

Ασθενής με Συστηματικό Ερυθηματώδη Λύκο χωρίς όργανο στόχο αλλά με υψηλό SLEDAI

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ΔΕΝ ΥΠΑΡΧΕΙ ΣΥΓΚΡΟΥΣΗ ΣΥΜΦΕΡΟΝΤΩΝ

ΠΕΡΙΕΧΟΜΕΝΑ ΠΑΡΟΥΣΙΑΣΗΣ

- Παρουσίαση κλινικής περίπτωσης
- Προβληματισμοί –κριτική αξιολόγηση
- Κατευθυντήριες οδηγίες
- Τ2Τ στον ΣΕΛ- Δείκτες παρακολούθησης
- Πρώιμη χρήση bDMARDS
- Take Home Messages

Παρουσίαση κλινικής περίπτωσης



- Άνδρας, 42
- Ελεύθερο α/α , πρόσφατο σύνδρομο λοιμώδους μονοπυρήνωσης
- Εμμονή κόπωσης, αρθραλγιών, δεκατικής πυρετικής κίνησης και εξάνθημα
- Εργαστηριακό φλεγμονώδες σύνδρομο-αναιμία
- ANA (1/640 πυρηνίων) ENA (SSA/Ro60+) C3,C4 ↓
- ACA, b2GPI IgG X2 Elisa

HCQ 400mg Prednisone 10mg Salospir 80mg

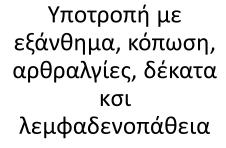
Παρουσίαση κλινικής περίπτωσης

Έναρξη **MTX** 10mg + Φολικό οξύ 5mg /εβδ

- Τιτλοποίηση δόσης
 ως 20mg (4+4 tb pos)
 - •δεν επιθυμεί inj sc

Προσθήκη CsA 50mg (1tb) Τιτλοποίηση δόσης ως 100mg (2tb pos)

Υπερτασικές αιχμέςδιακοπή CsA



Παρουσίαση κλινικής περίπτωσης



- Δεν επιθυμεί να τεθεί σε belimumab
- Παραμένει σε Pz 5-15mg χωρίς ύφεση και MTX +HCQ
- Alprazolame+
 Duloxetine

Προβληματισμοί

- Γιατί δεν μπήκε ποτέ σε ύφεση; Παίζει ρόλο η ορολογική ενεργότητα;
- Εχει damage παρολο που δεν έχει όργανο στόχο-τι φταίει;
- Τι θα μπορούσαμε να κάνουμε διαφορετικά;

Κατευθυντήριες οδηγίες

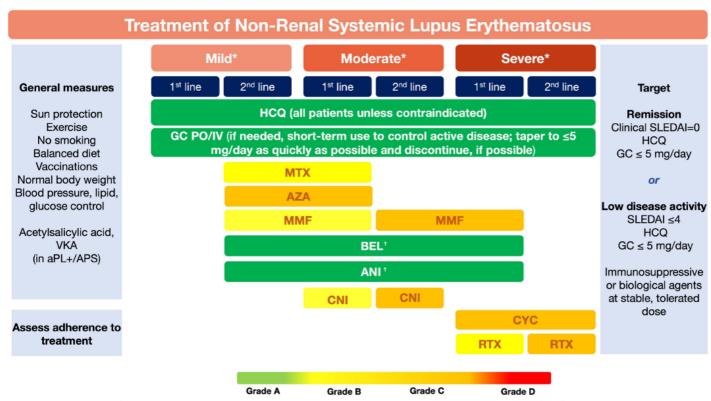
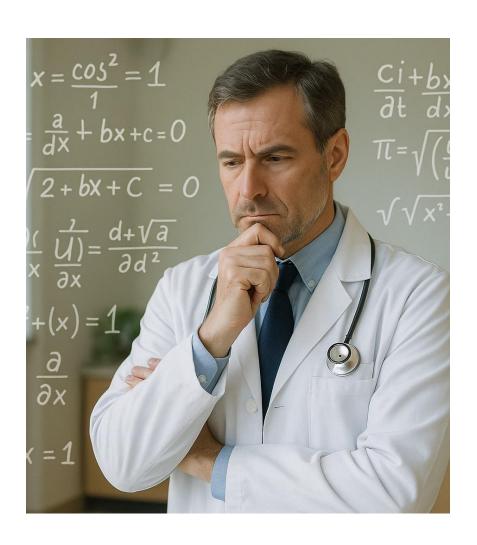


