Η εφαρμογή των επικαιροποιημένων συστάσεων EULAR στην κλινική πράξη

Γιατί είναι σημαντική η έγκαιρη παρέμβαση με βιολογικό παράγοντα στον ΣΕΛ;

Ανδρέας Μπούνας

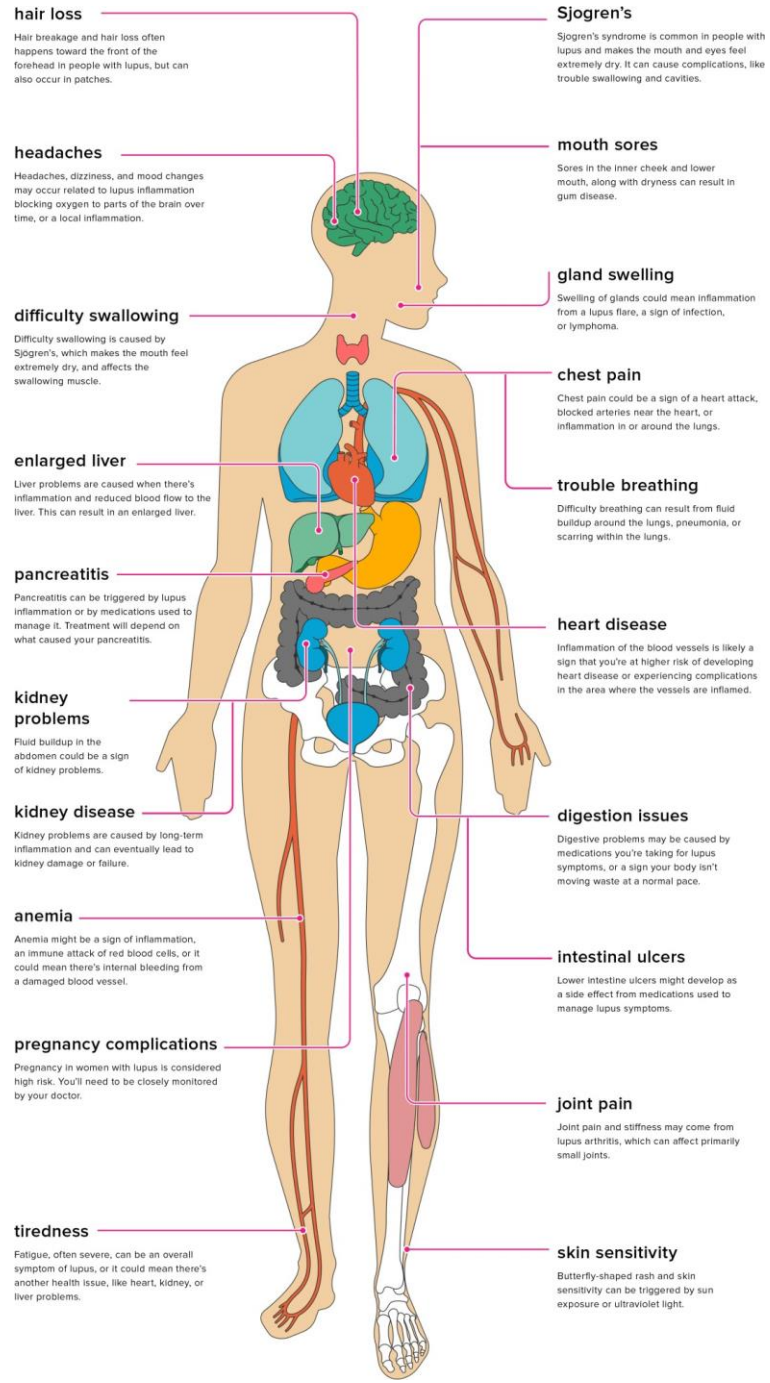
ΣΥΓΚΡΟΥΣΗ ΣΥΜΦΕΡΟΝΤΩΝ

- **Speaker/ Consaltant of [last 2 years]:**
  Abbvie, Aenorasis, Amgen, Bausch Health, FARAN, Genesis Pharma, GSK, Janssen, MSD, Novartis, Pfizer, UCB

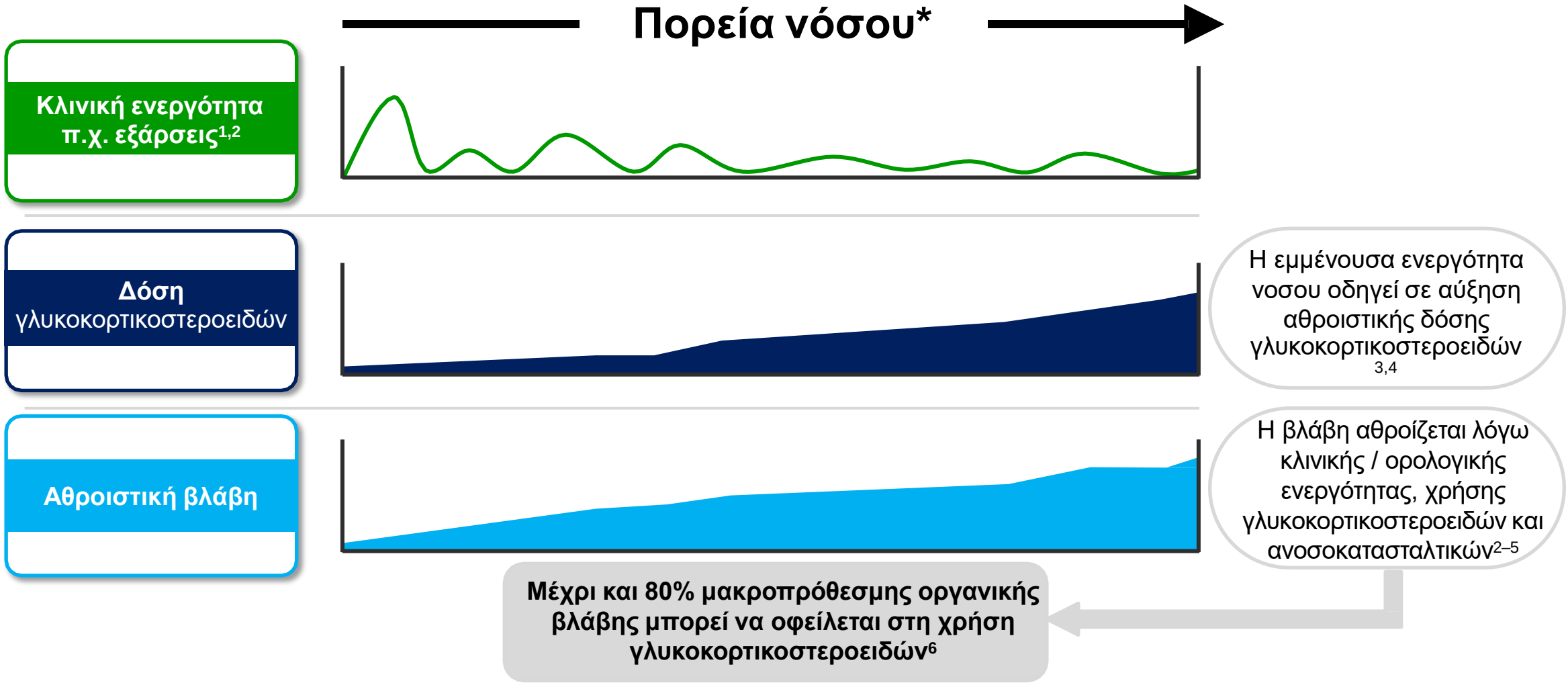
  Grant/ research support from:
  Abbvie, Amgen, Genesis , MSD, Novartis, Pfizer

- Για τη συγκεκριμένη ομιλία έχω λάβει τιμητική αμοιβή από την GSK

SYSTEMIC LUPUS ERYTHEMATOSUS



Η οργανική βλάβη στο ΣΕΛ προκαλείται από την εμμένουσα ενεργότητα της νόσου και από την αθροιστική δόση των κορτικοστεροειδών

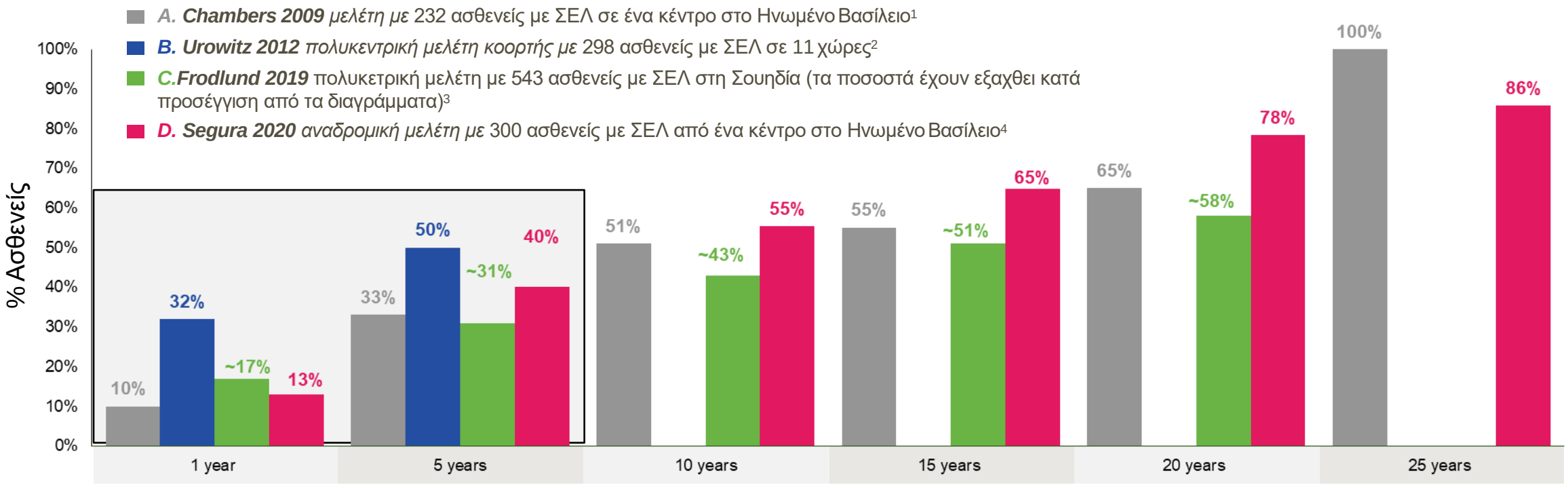


* Η γραφική παράσταση είναι αναπαράσταση υποθετικής πορείας ασθενούς με Συστηματικό Ερυθηματώδη Λύκο

1. Petri M, et al. J Rheumatol 2009;36:2476–2480; 2. Petri M, et al. Arthritis Rheum 2012;64:4021–4028;
3. ACR Ad Hoc Committee on SLE Guidelines. Arthritis Rheum 1999;42:1785–1796;
4. Thamer M, et al. J Rheumatol 2009;36:560–564;
5. Legge A, et al. J Rheumatol 2016;43:1050–1056; 6. Gladman DD, et al. J Rheumatol 2003;30:1955–1959.

