l) was compared to all others. Longitudinal linear mixed-effects models were developed using 12 CIMT and other secondary APPLE outcomes (lipids, hsCRP, disease activity and damage, and quality of life). Three way interaction effects were assessed for models.

RESULTS: Significant interaction effects with trends of less CIMT progression in atorvastatin-treated participants were observed in pubertal (3 CIMT segments), high hsCRP (2 CIMT segments), and the combined high hsCRP and pubertal group (5 CIMT segments). No significant treatment effect trends were observed across subgroups defined by age, SLE duration, LDL for CIMT or other outcome measures.

CONCLUSIONS: Pubertal status and higher hsCRP were linked to lower CIMT progression in atorvastatin-treated subjects, with most consistent decreases in CIMT progression in the combined pubertal and high hsCRP group. While secondary analyses must be interpreted cautiously, results suggest further research is needed to determine whether pubertal lupus patients with high CRP benefit from statin therapy.

CLINICALTRIALSGOV IDENTIFIER: NCT00065806.

Table 4 Comparison of atorvastatin and placebo treatment effects on CIMT progression in subgroups defined by hsCRP

		hsCRP<1.5 mg/l			hsCRP≥1.5 mg/l		
CIMT measurements	Interaction p value	Progression rate of atorvastatin estimates (95% CI)	Progression rate of placebo estimates (95% CI)	p Value	Progression rate of atorvastatin estimates (95% CI)	Progression rate of placebo estimates (95% CI)	p Value
Mean–mean common	0.049	0.0015 (–0.0005 to 0.0035)	0.0011 (–0.0009 to 0.0031)	0.795	–0.0007 (–0.0036 to 0.0023)	0.0042 (0.0010 to 0.0075)	0.029
Mean–max	0.413	0.0025 (–0.0002 to 0.0052)	0.0043 (0.0016 to 0.0069)	0.357	0.0055 (0.0016 to 0.0094)	0.0102 (0.0059 to 0.0145)	0.117
Mean–mean	0.093	0.0025 (0.0007 to 0.0043)	0.0031 (0.0014 to 0.0049)	0.633	0.0041 (0.0015 to 0.0067)	0.0087 (0.0058 to 0.0115)	0.021
Mean–max common	0.710	0.0002 (–0.0028 to 0.0032)	–0.0004 (–0.0035 to 0.0026)	0.769	0.0013 (–0.0032 to 0.0057)	0.0021 (–0.0028 to 0.0070)	0.801
Mean–max internal	0.879	0.0047 (0.0001 to 0.0093)	0.0099 (0.0053 to 0.0146)	0.114	0.0174 (0.0107 to 0.0242)	0.0236 (0.0161 to 0.0311)	0.231
Mean–mean internal	0.919	0.0032 (0.0000 to 0.0064)	0.0057 (0.0025 to 0.0089)	0.277	0.0125 (0.0078 to 0.0171)	0.0154 (0.0102 to 0.0206)	0.412
Mean–max bifurcation	0.232	0.0039 (–0.0000 to 0.0079)	0.0061 (0.0021 to 0.0100)	0.445	0.0014 (–0.0044 to 0.0072)	0.0099 (0.0035 to 0.0163)	0.056
Mean–mean bifurcation	0.176	0.0028 (0.0003 to 0.0053)	0.0042 (0.0017 to 0.0068)	0.435	0.0030 (–0.0007 to 0.0067)	0.0089 (0.0048 to 0.0129)	0.035
Mean–max far wall	0.831	0.0028 (–0.0005 to 0.0061)	0.0063 (0.0030 to 0.0096)	0.143	0.0080 (0.0031 to 0.0128)	0.0105 (0.0051 to 0.0159)	0.489
Mean–mean far wall	0.858	0.0031 (0.0010 to 0.0052)	0.0052 (0.0031 to 0.0073)	0.155	0.0062 (0.0031 to 0.0093)	0.0089 (0.0055 to 0.0123)	0.258
Mean–max near wall	0.087	0.0019 (–0.0014 to 0.0053)	0.0013 (–0.0021 to 0.0047)	0.796	0.0026 (–0.0024 to 0.0076)	0.0097 (0.0042 to 0.0152)	0.062
Mean–mean near wall	0.011	0.0019 (–0.0005 to 0.0042)	0.0003 (–0.0020 to 0.0027)	0.370	0.0017 (–0.0018 to 0.0052)	0.0082 (0.0043 to 0.0120)	0.014