Figure 1 Treatment of non-renal systemic lupus erythematosus. Top-to bottom sequence does not imply order of preference (eg, MTX, AZA and MMF are equal options for second-line therapy in mild disease or first-line therapy in moderate disease). *Mild disease: constitutional symptoms; mild arthritis; rash ≤9% body surface area; platelet count (PLTs) 50–100 × 10⁹/L; SLEDAI≤6; BILAG C or ≤1 BILAG B manifestation. *Moderate disease: moderate—severe arthritis ('RA-like'; rash 9%–18% BSA; PLTs 20–50×10⁹/L; serositis; SLEDAI 7–12; ≥2 BILAG B manifestations). *Severe disease: major organ threatening disease (cerebritis, myelitis, pneumonitis, mesenteric vasculitis); thrombocytopenia with platelets<20×10⁹/L; TTP-like disease or acute haemophagocytic syndrome; rash>18% BSA SLEDAI>12; ≥1 BILAG A manifestations. †Recommendation of belimumab and anifrolumab as first-line therapy in severe disease refers to cases of extrarenal SLE with non-major organ involvement, but extensive disease from skin, joints, and so on. The use of anifrolumab as add-on therapy in severe disease refers mainly to severe skin disease. For patients with severe neuropsychiatric disease, anifrolumab and belimumab are not recommended. ANI, anifrolumab; aPL, antiphospholipid antbodies; APS, antiphospholipid syndrome; AZA, azathioprine; BEL, belimumab; BILAG, British Isles Lupus Assessment Group; CNI, calcineurin inhibitor; CYC, cyclophosphamide; GC, glucocortocoids; HCQ, hydroxychloroquine; IV, intravenous; MMF, mycophenolate mofetil; MTX, methotrexate; PO, per os; RTX, rituximab; SLEDAI, SLE Disease Activity

Δείκτες παρακολούθησης



- ΣΕΛ → μεγάλη ετερογένεια
- Δείκτες
 παρακολούθησης →
 δύσκολοι και
 περίπλοκοι;

Δείκτες παρακολούθησης

Instrument	Description	Example of typical use	
Disease activity			
SLE disease activity index (SLEDAI) with versions including the SELENA-SLEDAI and SLEDAI-2K	Composite weighted global activity score based on the presence or absence of 24 manifestations that are attributable to active SLE	Most common instrument used in observational research Used in clinical trials as part of composite efficacy endpoints Feasible for clinical practice	
British Isles Lupus Assessment Group (BILAG) with versions including the BILAG-2004 and easy-BILAG	Organ-based index grading disease activity in nine different organ systems	Used in clinical trials as part of composite efficacy endpoints Use in observational research and clinical practice limited by its complexity, however the Easy-BILAG may address this limitation	
Physician global assessment (PGA)	Clinician rating of global disease activity on a 0–3 visual analogue scale	Used in observational research and clinical trial endpoints, typically alongside other activity measures Feasible for use in clinical practice	
Cutaneous lupus activity and severity index (CLASI)	Organ-specific measure assessing mucocutaneous disease activity (and damage)	Used in clinical trials and observational research specifically for mucocutaneous lupus Feasible for use in clinical practice	
Flare			
SELENA-SLEDAI flare index (SFI)	Defines severe and mild/moderate flares based on changes in SLEDAI and other criteria	Used in observational research and clinical trials Feasible for use in clinical practice	
BILAG flare index	Definitions of severe, moderate, and mild flares derived from the organ-based grading of the BILAG	Used in clinical trials Use in observational research and clinical practice limited by the complexity of the BILAG	
Treat to target state			
Lupus low disease activity state (LLDAS)	Target disease state based on SLEDAI, PGA and medication criteria	Increasingly used in observational research, clinical trials, and clinical practice	
DORIS remission	More stringent target disease state based on SLEDAI, PGA and medication criteria	Increasingly used in observational research, clinical trials, and clinical practice	
Treatment response			
SLE responder index (SRI)	Defines improvement based on reduction in SLEDAI with no worsening of BILAG or PGA	Used in clinical trials as a primary or secondary efficacy endpoint Not typically used in clinical practice or observational research	
BILAG-based composite lupus assessment (BICLA)	Defines improvement based on improvement in BILAG organ grades with no worsening of SLEDAI or PGA	Used in clinical trials as a primary or secondary efficacy endpoint Not typically used in clinical practice or observational research	
Renal response	Various definitions based on reduction in proteinuria with no worsening of renal function	Used in clinical trials, observational research and clinical practice specifically for lupus nephritis	