Η οργανική βλάβη στον ΣΕΛ μπορεί να εμφανιστεί **μέσα σε ένα χρόνο από τη διάγνωση** και μέχρι και στο **50% των ασθενών στα 5 χρόνια** παρά τη θεραπεία

Ποσοστό ασθενών με ΣΕΛ με μόνιμη οργανική βλάβη (SDI > 0)



Μελέτες από διαφορετικές κοορτές που συμπεριλαμβάνονται στο ίδιο διάγραμμα για επεξηγηματικούς λόγους μόνο

SDI = SLICC (Systemic Lupus International Collaborating Clinics)/ACR (American College of Rheumatology) Damage Index; SLE = systemic lupus erythematosus.

1. Chambers SA, et al. Rheumatology. 2009;48(6):673–675. 2. Urowitz MB, et al. Arthritis Care Res. 2012;64(1):132–137. 3. Frodlund M, et al. Lupus. 2019;28(10):1261–1272. 4. Segura BT, et al. Rheumatology. 2020;59(3):524–533.

BMJ Open

Association between organ damage and mortality in systemic lupus erythematosus: a systematic review and meta-analysis

Irene B Murimi-Worstell,[1,2] Dora H Lin,[3] Henk Nab,[4] Hong J Kan,[5] Oluwadamilola Onasanya,[2,6] Jonothan C Tierce,[1,2] Xia Wang,[7] Barnabas Desta,[7] G Caleb Alexander,[1,2,8] Edward R Hammond[7]

To cite: Murimi-Worstell IB, Lin DH, Nab H, *et al*. Association between organ damage and mortality in systemic lupus erythematosus: a systematic review and meta-analysis. *BMJ Open* 2020;**10**:e031850. doi:10.1136/bmjopen-2019-031850

► Prepublication history and additional material for this

ABSTRACT

Objective At least half of patients with systemic lupus erythematosus (SLE) develop organ damage as a consequence of autoimmune disease or long-term therapeutic steroid use. This study synthesised evidence on the association between organ damage and mortality in patients with SLE.

Design Systematic review and meta-analysis.

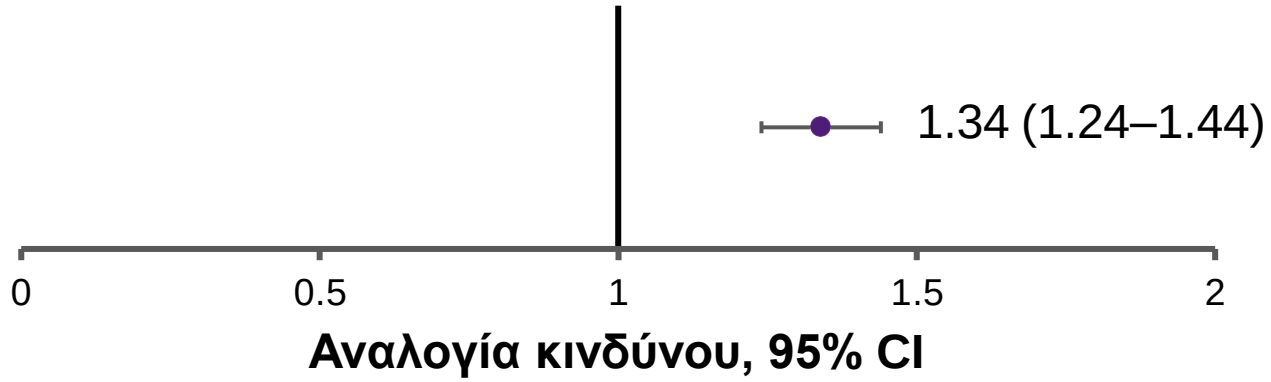
Methods Electronic searches were performed in PubMed, Embase, Cochrane Library and Latin

Strengths and limitations of this study

- We report a systematic review with meta-analysis of high-quality studies across four continents that demonstrates a consistent association between systemic lupus erythematosus (SLE)-related organ damage and increased mortality.
- To our knowledge, this is the first meta-analysis informed by a systematic literature review investigating the association between organ damage, assessed

Η βαθμολογία SDI > 0 αυξάνει τον κίνδυνο θανάτου, με σημαντική μείωση της επιβίωσης σε ασθενείς με πρώιμη οργανική βλάβη

Συγκεντρωτική αναλογία κινδύνου από μία μετα-ανάλυση 10 μελετών που αναφέρουν τον κίνδυνο θανάτου ανά 1 μονάδα αύξηση στη βαθμολογία SDI[1]



34%

Αύξηση στον κίνδυνο θανάτου για κάθε 1 επιπλέον μονάδα στη βαθμολογία SDI
(*P* < 0.001)

Μία άλλη μελέτη έδειξε ότι σε σύγκριση με ασθενείς χωρίς πρώιμη οργανική βλάβη (SDI = 0), όσοι είχαν πρώιμη οργανική βλάβη (SDI > 0) είχαν σημαντικά χαμηλότερο ποσοστό επιβίωσης στα 10 έτη παρακολούθησης[2]

263 ασθενείς με ΣΕΛ που εντάχθηκαν 1 χρόνο μετά τη διάγνωση

Τουλάχιστον 10 έτη πρακολούθησης

Η μελέτη σχεδιάστηκε για να προσδιορίσει αν πρώιμη οργανική βλάβη μπορεί να προβλέψει τη θνητότητα

CI = confidence interval;
SDI = Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.

1. Murimi-Worstell IB, et al. BMJ open 2020;10:e031850;
2. Rahman P, et al. Lupus 2001;10:93–96.

English Edition

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NEWS & PERSPECTIVE DRUGS & DISEASES CME & EDUCATION VIDEO DECISION POINT

Drugs & Diseases > Calculators

Calculator About References

SLICC/ACR Damage Index

Measure accumulated damage since onset of lupus

Questions

1. Retinal change or optic atrop... Yes, single epis...
2. **Cataract?** **Yes**
3. Cognitive Impairment or Maj...
4. Seizures requiring therapy fo...
5. Cerebrovascular Accident?
6. Cranial or Peripheral Neurop...
7. Transverse Myelitis?
8. Estimated or Measured GFR ...
9. Proteinuria ≥3.5 g/24 hours?
10. End-stage renal disease?
11. Pulmonary Hypertension?
12. Pulmonary Fibrosis?
13. Shrinking Lung?
14. Pleural Fibrosis?
15. Pulmonary Infarction?
16. Angina or Coronary Artery By...
17. Myocardial Infarction?

Default Units

2. Cataract?

Yes ✓

No

More Information

A lens opacity in either eye, ever, whether primary or secondary to steroid therapy, documented by ophthalmoscopy

Created by QxMD

17. Myocardial Infarction? No
18. Cardiomyopathy? No
19. Valvular disease? No
20. Pericarditis or Pericardiecto... No
21. Claudication? No
22. Minor Tissue Loss from Perip... No
23. Significant Tissue Loss from ... No
24. Venous Thrombosis with Sw... No
25. Infarction or Resection of Bo... No
26. Mesenteric Insufficiency? No
27. Chronic Peritonitis? No
28. Stricture or Upper Gastrointe... No
29. Pancreatic Insufficiency Requ... No
30. Muscle Atrophy or Weakness? No
31. **Deforming or Erosive Arthr...** **No**
32. Osteoporosis with Fracture o... No
33. Avascular Necrosis? No
34. Scarring Chronic Alopecia? No
35. Extensive Scarring of Pannic... No
36. Skin Ulceration (excluding th... No
37. Premature Gonadal Failure? No
38. Diabetes Requiring Therapy? No
39. Malignancy? No

About

The systemic lupus international collaborating clinics American College of Rheumatology Damage index (SLICC/ACR DI) was developed to quantify damage that has occurred since onset of lupus.

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Drugs & Diseases > Calculators

Calculator About References

SLICC/ACR Damage Index

Measure accumulated damage since onset of lupus

Questions

1. Retinal change or optic atrop... No
2. Cataract? Yes
3. Cognitive Impairment or Maj... No
4. Seizures requiring therapy fo... No

Default Units

Results Copy Results

SLICC/ACR Damage Index
1

Created by QxMD

About

The systemic lupus international collaborating clinics American College of Rheumatology Damage index (SLICC/ACR DI) was developed to quantify damage that has occurred since onset of lupus.

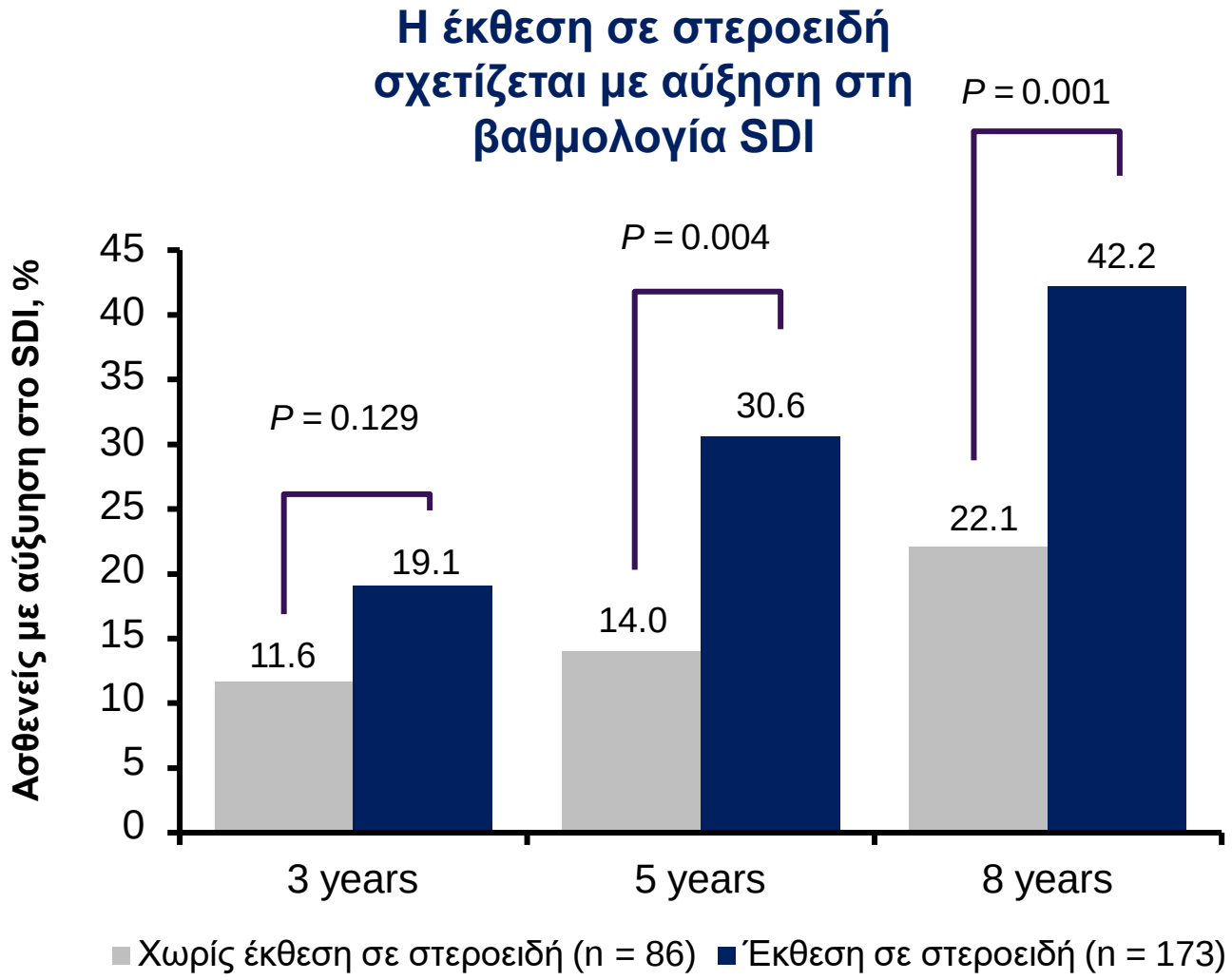
It has been shown to be a valid measure for damage and correlates with mortality.