The interaction p value assesses differences in the progression rate for atorvastatin/placebo and subgroups.
The p values in the hsCRP<1.5 mg/l and hsCRP≥1.5 mg/l groups assess differences in the progression rate for atorvastatin/placebo groups.
CIMT, carotid intima media thickness; hsCRP, high sensitivity C reactive protein.

J Clin Invest. 2014 May 1;124(5):2234-45. doi: 10.1172/JCI73411. Epub 2014 Mar 25.

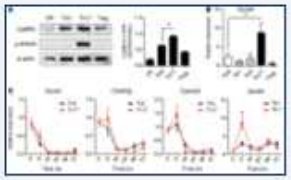
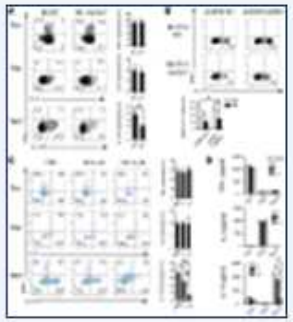
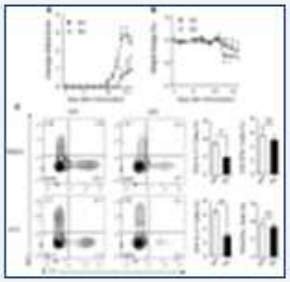
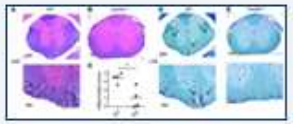
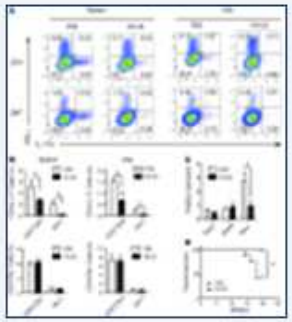
CaMK4-dependent activation of AKT/mTOR and CREM-α underlies autoimmunity-associated Th17 imbalance.

Koga T, Hedrich CM, Mizui M, Yoshida N, Otomo K, Lieberman LA, Rauen T, Crispín JC, Tsokos GC.

Abstract

Tissue inflammation in several autoimmune diseases, including SLE and MS, has been linked to an imbalance of IL-17-producing Th (Th17) cells and Tregs; however, the factors that promote Th17-driven autoimmunity are unclear. Here, we present evidence that the calcium/calmodulin-dependent protein kinase IV (CaMK4) is increased and required during Th17 cell differentiation. Isolation of naive T cells from a murine model of lupus revealed increased levels of CaMK4 following stimulation with Th17-inducing cytokines but not following Treg, Th1, or Th2 induction. Furthermore, naive T cells from mice lacking CaMK4 did not produce IL-17. Genetic or pharmacologic inhibition of CaMK4 decreased the frequency of IL-17-producing T cells and ameliorated EAE and lupus-like disease in murine models. Inhibition of CaMK4 reduced Il17 transcription through decreased activation of the cAMP response element modulator α (CREM-α) and reduced activation of the AKT/mTOR pathway, which is known to enhance Th17 differentiation. Importantly, silencing CaMK4 in T cells from patients with SLE and healthy individuals inhibited Th17 differentiation through reduction of IL17A and IL17F mRNA. Collectively, our results suggest that CaMK4 inhibition has potential as a therapeutic strategy for Th17-driven autoimmune diseases.