Δείκτες παρακολούθησης



► ACR Open Rheumatol. 2022 Aug 12;4(10):923–930. doi: 10.1002/acr2.11451 🗷

External Validation of the Lupus Multivariable Outcome Score for Systemic Lupus Erythematosus Trials

Michal Abrahamowicz ¹, Maria Izabela Abrahamowicz, Peter E Lipsky ^{2,™}

► Author information ► Article notes ► Copyright and License information PMCID: PMC9555192 PMID: 35962577

Abstract

Objective

Development of new systemic lupus erythematosus (SLE) treatments requires an effective responder index. Toward this end, we have recently developed a new Lupus Multivariable Outcome Score (LuMOS) to optimize discrimination between actively treated patients and those on placebo. We now report on external validation of LuMOS in two independent clinical trials.

Observational Study > Ann Rheum Dis. 2021 Dec;80(12):1568-1574. doi: 10.1136/annrheumdis-2021-220363. Epub 2021 Aug 18.

Systemic Lupus Erythematosus Disease Activity Score (SLE-DAS) enables accurate and user-friendly definitions of clinical remission and categories of disease activity

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Affiliations + expand

PMID: 34407927 DOI: 10.1136/annrheumdis-2021-220363
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Abstract

SDI

Table 1 SLICC SLE damage index. Damage (non-reversible change, not related to active inflammation) occurring since onset of lupus, ascertained by clinical assessment and present for at least 6 months unless otherwise stated. Repeat episodes mean at least 6 months apart to score 2. The same lesion cannot be scored twice

llem	Score	
Ocular (Either eye, by clinical assessment)		
Any cataract ever	1	
Retinal change OR optic atrophy	1	
Neuropsychiatric		
Cognitive impairment (e.g. memory deficit, difficulty with calculation, poor concentration, difficult in spoken or written language, impaired performance level)	1	
DR major psychosis	1	
Seizures requiring therapy for 6 months	1	
Cerebral vascular accident ever (score 2 if 1) OR resection not for malignancy	1	
Cranial OR peripheral neuropathy (excluding optic)	1	
Fransverse myelitis	1	
Renal	_	
Estimated or measured GFR < 50%	1	
Proteinuria 24 h ≥ 3.5 g OR	1	
End-stage renal disease (regardless of dialysis or transplantation)	3	
Pulmonary		
Pulmonary hypertension (right ventricular prominence, or loud P2)	1	
Pulmonary fibrosis (physical and X-ray)	1	
Shrinking lung (X-ray) Pleural fibrosis (X-ray)	i	
Pulmonary infarction (X-ray) OR resection not for malignancy	i	
unionaly infaction (x-ray) OK resection for for manginancy	i	
Cardiovascular		
Angina OR coronary artery bypass	1	
Myocardial infarction ever (score 2 if > 1)	i	
Cardiomyopathy (ventricular dysfunction)	i	
Valvular disease (diastolic murmur, or a systolic murmur > 3/6)	1	
Pericarditis × 6 months, OR pericardiectomy	1	
Peripheral Vascular		
Claudication × 6 months	1	
Minor tissue loss (pulp spae)	1	
Significant tissue loss ever (e.g. loss of digit or limb) (Score 2 if > one site)	1	
Venous thrombosis with swelling, ulceration, OR venous stasis	1	
Gastrointestinal		
nfarction or resection of bowel below duodenum, spleen, liver or gall bladder ever, for whatever cause (score 2 if > one site)	1	
Mesenteric insufficiency	1	
Chronic peritonitis	1	
Stricture OR upper gastrointestinal tract surgery ever	1	
ancreatitis: insufficiency requiring enzyme replacement or with pseudocyst	1	
Musculoskeletal		
Muscle atrophy or weakness	1	
Deforming or erosive arthritis (including reducible deformities, excluding avascular necrosis)	1	
Osteoporosis with fracture or vertebral collapse (excluding avascular necrosis) Avascular necrosis (score 2 of > 1)	1	
Steomyelitis	i	
Augusted tendon	i	
kin		
isani Scarring chronic alopecia	1	
Extensive scarring or panniculum other than scalp and pulp space	i	
Skin ulceration (not due to thrombosis) for more than 6 months	i	
Premature gonodal failure	i	
Diabetes (regardless of treatment)	i	
Malignancy (exclude dysplasia) (score 2 if > one site)	i	
6	2	