In this index, damage is defined a non-reversible change, **not related** to active inflammation, occurring since the onset of lupus, ascertained by clinical assessment and present for at least 6 months. 'Repeat' episodes mean at least 6 months apart to score 2. The same lesion cannot be scored twice.

References

Gladman DD, Goldsmith CH, Urowitz MB, Bacon P, Fortin P, Ginzler E, Gordon C, Hanly JG, Isenberg DA, Petri M, Nived O, Snaith M, Sturfelt G.
The Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index for Systemic Lupus Erythematosus International Comparison.
Journal of Rheumatology 2000, 27 (2): 373-6

Η χρήση στεροειδών σχετίζεται με οργανική βλάβη

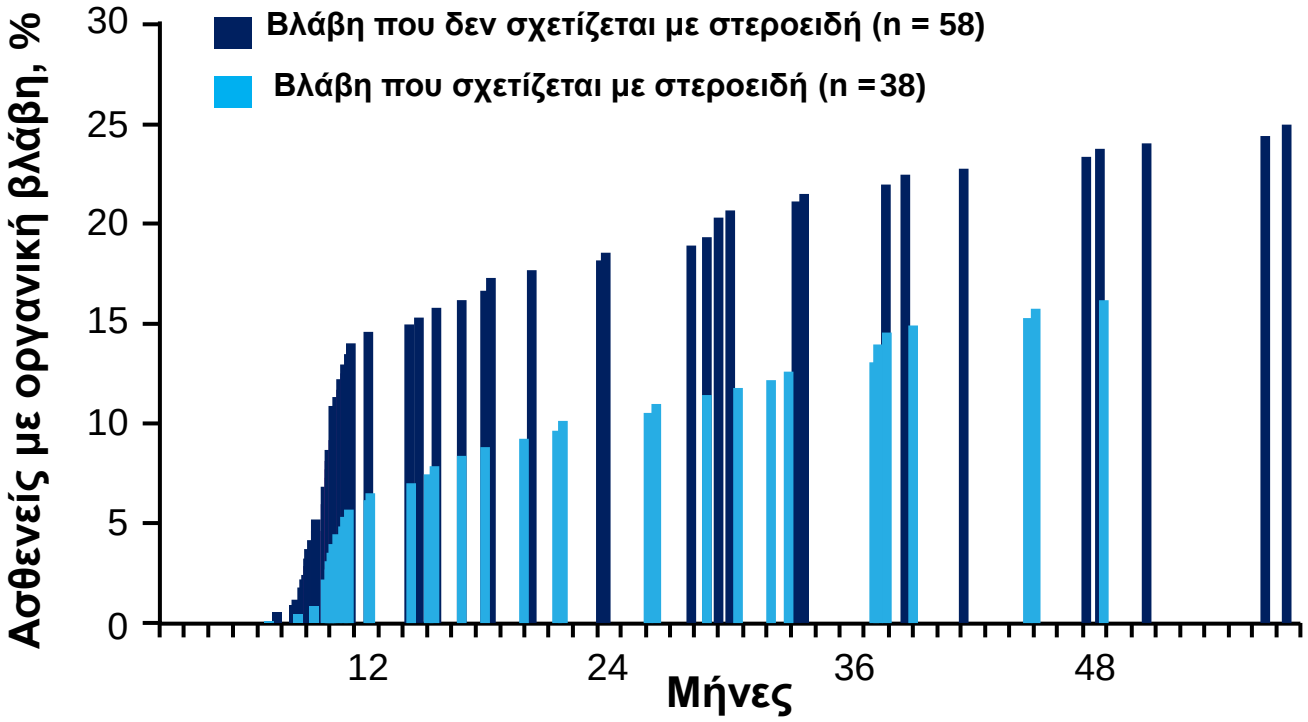


SDI = Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.

Προσαρμογή από:
Sheane BJ, et al. Arthritis Care Res (Hoboken) 2017;69:252–256.

Η οργανική βλάβη αθροίζεται ταχέως στα πρώιμα στάδια του λύκου

Η πρώιμη βλάβη συσχετίστηκε με την ενεργότητα της νόσου και τη χρήση κορτικοστεροειδών



Κατά την πορεία της νόσου, **η πρώιμη βλάβη** αποδίδεται τόσο στην **ενεργότητα της νόσου** (εξάρσεις και εμμένουσα ενεργότητας), όσο και στη **χρήση κοστικοστεροειδών**

N = 230

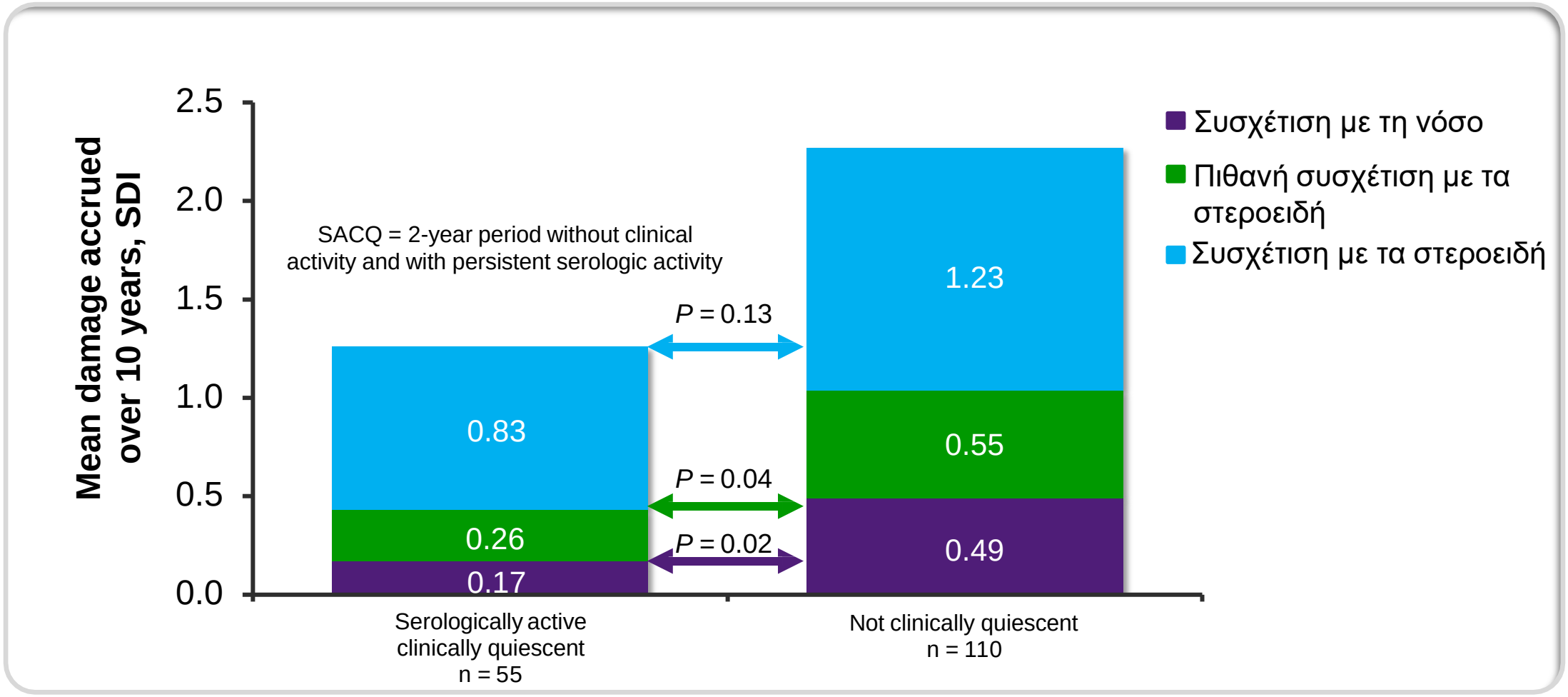
Διάρκεια νόσου
< 12 μήνες από την ένταξη

Μέση διάρκεια παρακολούθησης:
27,4 μήνες

GC = glucocorticosteroids.

Adapted from Figure 1B of
Piga M, Iaccarino L, et al. Rheumatology (Oxford) 2020;59:2272–2281.

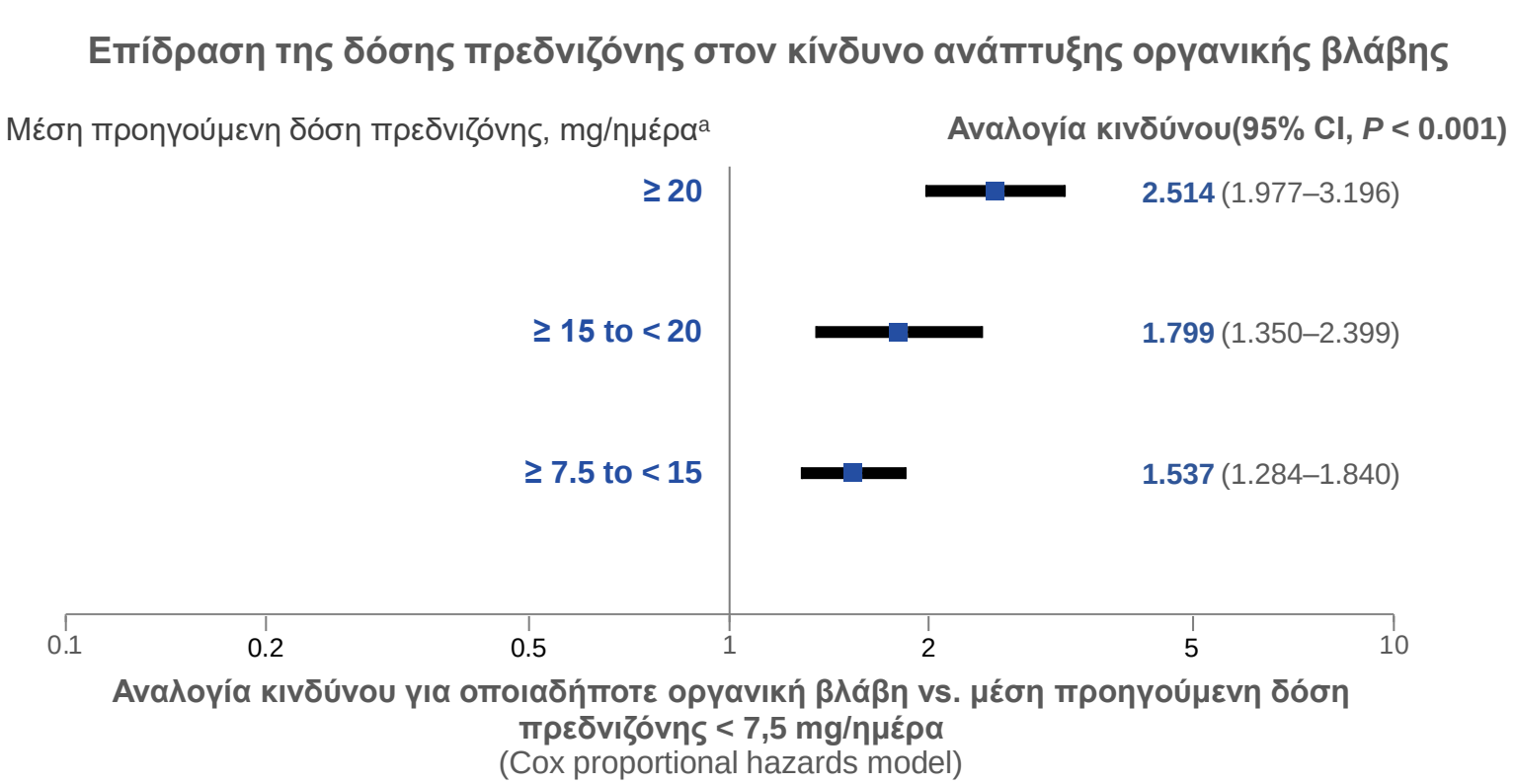
Τα στεροειδή συσχετίζονται με οργανική βλάβη ανεξάρτητα της ενεργότητας της νόσου



SACQ = serologically active clinically quiescent.