PMID: 24667640 [PubMed - indexed for MEDLINE] PMCID: PMC4001553 **Free PMC Article**

J Biol Chem. 2013 Nov 1;288(44):31880-7. doi: 10.1074/jbc.M113.508655. Epub 2013 Sep 18.

cAMP-responsive element modulator α (CREMα) trans-represses the transmembrane glycoprotein CD8 and contributes to the generation of CD3+CD4-CD8- T cells in health and disease.

Hedrich CM[1], Rauen T, Crispin JC, Koga T, Ioannidis C, Zajdel M, Kyttaris VC, Tsokos GC.

Author information

Abstract

T cell receptor-αβ(+) CD3(+)CD4(-)CD8(-) "double-negative" T cells are expanded in the peripheral blood of patients with systemic lupus erythematosus and autoimmune lymphoproliferative syndrome. In both disorders, double-negative T cells infiltrate tissues, induce immunoglobulin production, and secrete proinflammatory cytokines. Double-negative T cells derive from CD8(+) T cells through down-regulation of CD8 surface co-receptors. However, the molecular mechanisms orchestrating this process remain unclear. Here, we demonstrate that the transcription factor cAMP-responsive element modulator α (CREMα), which is expressed at increased levels in T cells from systemic lupus erythematosus patients, contributes to transcriptional silencing of CD8A and CD8B. We provide the first evidence that CREMα trans-represses a regulatory element 5' of the CD8B gene. Therefore, CREMα represents a promising candidate in the search for biomarkers and treatment options in diseases in which double-negative T cells contribute to the pathogenesis.

J Intern Med. 2014 Apr;275(4):398-408. doi: 10.1111/joim.12155. Epub 2013 Nov 22.

Autoimmune disorders and quadrivalent human papillomavirus vaccination of young female subjects.

Grimaldi-Bensouda L[1], Guillemot D, Godeau B, Bénichou J, Lebrun-Frenay C, Papeix C, Labauge P, Berquin P, Penfornis A, Benhamou PY, Nicolino M, Simon A, Viallard JF, Costedoat-Chalumeau N, Courcoux MF, Pondarré C, Hilliquin P, Chatelus E, Foltz V, Guillaume S, Rossignol M, Abenhaim L; PGRx-AID Study Group.

Collaborators (162)

Author information

Abstract

OBJECTIVES: The aim of this study was to investigate whether the quadrivalent human papillomavirus (HPV) vaccine Gardasil is associated with a change in the risk of autoimmune disorders (ADs) in young female subjects.

DESIGN: Systematic case-control study of incident ADs associated with quadrivalent HPV vaccination in young women across France.

PARTICIPANTS AND SETTING: A total of 113 specialised centres recruited (from December 2007 to April 2011) females aged 14-26 years with incident cases of six types of ADs: idiopathic thrombocytopenic purpura (ITP), central demyelination/multiple sclerosis (MS), Guillain-Barré syndrome, connective tissue disorders (systemic lupus erythematosus, rheumatoid arthritis/juvenile arthritis), type 1 diabetes mellitus and autoimmune thyroiditis. Control subjects matched to cases were recruited from general practice.

ANALYSIS: Multivariate conditional logistic regression analysis; factors included age, geographical origin, smoking, alcohol consumption, use of oral contraceptive(s) or vaccine(s) other than Gardasil received within 24 months before the index date and personal/family history of ADs.

RESULTS: Overall, 211 definite cases of ADs were matched to 875 controls. The adjusted odds ratio (OR) for any quadrivalent HPV vaccine use was 0.9 [95% confidence interval (CI) 0.5-1.5]. The individual ORs were 1.0 (95% CI 0.4-2.6) for ITP, 0.3 (95% CI 0.1-0.9) for MS, 0.8 (95% CI 0.3-2.4) for connective disorders and 1.2 (95% CI 0.4-3.6) for type 1 diabetes. No exposure to HPV vaccine was observed in cases with either Guillain-Barré syndrome or thyroiditis.

CONCLUSIONS: No evidence of an increase in the risk of the studied ADs was observable following vaccination with Gardasil within the time periods studied. There was insufficient statistical power to allow conclusions to be drawn regarding individual ADs.