T2T

Box 1 | Definitions of SLE targets for remission and low disease activity

Remission has been endorsed as the long-term target to achieve in systemic lupus erythematosus (SLE), and Low Lupus Disease Activity State (LLDAS) might represent a suitable intermediate target, at least in the medium term.

DORIS definition:

- Clinical SLE Disease Activity Index (cSLEDAI) = 0
- Physician's global activity (PGA) (scale 0-3) score <0.5
- Irrespective of serology
- The patient may be on antimalarial, low-dose glucocorticoids (prednisolone <5 mg daily) and/or stable immunosuppressive drugs including biologics

LLDAS definition:

- SLEDAI 2000 (SLEDAI-2K) score ≤4, with no activity in major organ systems (including renal, central nervous system, cardiopulmonary, vasculitis and fever)¹⁸ and no haemolytic anaemia or gastrointestinal activity
- No new features of lupus disease activity (according to SLEDAI-2K) compared with the previous assessment
- SELENA SLEDAI-PGA (scale 0-3) score ≤1
- Current prednisolone (or equivalent) dose ≤7.5 mg daily
- Well-tolerated standard maintenance doses of immunosuppressive drugs and approved biological agents

DORIS, Definition of Remission in SLE.

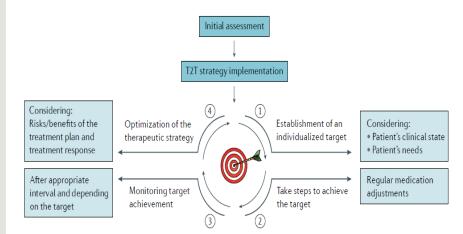


Fig. 1 | Treat-to-target therapeutic strategy for treatment of systemic lupus erythematosus. The proposed treat-to-target (T2T) therapeutic strategy can be summarized in four key sequential steps: first, establish a relevant individualized target; second, take steps to achieve that target; third, monitor if the target has been achieved after an appropriate interval; and fourth, adjust the therapy if the target is not attained. Decision-making regarding therapy adjustments should be based on the assessment of the disease, the physician's judgement, the risk/benefit ratio of the treatment plan and the patients' view of their own disease ²⁸⁻²⁸.

T2T

- Υπέρταση , διαβήτης, υπερουριχαιμία ,
- Ρευματοειδής Αρθρίτιδα
- Μείωση θνητότητας, νοσηρότητας, αποφυγή εξάρσεων και τοξικότητα από θεραπεία, βελτίωση ποιότητας ζωής
- LLDAS μέσα στους πρώτους 3 μήνες → μείωση ανθεκτικών υποτροπών μακροπρόθεσμα
- Ήπιες προς μέτριες βλεννογονοδερματικές υποτροπές σε ασθενείς με δερματική προσβολή >> χαμηλά ποσοστά ύφεσης/ LLDAS

Κορτικοστεροειδή και ΣΕΛ

Side effects based on dose and treatment duration.