Steiman AJ, et al. Arthritis Care Res 2012;64:511–518.

Αυξημένος κίνδυνος εξέλιξης οργανικής βλάβης όσο μεγαλύτερη η μέση δόση πρεδνιζόνης



Οι ασθενείς που είχαν εκτεθεί σε μέση προηγούμενη **δόση πρεδνιζόνης ≥ 7,5 mg/ημέρα** είχαν **1,7 φορές** μεγαλύτερο κίνδυνο να αναπτύξουν οποιαδήποτε νέα οργανική βλάβη σε σύγκριση με εκείνους που είχαν εκτεθεί σε μέση προηγούμενη δόση πρεδνιζόνης < 7,5 mg/ημέρα (HR = 1.742, 95% CI 1.489 to 2.039, *P* < 0.001).

Με κάθε **1 mg αύξηση της μέσης ημερήσιας δόσης πρεδνιζόνης** (ανεξάρτητα από την αρχική δόση πρεδνιζόνης), ο κίνδυνος εμφάνισης οποιασδήποτε νέας οργανικής βλάβης αυξήθηκε κατά περίπου **3%** (HR = 1.028, 95% CI 1.022 to 1.035, *P* < 0.001).

- Η μελέτη της κοορτής ασθενών με ΣΕΛ από το Hopkins ήταν μία προοπτική διαχρονική μελέτη που παρακολουθούσε ασθενείς με ΣΕΛ μέσω τριμηνιαίων (ή πιο συχνών) επισκέψεων, συμπεριέλαβε 2265 ασθενείς που παρακολουθήθηκαν στην πορεία 26 ετών μεταξύ 1987 και 2012, με μία μέση διάρκεια παρακολούθησης τα 6,2 έτη.

[a]Average prednisone dose during prior cohort follow-up
CI = confidence interval; HR = hazard ratio; LLDAS = Lupus Low Disease Activity State; RR = relative risk; SDI = Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index
Al Sawah S, et al. Lupus Sci Med. 2015:2:e000066.

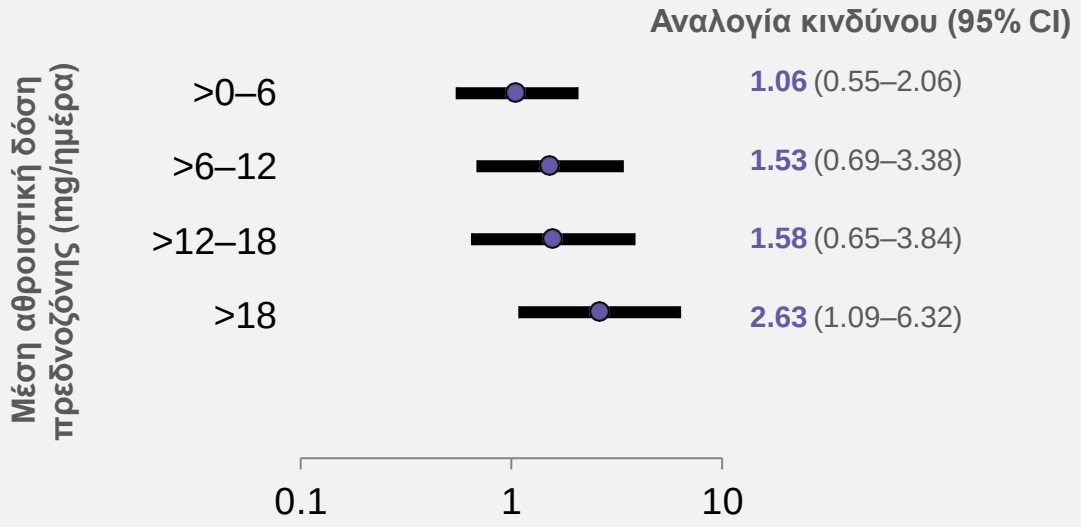
Ακόμα και χαμηλή δόση στεροειδών μπορεί να προκαλέσει ανεπιθύμητες ενέργειες

Τα δεδομένα βασίζονται σε μία μελέτη και μπορεί να μην εφαρμόζονται σε όλους τους ασθενείς και πληθυσμούς ασθενών

1. Ruiz-Irastorza G, et al. Rheumatology (Oxford) 2012;51:1145–1153;
2. Nevskaya T, et al. Clin Exp Rheum 2017;35:700–710;
3. Stojan G, et al. Curr Treatm Opt Rheumatol 2017;3:164–172.

Ιδανική η επίτευξη της χαμηλότερης δυνατής δόσης κορτικοστεροειδών στο Συστηματικό Ερυθηματώδη Λύκο

Η χαμηλότερη δόση πρεδνιζονης έχει μικρότερο κίνδυνο μη αναστρέψιμης οργανικής βλάβης[1a]



Τ̈απιο αυστηρό όριο δόσης πρεδνιζονης μπορεί να σχετίζεται με μειωμένη οργανική βλάβη[2]

	≤ 5 mg/ημέρα	≤ 7.5 mg/ημέρα
RR για αύξηση στο SDI ≥ 1	**0.38**	**0.47**
(95% CI)	0.21–0.70	0.28–0.79
***P* value**	*P* = 0.002	*P* = 0.005

Μία μελέτη με στόχο τον προσδιορισμό και την πιστοποίηση του LLDAS πρότεινε ότι ένα πιο αύστηρο όριο από ≤ 7.5 mg/ημέρα για τη δόση πρεδνιζόνης στο LLDAS μπορεί να σχετίζεται με περαιτέρω προστασία από την αθροιστική οργανική βλάβη[2]

[a]Weighted secondary analysis estimating hazard ratio of organ damage by cumulative prednisone dose model that appropriately adjusts for measured confounders in n=141 patients.
CI = confidence interval; LLDAS = Lupus Low Disease Activity State; RR = relative risk; SDI = Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.
1. Thamer M, et al. J Rheumatol. 2009;36(3):560-564. 2. Franklyn K, et al. Ann Rheum Dis. 2016;75:1615-1621.

EULAR recommendations for the management of systemic lupus erythematosus: 2023 update

Antonis Fanouriakis ,[1] Myrto Kostopoulou ,[1] Jeanette Andersen,[2] Martin Aringer ,[3] Laurent Arnaud ,[4] Sang-Cheol Bae ,[5] John Boletis,[6] Ian N Bruce,[7] Ricard Cervera,[8] Andrea Doria ,[9] Thomas Dörner ,[10] Richard A Furie ,[11] Dafna D Gladman ,[12] Frederic A Houssiau ,[13] Luís Sousa Inês ,[14] David Jayne ,[15] Marios Kouloumas,[16] László Kovács,[17] Chi Chiu Mok ,[18] Eric F Morand ,[19] Gabriella Moroni,[20] Marta Mosca,[21] Johanna Mucke ,[22] Chetan B Mukhtyar ,[23] György Nagy ,[24,25,26] Sandra Navarra,[27] Ioannis Parodis ,[28,29,30] José M Pego-Reigosa,[31] Michelle Petri ,[32] Bernardo A Pons-Estel,[33] Matthias Schneider,[22] Josef S Smolen,[34] Elisabet Svenungsson ,[28,29] Yoshiya Tanaka ,[35] Maria G Tektonidou ,[36] YK Onno Teng ,[37] Angela Tincani ,[38] Edward M Vital ,[39] Ronald F van Vollenhoven ,[40] Chris Wincup ,[41] George Bertsias ,[42] Dimitrios T Boumpas [1,43,44]

Handling editor David S Pisetsky

► Additional supplemental

ABSTRACT

Objectives To update the EULAR recommendations for the management of systemic lupus erythematosus (SLE) based on emerging new evidence

be considered. Updated specific recommendations are also provided for cutaneous, neuropsychiatric and haematological disease, SLE-associated antiphospholipid syndrome, kidney protection, as well as preventative

Table 1 EULAR Recommendations for the management of patients with systemic lupus erythematosus—2023 update