Low Doses (<5-7.5)			High Doses		
Early (<6 Months)	Long-Term (>6 Months)	Immediate Pulses	Early (<6 Months)	Long-Term (>6 Months)	
Osteoporosis	Cataracts	Acute vascular events	Cardiovascular and cerebrovascular events	• Infections	
 Hyperglycemia 	• Psychiatric disorders	Hyperglycemia	Avascular necrosis	• Cushingoid features	
• Cushing syndrome	 Osteoporosis 	• Hypertension,	Myopathy	• Insulin resistance	
 Hypertension 	• Infections	• Avascular necrosis	Mood disorders	 Osteoporosis 	
• Glaucoma	• Cardiovascular disease	• Psychosis	Psychiatric disorders	• Cataracts	
• Psychiatric disease	 Dermatological 		• Insulin resistance	• Glaucoma	
• Sleep disorders			Dyslipidemia	 Dermatological 	
 Dermatological 			Glaucoma	• Infections	
			Osteoporosis	Dyslipidemia	
			Dermatological	• Hypertension	

Ορολογική ενεργότητα- σημασία

The association between lupus serology and disease outcomes: A systematic literature review to inform the treat-to-target approach in systemic lupus erythematosus



Abstract

Introduction

Serological markers such as anti-double stranded (ds)DNA antibodies and complement fractions C3/C4, are integral components of disease activity assessment in patients with systemic lupus erythematosus (SLE). However, it remains uncertain whether treatment should aim at restoration of serological abnormalities.

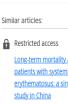
Objectives

To analyze and critically appraise the literature on the prognostic impact of active lupus serology despite clinical disease quiescence.

Methods

A systematic literature review was performed in PubMed and EMBASE using the PICOT(S) (population, index, comparator, outcome(s), timing, setting) system to identify studies evaluating the association of serum anti-dsDNA, C3 and C4 levels assessed at the time of clinical remission or during the disease course, against the risk for impending flares and organ damage. Risk of bias was determined by the Quality in Prognosis Studies





Results

Fifty-three studies were eligible, the majority having moderate (70.6%) or high (11.8%) risk of bias and not adequately controlling for possible confounders. C3 hypocomplementemia during stable/inactive disease was associated with increased risk (2.0 to 3.8-fold) for subsequent flare in three out of seven relevant studies. Three out of four studies reported a significant effect of C4 hypocomplementemia on flare risk, including one study in lupus nephritis (likelihood ratio-positive 12.0). An increased incidence of flares (2.0 to 2.8-fold) was reported in 11 out of 16 studies assessing the prognostic effect of high anti-dsDNA, and similarly, the majority of studies yielded significant relationships with renal flares. Six studies examined the effect of combined (rather than individual) serological activity, confirming the increased risk (2.0 to 2.7-fold) for relapses. No consistent association was found with organ damage.

Conclusion

Notwithstanding the heterogeneity and risk of bias, existing evidence indicates a modest association between abnormal serology and risk for flare in patients with stable/inactive SLE. These findings provide limited support for inclusion of serology in the treat-to-target approach but rationalize to further investigate their prognostic implications especially in lupus nephritis.

Early bDMARD use

Lupus



ORIGINAL RESEARCH

Analysis of belimumab prescription and outcomes in a 10-year monocentric cohort: is there an advantage with early use?

Chiara Tani 0, 1,2 Dina Zucchi 0, 1,2 Chiara Cardelli 0, 1 Elena Elefante 0, 1 Viola Signorini, Davide Schilirò, Giancarlo Cascarano, Luca Gualtieri, Anastasiya Valevich, 1 Giulia Puccetti, 1 Linda Carli, 1 Chiara Stagnaro, 1 Marta Mosca¹

To cite: Tani C. Zucchi D. Cardelli C, et al. Analysis of belimumab prescription and outcomes in a 10year monocentric cohort: is there an advantage with early use?. RMD Open rmdopen-2023-003981

CT and DZ contributed equally.

Received 7 December 2023 Accepted 19 March 2024

Objective The objective is to evaluate perscriptions of belimumab (BEL), how these have changed over the years and their impact on clinical outcomes in patients with systemic lupus erythematosus (SLE)

Methods This is a retrospective analysis of prospectively 2024;10:e003981. doi:10.1136/ collected data. We retrieved demographic and clinical data and concomitant therapies at BEL starting (baseline). Disease activity was assessed at baseline and after 6 and 12 months and organ damage at baseline and at the last

> Results From 422 patients followed in the Pisa SLE cohort, 102 patients received BEL and were included and 22 (21.6%) were immunosuppressant (IS)-naïve. Lupus Low Disease Activity State (LLDAS) with a glucocorticoid (GC) dosage ≤5 mg/day (LLDAS5) and remission were achieved by 47% and 38% of patients at 6 months, and by 75% and 66% at 12 months. Comparing IS-naïve patients with those who received BEL after at least one conventional IS, we did not find significant differences in baseline characteristics and in the achievement of LLDAS5 and remission. Despite at baseline we did not observe significant differences in mean GC daily dosage, IS-naïve patients were taking a significantly lower GC daily dose at 6 and 12 months. Interestingly, IS-naïve patients were more common in the most recent years.

> Conclusions Our data confirm that BEL is effective in controlling disease activity, and in recent years BEL has been considered as an earlier treatment option before other IS. Early introduction of BEL can be at least as effective as a step-up approach and can help to reduce the

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ More than 10 years have passed since the approval of belimumab (BEL) for systemic lupus erythematosus (SLE), and data on real-life use of this drug are more and more emerging. However, little is known on the early use of biological drugs in extrarenal manifestations, especially in immunosuppressant (IS)-naïve patients.

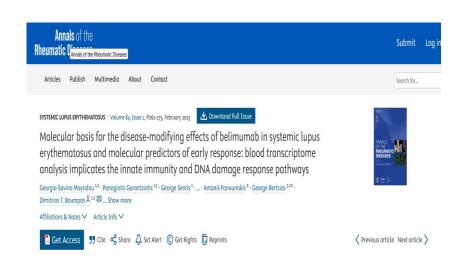
WHAT THIS STUDY ADDS

- ⇒ The approach to treatment with BEL seems to have changed over the years, as in the first years BEL was prescribed mainly to patients with a refractory disease treated with more than one IS drug, while in the most recent years it has been considered as an earlier treatment option before other ISs.
- ⇒ In our cohort, we did not observe significant differences in response between patients treated or not treated with conventional IS drugs before BEL, but in IS-naïve patients we observed a significant glucocorticoid (GC) sparing effect at 6 and 12 months with respect to the other patients.

HOW THIS STUDY MIGHT AFFECT RESEARCH. PRACTICE OR POLICY

⇒ These data suggest that BEL is effective in controlling disease activity and reducing the daily dose of GCs in SLE, and can be considered as an early treatment option before conventional IS.

conventional immunosuppressants (IS) and



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Early bDMARD use

ARTICLES · Volume 6, Issue 11, E751-E761, November 2024



Attainment of remission and low disease activity after treatment with belimumab in patients with systemic lupus erythematosus: a post-hoc analysis of pooled data from five randomised clinical trials

Ioannis Parodis, MD a.b. Julius Lindblom, MD a. Prof Roger A Levy, MD 2 Margherita Zen, MD d. Nursen Cetrez, MD a. Alvaro Gomez, MD a · et al. Show more

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Summary

Background

Disease remission or low disease activity are key treatment targets for patients with systemic lupus erythematosus (SLE). Pivotal trials of belimumab were conducted before the introduction of these targets. In this study, we aimed to pool data across trials to assess attainment of remission and low disease activity in a large, racially and culturally diverse patient population with SLE.