	Level of agreement	
	Mean (SD)	% with score ≥8
Overarching principles		
A. SLE requires multidisciplinary, individualised management with patient education and shared decision-making, taking into consideration the costs to patient and society.	9.88 (0.40)	100
B. SLE disease activity should be assessed at each clinic visit (the frequency depending on physician's discretion), with evaluation of organ damage (at least annually), using validated instruments.	9.74 (0.63)	100
C. Non-pharmacological interventions, including sun protection, smoking cessation, healthy, balanced diet, regular exercise and measures to promote bone health are important to improve long-term outcomes	9.90 (0.37)	100
D. Pharmacological interventions are directed by patient characteristics, type and severity of organ involvement, treatment-related harms, comorbidities, risk for progressive organ damage, and patient preferences.	10 (0)	100
E. Early SLE diagnosis (including serological assessment), regular screening for organ involvement (especially nephritis), prompt initiation of treatment aiming at remission (or low disease activity if remission is not possible) and strict adherence to treatment are essential to prevent flares and organ damage, improve prognosis and enhance quality of life.	9.81 (0.51)	100
Recommendation/statement		
1. Hydroxychloroquine is recommended for all patients (**1b/A**), unless contraindicated, at a target dose of 5 mg/kg real body weight/day (**2b/B**) but individualised based on risk for flare (**2b/B**) and retinal toxicity.	9.21 (1.35)	90.4
2. Glucocorticoids, if needed, are dosed based on the type and severity of organ involvement (**2b/C**), and should be reduced to maintenance dose of ≤5 mg/day (prednisone equivalent) (**2a/B**) and, when possible, withdrawn; in patients with moderate-to-severe disease, pulses of intravenous methylprednisolone (125–1000 mg/day, for 1–3 days) (**3b/C**) can be considered.	9.57 (0.77)	97.6
3. In patients not responding to hydroxychloroquine (alone or in combination with glucocorticoids) or patients unable to reduce glucocorticoids below doses acceptable for chronic use, addition of immunomodulating/immunosuppressive agents (eg, methotrexate (**1b/B**), azathioprine (**2b/C**) or mycophenolate (**2a/B**)) and/or biological agents (eg, belimumab (**1a/A**) or anifrolumab (**1a/A**)) should be considered.	9.32 (0.91)	95.2
4. In patients with organ-threatening or life-threatening disease, intravenous cyclophosphamide (**2b/C**) should be considered; in refractory cases, rituximab (**2b/C**) may be considered.	9.38 (0.99)	95.2
5. Treatment of active skin disease should include topical agents (glucocorticoids, calcineurin inhibitors) (**2b/B**), antimalarials (hydroxychloroquine, chloroquine) (**1a/A**), and/or systemic glucocorticoids (**4/C**) as needed, with methotrexate (**1b/B**), mycophenolate (**4/C**), anifrolumab (**1a/A**), or belimumab (**1a/B**) considered as second-line therapy.	9.35 (1.06)	95.2
6. In active neuropsychiatric disease attributed to SLE, glucocorticoids and immunosuppressive agents for inflammatory manifestations (**1b/A**) and antiplatelet agents/anticoagulants for atherothrombotic/aPL-related manifestations (**2b/C**) should be considered.	9.68 (0.81)	97.6
7. For acute treatment of severe autoimmune thrombocytopenia, high-dose glucocorticoids (including pulses of intravenous methylprednisolone) (**4/C**), with or without intravenous immunoglobulin G (**4/C**), and/or rituximab (**2b/B**), and/or high-dose intravenous cyclophosphamide (**4/C**), followed by maintenance therapy with rituximab (**2b/B**), azathioprine (**2b/C**), mycophenolate (**2b/C**), or cyclosporine (**4/C**) should be considered.	9.48 (0.86)	97.6
8. Patients with active proliferative lupus nephritis should receive low-dose (EuroLupus) intravenous cyclophosphamide (**1a/A**) or mycophenolate (**1a/A**) and glucocorticoids (pulses of intravenous methylprednisolone followed by lower oral doses); combination therapy with belimumab (either with cyclophosphamide or mycophenolate (**1b/A**)) or calcineurin inhibitors (especially voclosporin or tacrolimus, combined with mycophenolate, **1b/A**) should be considered.	9.36 (1.06)	92.8

Τα γλυκοκορτικοστεροειδή ως θεραπεία «γέφυρα»

EULAR Recommendation/Statement

Σύσταση

Τα γλυκοκορτικοστεροειδή, εάν απαιτούνται, δίνονται σε δόση που βασίζεται στον τύπο και τη σοβαρότητα της οργανικής συμμετοχής (2b/C) και θα πρέπει να μειώνονται σε **δόση συντήρησης ≤ 5 mg/ημέρα** (ανάλογο πρεδνιζόνης) (2a/B) και **όταν είναι δυνατό, να αποσύρονται,** σε ασθενείς με μέτρια ως σοβαρή νόσο, ώσεις ενδοφλέβιας μεθυλπρεδνιζολόνης (125–1000 mg per ημέρα, for 1–3 days) (3b/C) μπορούν να χορηγηθούν.

Επιπλέον πληροφορίες

- Η χρόνια έκθεση γλυκοκορτικοστεροειδή είναι ο βασικός κίνδυνος
- Χρήση γλυκοκορτικοστεροειδών ως ‘θεραπεία γέφυρα’ όπως στη ρευματοειδή αρθρίτιδα, χρησιμοποιώντας της χαμηλότερη δυνατή δόση για το μικρότερο δυνατό χρονικό διάστημα, με στόχο την πλήρη απόσυρση

GC = glucocorticoids; RA = rheumatoid arthritis.
Fanouriakis A, et al. Ann Rheum Dis. 2023. doi: 10.1136/ard-2023-224762 (online ahead of print).

of the disease, but also thereafter. This need for increased awareness for signs of new-onset kidney involvement was emphasised by several Task Force members, because LN represents a major milestone in the natural history of the disease and delaying its diagnosis has profound prognostic repercussions; (3) pursuing a treatment target, which should ideally be remission, as defined by the recent Definition Of Remission In SLE (DORIS) criteria,[21] or alternatively, a state of low disease activity, such as the Lupus Low Disease Activity state (LLDAS).[22] Both remission and LLDAS have been extensively validated and proven to reduce the risk for damage and other adverse outcomes in patients with SLE (a detailed analysis of the favourable outcomes associated with remission and LLDAS is given in the online supplemental appendix); and (4) the importance of patient adherence to treatment. Specific reference to the issue of adherence in the overarching principles was emphasised by several panellists, including the patient research partners, because medication non-adherence, despite reported wide variations, is considered a major cause of treatment failure.[23] A trusting relationship between the physician and patient forms the basis for the minimisation of the risk of non-adherence. Mean (SD) LoA for the final overarching principle was 9.81 (0.51).

Individual recommendations

1. Hydroxychloroquine is recommended for all patients (1b/A), unless contraindicated, at a target dose of 5 mg/kg real body weight/day (2b/B), but individualised based on risk for flare (2b/B) and retinal toxicity.

HCQ is the mainstay of treatment for patients with SLE and the current SLR extended the existing body of evidence regarding the multiple beneficial effects of HCQ in various aspects of the disease. In the 2019 recommendations, emphasis was placed on the specification that HCQ dose 'should not exceed 5 mg/kg real body weight/day', in view of data which suggested a higher than HCQ (mainly for retinal toxicity).[24] Finally, quinacrine can be considered in patients with cutaneous manifestations and HCQ-induced retinopathy. The statement on HCQ was agreed on by 77.8% of participants following one round of amendments (the only statement where this was needed) and mean (SD) LoA was 9.21 (3.35).

2. Glucocorticoids, if needed, are dosed based on the type and severity of organ involvement (2b/C), and should be reduced to maintenance dose of ≤5 mg/day (prednisone equivalent) (2a/B) and, when possible, withdrawn; in patients with moderate-to-severe disease, pulses of intravenous methylprednisolone (125–1000 mg per day, for 1–3 days) (3b/C) can be considered.

Minimisation of GC use, in view of their detrimental effects, was a major theme of discussion during the Task Force meetings. Numerous studies in the current SLR confirmed associations of different cut-offs for daily prednisone dose with adverse outcomes, most of which pointed to the threshold of 5 mg/day. Although a controlled trial of different GC tapering regimens or maintenance doses is still lacking in SLE, the Task Force elected to lower the 'acceptable' threshold of daily prednisone dose for maintenance treatment to maximum 5 mg/day prednisone equivalent, as compared with 7.5 mg/day in the 2019 recommendations. Ideally, one could envision the use of GC only as 'bridging therapy' in SLE, similar to rheumatoid arthritis (lowest possible dose for the shortest possible period), and the complete withdrawal of GC is the optimal target.

Intravenous pulses of methylprednisolone (MP) of various doses (depending on disease severity and patient weight) capitalise on the immediate non-genomic effects of GC,[28] and may allow for a faster tapering of per os (PO) GC.[29] Importantly, pulse IV MP has not been linked to certain established GC-related harms, like avascular necrosis.[30] Initial PO dose also depends on disease severity; a retrospective study in 206 patients with LN using propensity score matching found higher rates of

Table 1 EULAR Recommendations for the management of patients with systemic lupus erythematosus—2023 update

	Level of agreement	
	Mean (SD)	% with score ≥8
Overarching principles		
A. SLE requires multidisciplinary, individualised management with patient education and shared decision-making, taking into consideration the costs to patient and society.	9.88 (0.40)	100
B. SLE disease activity should be assessed at each clinic visit (the frequency depending on physician's discretion), with evaluation of organ damage (at least annually), using validated instruments.	9.74 (0.63)	100
C. Non-pharmacological interventions, including sun protection, smoking cessation, healthy, balanced diet, regular exercise and measures to promote bone health are important to improve long-term outcomes	9.90 (0.37)	100
D. Pharmacological interventions are directed by patient characteristics, type and severity of organ involvement, treatment-related harms, comorbidities, risk for progressive organ damage, and patient preferences.	10 (0)	100
E. Early SLE diagnosis (including serological assessment), regular screening for organ involvement (especially nephritis), prompt initiation of treatment aiming at remission (or low disease activity if remission is not possible) and strict adherence to treatment are essential to prevent flares and organ damage, improve prognosis and enhance quality of life.	9.81 (0.51)	100
Recommendation/statement		
1. Hydroxychloroquine is recommended for all patients (**1b/A**), unless contraindicated, at a target dose of 5 mg/kg real body weight/day (**2b/B**) but individualised based on risk for flare (**2b/B**) and retinal toxicity.	9.21 (1.35)	90.4
2. Glucocorticoids, if needed, are dosed based on the type and severity of organ involvement (**2b/C**), and should be reduced to maintenance dose of ≤5 mg/day (prednisone equivalent) (**2a/B**) and, when possible, withdrawn; in patients with moderate-to-severe disease, pulses of intravenous methylprednisolone (125–1000 mg/day, for 1–3 days) (**3b/C**) can be considered.	9.57 (0.77)	97.6
3. In patients not responding to hydroxychloroquine (alone or in combination with glucocorticoids) or patients unable to reduce glucocorticoids below doses acceptable for chronic use, addition of immunomodulating/immunosuppressive agents (eg, methotrexate (**1b/B**), azathioprine (**2b/C**) or mycophenolate (**2a/B**)) and/or biological agents (eg, belimumab (**1a/A**) or anifrolumab (**1a/A**)) should be considered.	9.32 (0.91)	95.2
4. In patients with organ-threatening or life-threatening disease, intravenous cyclophosphamide (**2b/C**) should be considered; in refractory cases, rituximab (**2b/C**) may be considered.	9.38 (0.99)	95.2
5. Treatment of active skin disease should include topical agents (glucocorticoids, calcineurin inhibitors) (**2b/B**), antimalarials (hydroxychloroquine, chloroquine) (**1a/A**), and/or systemic glucocorticoids (**4/C**) as needed, with methotrexate (**1b/B**), mycophenolate (**4/C**), anifrolumab (**1a/A**), or belimumab (**1a/B**) considered as second-line therapy.	9.35 (1.06)	95.2
6. In active neuropsychiatric disease attributed to SLE, glucocorticoids and immunosuppressive agents for inflammatory manifestations (**1b/A**) and antiplatelet agents/anticoagulants for atherothrombotic/aPL-related manifestations (**2b/C**) should be considered.	9.68 (0.81)	97.6
7. For acute treatment of severe autoimmune thrombocytopenia, high-dose glucocorticoids (including pulses of intravenous methylprednisolone) (**4/C**), with or without intravenous immunoglobulin G (**4/C**), and/or rituximab (**2b/B**), and/or high-dose intravenous cyclophosphamide (**4/C**), followed by maintenance therapy with rituximab (**2b/B**), azathioprine (**2b/C**), mycophenolate (**2b/C**), or cyclosporine (**4/C**) should be considered.	9.48 (0.86)	97.6
8. Patients with active proliferative lupus nephritis should receive low-dose (EuroLupus) intravenous cyclophosphamide (**1a/A**) or mycophenolate (**1a/A**) and glucocorticoids (pulses of intravenous methylprednisolone followed by lower oral doses); combination therapy with belimumab (either with cyclophosphamide or mycophenolate (**1b/A**)) or calcineurin inhibitors (especially voclosporin or tacrolimus, combined with mycophenolate, **1b/A**) should be considered.	9.36 (1.06)	92.8
9. Following renal response, treatment of lupus nephritis should continue for at least 3 years (**2b/B**); patients initially treated with mycophenolate alone or in combination with belimumab or a calcineurin inhibitor should remain on these drugs (**1a/A**), whereas azathioprine or mycophenolate should replace cyclophosphamide for those initially treated with	9.56 (0.81)	95.2

This statement emphasises the value of conventional and biological immunomodulatory/immunosuppressive drugs for the control of the disease and facilitation of GC tapering and withdrawal. Since no new, high-quality data emerged in the past 4 years regarding conventional immunosuppressive drugs, deliberations regarding this statement focused on two main issues: (1) inclusion of anifrolumab, following its approval in 2021,[33 34] as well as belimumab,[35] as biological agents with proven efficacy in controlling disease activity, reducing flares, and allowing for GC dose reduction. In the recommendation, there is no hierarchy in the choice between anifrolumab and belimumab, as the two drugs have not been compared in a head-to-head trial and their approval was the result of RCTs in similar extrarenal SLE populations. The panel noted that there are more than 10 years of real-life clinical experience with belimumab, while no real-life data for anifrolumab had been published by the time of the SLR completion. (2) The positioning of biological agents in relation to conventional immunosuppressive drugs for the treatment of SLE. For the latter point, while considerations from specific countries, healthcare settings and biological reimbursement policies have to be taken into account, most panellists agreed that prior use of a conventional immunosuppressive drug (MTX, AZA, mycophenolate mofetil or mycophenolic acid (henceforth combined referred to as 'mycophenolate', see online supplemental table 1 for details), leflunomide[36] or others) should not be mandatory for initiating anifrolumab or belimumab. Of note, this is unchanged from the 2019 recommendations. The rationale driving this statement was that, despite their substantially higher cost, approved biological drugs have proven their efficacy in high-quality RCTs, while such data are lacking for

For the treatment of active skin disease in SLE, few new data have emerged since the 2019 recommendations, and a significant body of evidence continues to originate from studies in patients with cutaneous lupus erythematosus. Recommended first-line treatment (topical agents, antimalarials and/or systemic GC) has not changed in the statement. HCQ is the antimalarial of choice, but chloroquine may be used in the settings discussed earlier.[45] Quinacrine (mepacrine) may also be used in cases of inadequate response or toxic retinopathy, as add-on to HCQ or alternative therapy, respectively,[46] but its use is limited by frequent intolerance and unavailability in many countries.

For the ~40% of patients not responding to first-line therapy,[47] comparative studies among existing immunosuppressive drugs are lacking. Despite this paucity, recommended second-line drugs have partly changed from 2019, because the Task Force decided to recommend drugs more familiar to rheumatologists (such as MTX or mycophenolate, instead of dapsone or retinoids). A small retrospective study in 73 patients with refractory CLE to first-line therapy found similar response rates (~65%) between MTX and mycophenolate.[48] Anifrolumab and belimumab have both shown efficacy in mucocutaneous manifestations of SLE,[49 50] although only anifrolumab has used the Cutaneous Lupus Area and Severity Index in its clinical programme, whereas belimumab has reported responses according to the general instruments SLEDAI and BILAG (hence, the designation B in the Grading of Recommendation, despite positive RCT data). Importantly, the list of recommended drugs is indicative and other treatments may be considered as second-line or third-line options, including dapsone, retinoids, CNI, AZA, CYC and RTX, ideally in collaboration with dermatologists experienced in the treatment of

Recommendation

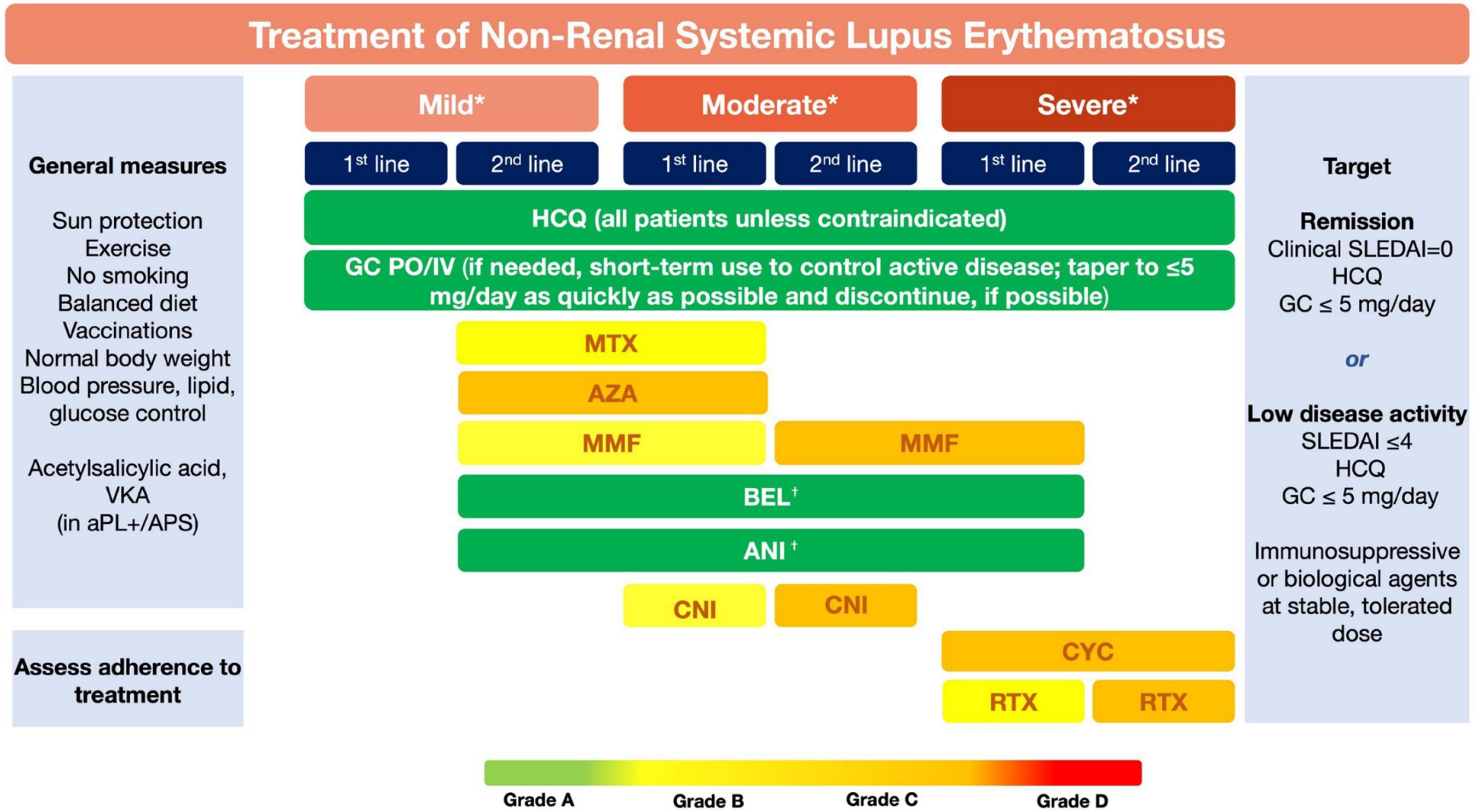
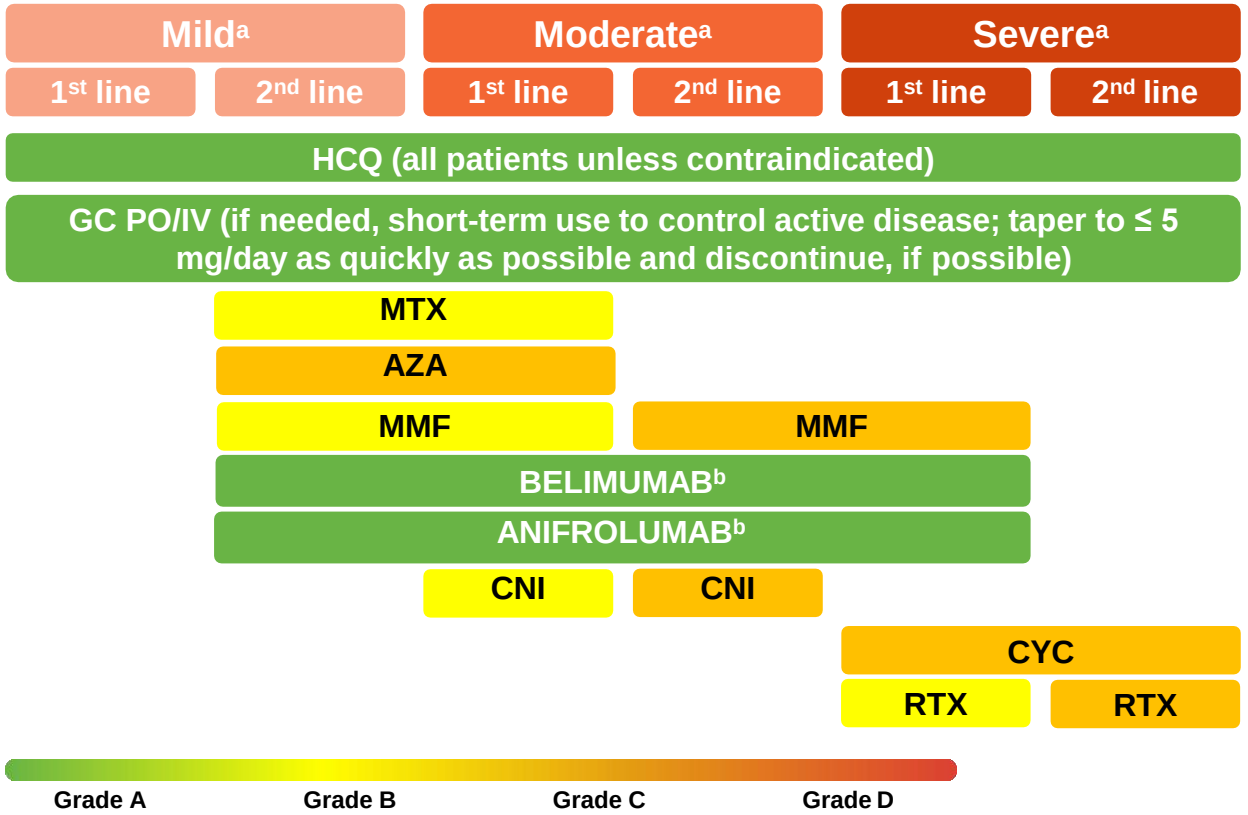


Figure 1 Treatment of non-renal systemic lupus erythematosus. Top-to bottom sequence does not imply order of preference (eg, MTX, AZA and MMF are equal options for second-line therapy in mild disease or first-line therapy in moderate disease). *Mild disease: constitutional symptoms; mild arthritis; rash ≤9% body surface area; platelet count (PLTs) 50–100 × 10^9/L; SLEDAI≤6; BILAG C or ≤1 BILAG B manifestation. *Moderate disease: moderate–severe arthritis ('RA-like'; rash 9%–18% BSA; PLTs 20–50×10^9/L; serositis; SLEDAI 7–12; ≥2 BILAG B manifestations). *Severe disease:

Συστάσεις EULAR 2023: Σκέψη για νωρίτερη χρήση βιολογικών παραγόντων

Θα πρέπει να εξετάζεται η προσθήκη βιολογικού παράγοντα για τον έλεγχο της νόσου, τη μείωση των εξάρσεων κι τη μείωση των κορτικοστεροειδών

Αλγόριθμος συστάσεων EULAR 2023 για τον εξωνεφρικό ΣΕΛ



- Θα πρέπει να εξετάζεται **η προσθήκη βιολογικού παράγοντα** σε ασθενείς που **δεν ανταποκρίνονται στην υδροξυχλωροκίνη (μόνη της ή σε συνδυσμό με κορτικοστεροειδή)** ή σε ασθενείς **με αδυναμία μείωσης κορτικοστεροειδών** σε δόσεις αποδεκτές για χρόνια χρήση
- **Δεν απαιτείται η προηγούμενη αποτυχία σε ένα ή περισσότερα ανοσοκατασταλτικά φάρμακα** πριν την έναρξη βιολογικού παράγοντα

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Top-to bottom sequence does not imply order of preference.