Methods

In this integrated post-hoc analysis, we pooled data from five phase 3 trials of belimumab (BLISS-76 [NCT00410384], BLISS-52 [NCT00424476], BLISS-NEA [NCT01345253], BLISS-SC [NCT01484496], and EMBRACE [NCT01632241]), in patients with active, autoantibody-positive SLE. Patients were randomly assigned to receive belimumab (10 mg/kg per month intravenously or 200 mg per week subcutaneously) or placebo, plus standard therapy. The proportion of patients with Definitions of Remission in SLE (DORIS) remission and lupus low disease activity state (LLDAS) were analysed every 4 weeks from week 4 to week 52 for belimumab versus placebo, using modified Poisson regression adjusted for trial variance, in all patients and in subgroups per baseline SLE Disease Activity Index-2000 score (<10 or ≥10); anti-double stranded DNA positivity (yes or no); low complement 3 (C3) or C4 levels (yes or no); anti-dsDNA positivity or low C3 or C4 levels (yes and no); prednisone-equivalent dose (\leq 7.5 mg per day or >7.5 mg per day); antimalarial use (yes or no); and by race (Black African ancestry or African American, Asian, Indigenous American, or White).

Findings

Data for 3086 patients (1869 in the belimumab group and 1217 in the placebo group) were analysed. 2913 (94%) of 3086 patients were women and 173 (6%) were men, and the median age was 36 years (IQR 28-45). The proportion of patients with DORIS remission was significantly higher in the belimumab group than the placebo group at weeks 28, 48, and 52 (week 52: 148 [8%] of 1869 participants vs 68 [6%] of 1217 participants; risk ratio 1·51 [95% CI 1·15-1·99]; p=0·0055). The proportion of patients who attained LLDAS was higher in the belimumab group than the placebo group at weeks 8, 24, 32-52 (week 52: 322 [17%] of 1869 participants vs 125 [10%] of 1217 participants; 1.74 [1.44-2.12]; p<0.0001). A higher proportion of patients had DORIS remission at week 52 in the belimumab group than the placebo group among all baseline subgroups denoting high disease activity, with the exception of those on a prednisone-equivalent dose higher than 7.5 mg per day in whom there was no difference for DORIS remission with belimumab versus placebo. The proportion of patients with LLDAS was significantly higher among patients in the belimuab group than those who received placebo from week 44 in all baseline subgroups denoting high disease activity or earlier in some subgroups, and the differences were maintained at week 52.

Interpretation

In adults with active SLE, belimumab plus standard therapy yielded greater benefit than placebo plus standard therapy in attaining DORIS remission (for which low rates were attained in both groups) and LLDAS, with differences observed as early as week 28 for DORIS remission and week 8 for LLDAS.

Τ2Τ- Ποιότητα ζωής





Impact of disease activity patterns on health-related quality of life (HRQoL) in patients with systemic lupus erythematosus (SLE)

Elena Elefante ¹ , Luca Gualtieri, Davide Schilirò, Chiara Stagnaro, Viola Signorini, Dina Zucchi ¹ , Chiara Cardelli ¹ , Linda Carli, Francesco Ferro, Chiara Tani, Marta Mosca

- συνολική πορεία της νόσου και όχι τόσο η ενεργότητα σε στιγμιότυπα
- Ήπιες εκδηλώσεις vs βλάβη οργάνου στόχου
 - Μακροχρόνια ύφεση) δεν βελτιώνει την καταθλιψη , την κόπωση, την λειτουργικότητα
- Ολιστική προσέγγιση;

Treat-to-target and shared decision-making in systemic lupus erythematosus from the patients' perspective: results from an international patient survey

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Abstract Objective

Treat-to-target (T2T) is being recognised as a promising concept to significantly improve the outcomes of patients with systemic lupus erythematosus (SLE). Despite its success being closely tied to patients' involvement, the patients' perspective regarding T2T has not been evaluated. We aimed to investigate patients' attitude towards T2T and their involvement in treatment decisions.

Take home messages

- Μη προσβολή οργάνου στόχου όχι απαραίτητα καλή πορεία νόσου
- Μείωση των κορτικοστεροειδών στα 5mg PZ ή και διακοπή το συντομότερο
- Τακτική παρακολούθηση με SLEDAI-2K/PGA και μια φορά ετησίως SDI
- Συμμετοχή του ασθενούς στο θεραπευτικό πλάνο
- Πρώιμη χορήγηση bDMARD → Επίτευξη πρώιμης ύφεσης

Zac euxaplotá