[a]Mild: constitutional symptoms/mild arthritis/rash ≤ 9% BSA/PLTs 50–100 × 10^9/L; SLEDAI ≤ 6; BILAG C or ≤ 1 BILAG B manifestation. Moderate: moderate-severe arthritis/rash 9–18% BSA/PLTs 20–50 × 10^9/L/serositis; SLEDAI 7–12; ≥ 2 BILAG B manifestations. Severe: major organ-threatening disease (cerebritis, myelitis, pneumonitis, mesenteric vasculitis); thrombocytopenia with platelets < 20 × 10^9/L; TTP-like disease or acute hemophagocytic syndrome; rash > 18% BSA; SLEDAI > 12; ≥ 1 BILAG A manifestations.

[b]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, etc. 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.

AZA = azathioprine; BILAG = British Lupus Assessment Group disease activity index; BSA = body surface area; CNI = calcineurin inhibitor; CYC = cyclophosphamide; EULAR = European Alliance of Associations for Rheumatology; GC = glucocorticoids; HCQ = hydroxychloroquine; IS = immunosuppressants; IV = intravenous; MMF = mycophenolate mofetil; MTX = methotrexate; PLT = platelet; PO = per os; RTX = rituximab; SLE = systemic lupus erythematosus; SLEDAI = Systemic Lupus Erythematosus Disease Activity Index; TTP = thrombotic thrombocytopenia purpura.

Fanouriakis A, et al. Ann Rheum Dis. 2023. doi: 10.1136/ard-2023-224762 (online ahead of print).

SLEDAI-2K score	Descriptor	Definition
8	**Seizure**	Recent onset, exclude metabolic, infectious or drug causes.
8	**Psychosis**	Altered ability to function in normal activity due to severe disturbance in the perception of reality.
8	**Organic brain syndrome**	Altered mental function with impaired orientation, memory or other intellectual function.
8	**Visual disturbance**	Retinal changes.
8	**Cranial nerve disorder**	New onset of sensory or motor neuropathy involving cranial nerves.
8	**Lupus headache**	Severe, persistent headache which may be migrainous, but must be nonresponsive to narcotic analgesia.
8	**Cerebrovascular accident**	New onset of cerebrovascular accident(s). Exclude arteriosclerosis.
8	**Vasculitis**	Ulceration, gangrene, tender finger nodules, periungual infarction, splinter haemorrhages, or biopsy or angiogram proof of vasculitis.
4	**Arthritis**	≥2 joints with pain and signs of inflammation (i.e. tenderness, swelling or effusion).
4	**Myositis**	Proximal muscle aching/weakness, associated with elevated creatine phosphokinase/aldolase or electromyogram changes or biopsy showing myositis.
4	**Urinary casts**	Heme granular or red blood cell casts.
4	**Haematuria**	>5 red blood cells/high power field. Exclude stone, infection or other cause.
4	**Proteinuria**	>0.5 gram/24 hours.
4	**Pyuria**	>5 white blood cells/high power field. Exclude infection.
2	**Rash**	Inflammatory type rash.
2	**Alopecia**	Abnormal, patchy or diffuse loss of hair.
2	**Mucosal ulcers**	Oral or nasal ulcerations.
2	**Pleurisy**	Pleuritic chest pain with pleural rub or effusion, or pleural thickening.
2	**Pericarditis**	Pericardial pain with at least 1 of the following: rub, effusion, or electrocardiogram or echocardiogram confirmation.
2	**Low complement**	Decrease in CH50, C3 or C4.
2	**Increased DNA binding**	Increased DNA binding by Farr assay.
1	**Fever**	>38°C. Exclude infectious cause.
1	**Thrombocytopenia**	<100 000 platelets / $x10^9$/L, exclude drug causes.
1	**Leukopenia**	<3000 white blood cells / $x10^9$/L, exclude drug causes.

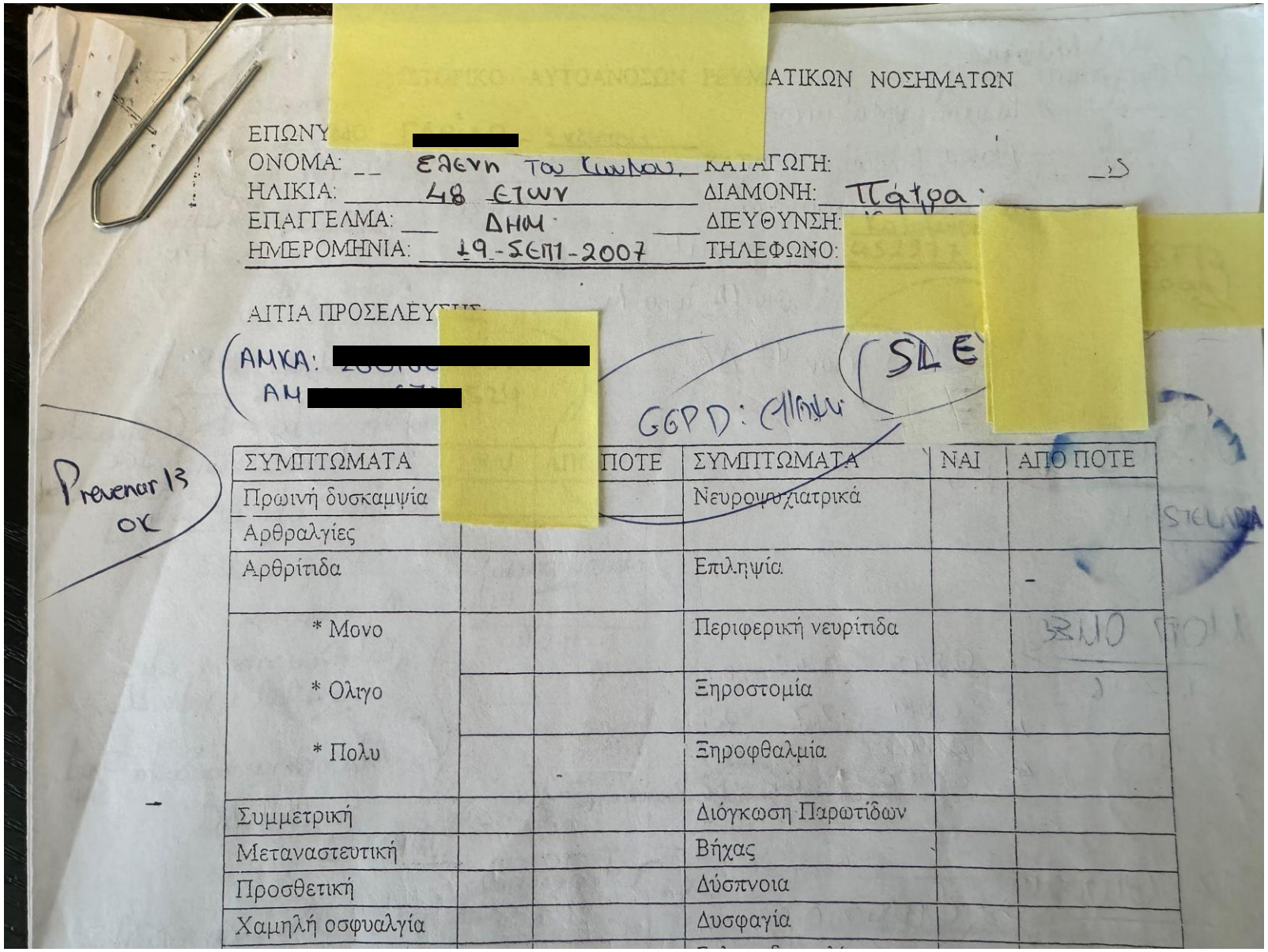
C3 = Complement protein 3, C4 = Complement protein 4, CH50 = 50% haemolytic complement activity, DNA = deoxyribonuclease, SLEDAI-2K = SLE disease activity index 2000

Summarized from *Gladman DD, Ibanez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000. J Rheumatol. 2002;29:288-91* (99).

CASE #1

- Γυναίκα 64 ετών
- ΣΕΛ από 30ετίας
- Στο ιατρείο από το 2007
- Υπό Υδροξυχλωροκίνη 200mg/d
- Καπνίστρια >20 τσιγάρα/ημέρα
- Ατομικό Αναμνηστικό: (-)

CASE #1



ΑΤΙΚΩΝ ΝΟΣΗΜΑΤΩΝ

ΕΠΩΝΥ
ΟΝΟΜΑ: Ελενη του Γιωνου, ΚΑΤΑΓΩΓΗ:
ΗΛΙΚΙΑ: 48 ετων ΔΙΑΜΟΝΗ: Πάτρα
ΕΠΑΓΓΕΛΜΑ: ΔΗΜ ΔΙΕΥΘΥΝΣΗ:
ΗΜΕΡΟΜΗΝΙΑ: 19-ΣΕΠ-2007 ΤΗΛΕΦΩΝΟ:

ΑΙΤΙΑ ΠΡΟΣΕΛΕΥΣΗΣ

ΑΜΚΑ:
ΑΜ

SLE

GGPD: Φ/ΑΡΝ

Prevenar 13 ΟΚ

ΣΥΜΠΤΩΜΑΤΑ	ΝΑΙ	ΑΠΟ ΠΟΤΕ	ΣΥΜΠΤΩΜΑΤΑ	ΝΑΙ	ΑΠΟ ΠΟΤΕ
Πρωινή δυσκαμψία			Νευροψυχιατρικά		
Αρθραλγίες					
Αρθρίτιδα			Επιληψία		-
* Μονο			Περιφερική νευρίτιδα		ΧΡΟΝΙΟ ΠΟΝΟ
* Ολιγο			Ξηροστομία		
* Πολυ			Ξηροφθαλμία		
Συμμετρική			Διόγκωση Παρωτίδων		
Μεταναστευτική			Βήχας		
Προσθετική			Δύσπνοια		
Χαμηλή οσφυαλγία			Δυσφαγία		

…CASE #1

- 09/2007
- Πολυαρθρίτιδα, δυσκαψία, αίσθημα κόπωσης

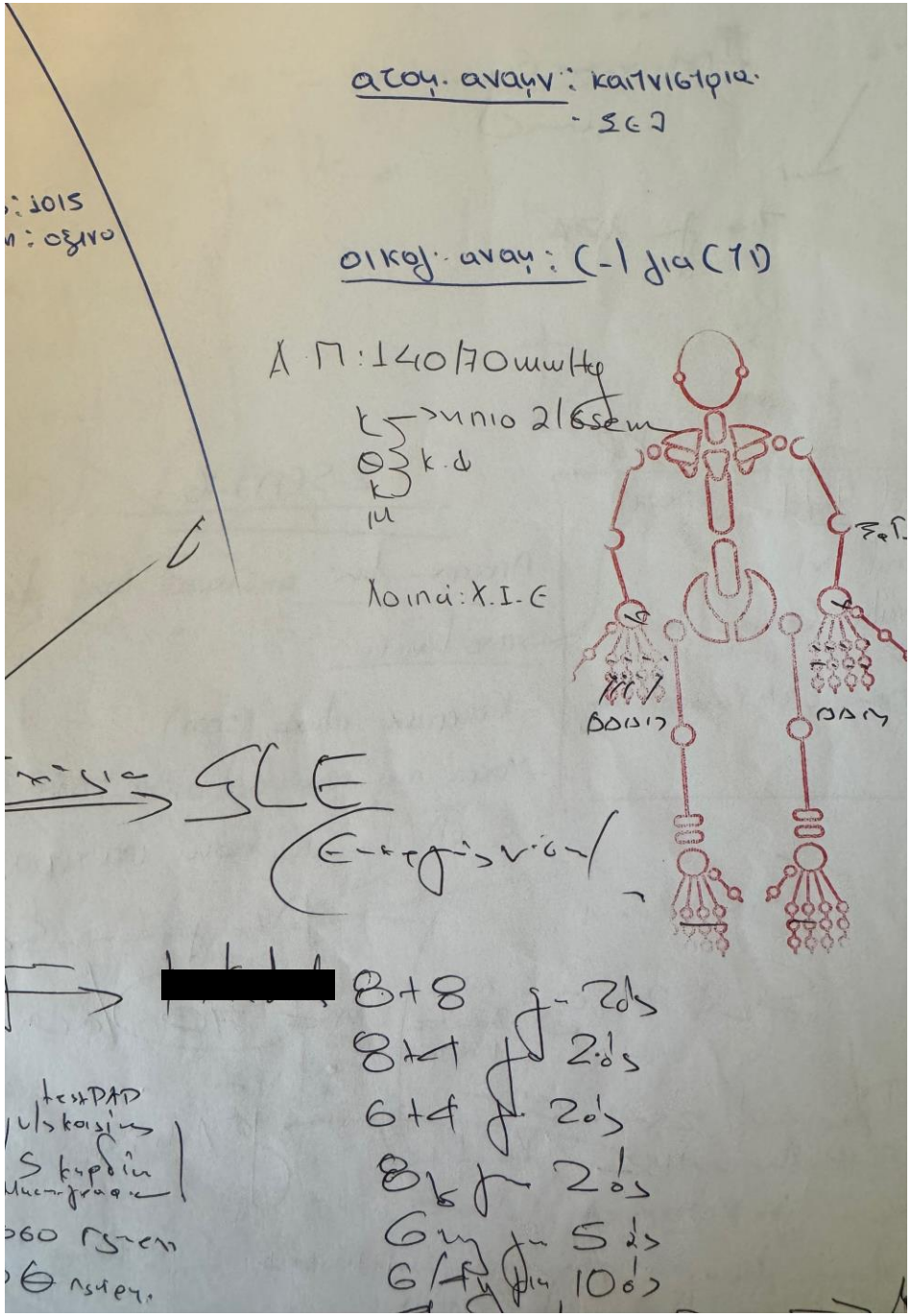
- ANA 1:1280 ομοιογενής, anti-dsDNA 750 (φτ<200),
- Hb 11,7g/dl

- SLEDAI 6, **SDI** 0

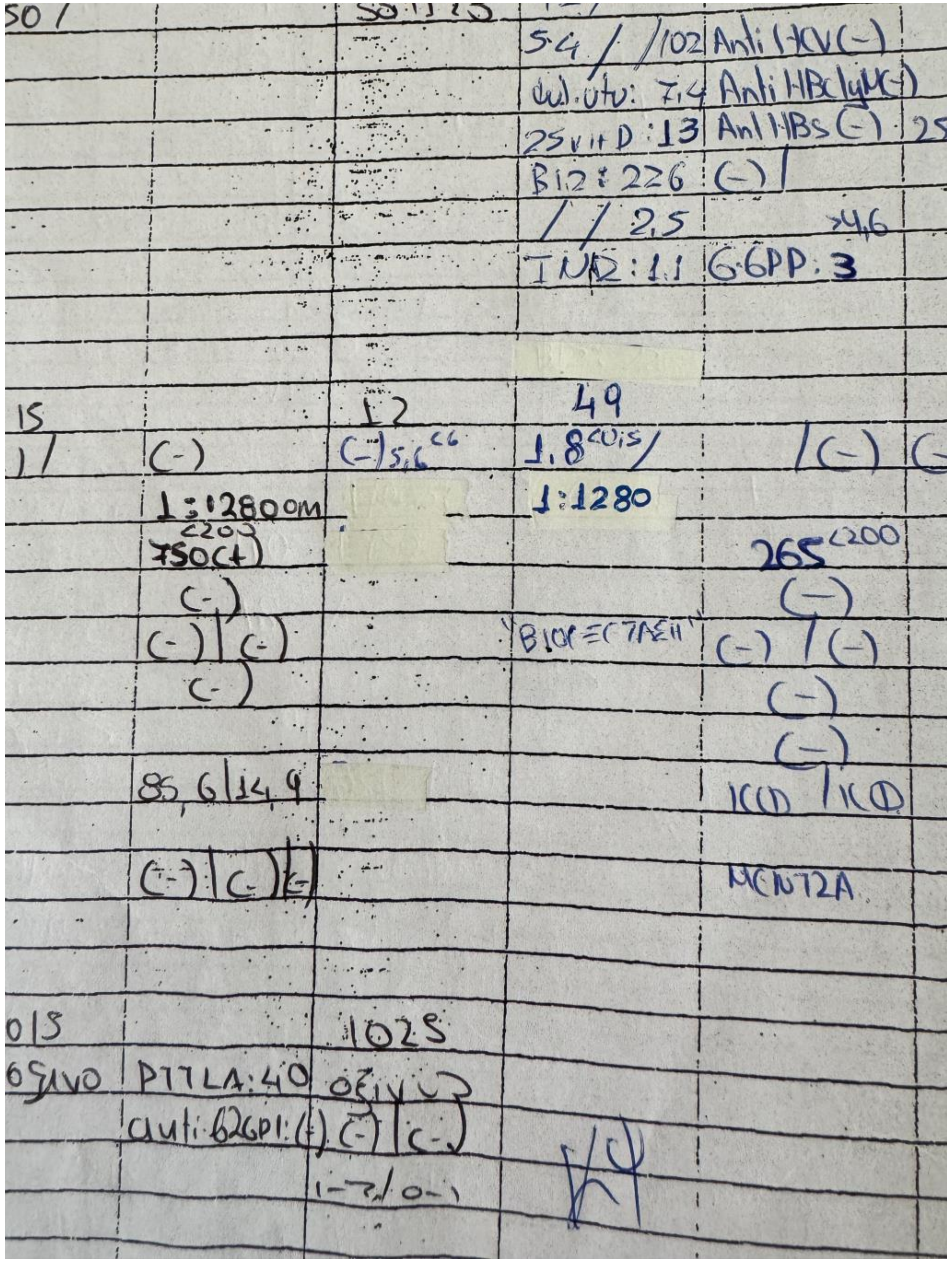
- Προσθήκη Μεθυλπρεδνιζολόνη 6mg/d, αλενδρονικό οξύ 5600/wk, AZA 100mg/d, διακοπή Υδροξυχλωροκίνης λόγω ανεπάρκειαςG6PD

Πραγματικά προφίλ ασθενών από προσωπικό αρχείο

CASE #1



CASE #1


Anti HCV(-)
Anti HBs (-)
B12: 226
G6PD: 3
1:1280
1:12800
750(+)
85,6/14,9
265
1025

…CASE #1

- Επανεμφανίζεται το 2016 (μετά από 9 έτη !!!)
- Υπό Μεθυλπρεδνιζολόνη 4mg/d… (διέκοψε AZA & αντιΟΠ αγωγή)
- Πολυαρθρίτιδα, δυσκαψία, αίσθημα κόπωσης,τριχόπτωση, βλάβες SCLE, cognitive impairment (γνωστική εξασθένηση)
- ANA 1:1280 ομοιογενής, anti-dsDNA 265 (φτ<200)
- Συννοσηρότητες: Καταρράκτης, Οστεοπόρωση εγκατεστημένη (Tscore -3,2), και σ. Cushing
- SLEDAI **11**, SDI **4**

Πραγματικά προφίλ ασθενών από προσωπικό αρχείο

…CASE #1

- ➔Μεθυλπρεδνιζολόνη 8mg, επανέναρξη AZA 100 mg/d, ρισεδρονικό οξύ 75mg(2tb)/m
- ΣΗΠ για Belimumab
- ΟΜΩΣ…….

- Επανέρχεται (και πάλι) μετά από 3 χρόνια (05/2019) λόγω αμέλειας και κατάθλιψης
- Μόνο υπό Μεθυλπρεδνιζολόνη 4 mg/d!
- Και καντεσαρτάνη 16 mg/d λόγω Υπέρτασης

Πραγματικά προφίλ ασθενών από προσωπικό αρχείο

CASE #1…

- Έχει αρθρίτιδα, εξανθήματα SCLE σε κορμό, άκρα και ψωριασιόμορφο φλυκταινώδες σε πέλματα

- ➔ Έναρξη MTX 15mg/wk, Μεθυλπρεδνιζολόνη **32**mg/d, λοιπή αγωγή ως είχε.

- …3 μήνες αργότερα (08/2019) ➔
  ➔ Μεγάλη βελτίωση κλινικά (σε αρθρίτιδα και εξάνθημα)
  Υπό Μεθυλπρεδνιζολόνη 6 mg/d, MTX 15mg/wk, λοιπή αγωγή ως είχε.

  Αναφέρει και δύσπνοια στην κόπωση!

Πραγματικά προφίλ ασθενών από προσωπικό αρχείο

CASE #1…

- … 3 μήνες αργότερα (12/2019) ➔

  ➔ ΕΞΑΡΣΗ ΝΟΣΟΥ (αρθρίτιδα, χείμετλα, εξάνθημα) υπό Μεθυλπρεδνιζολόνη 2mg/d

- Αύξηση δόσης Μεθυλπρεδνιζολόνης στα **16mg/d**

  Συνεχίζει MTX 15mg/wk

  Νέο ΣΗΠ για Belimumab ,σκέψη και για MMF

- Προσθήκη ustekinumab 45mg/12wks από Δερματολόγο λόγω ψωρίασης πελμάτων

Πραγματικά προφίλ ασθενών από προσωπικό αρχείο

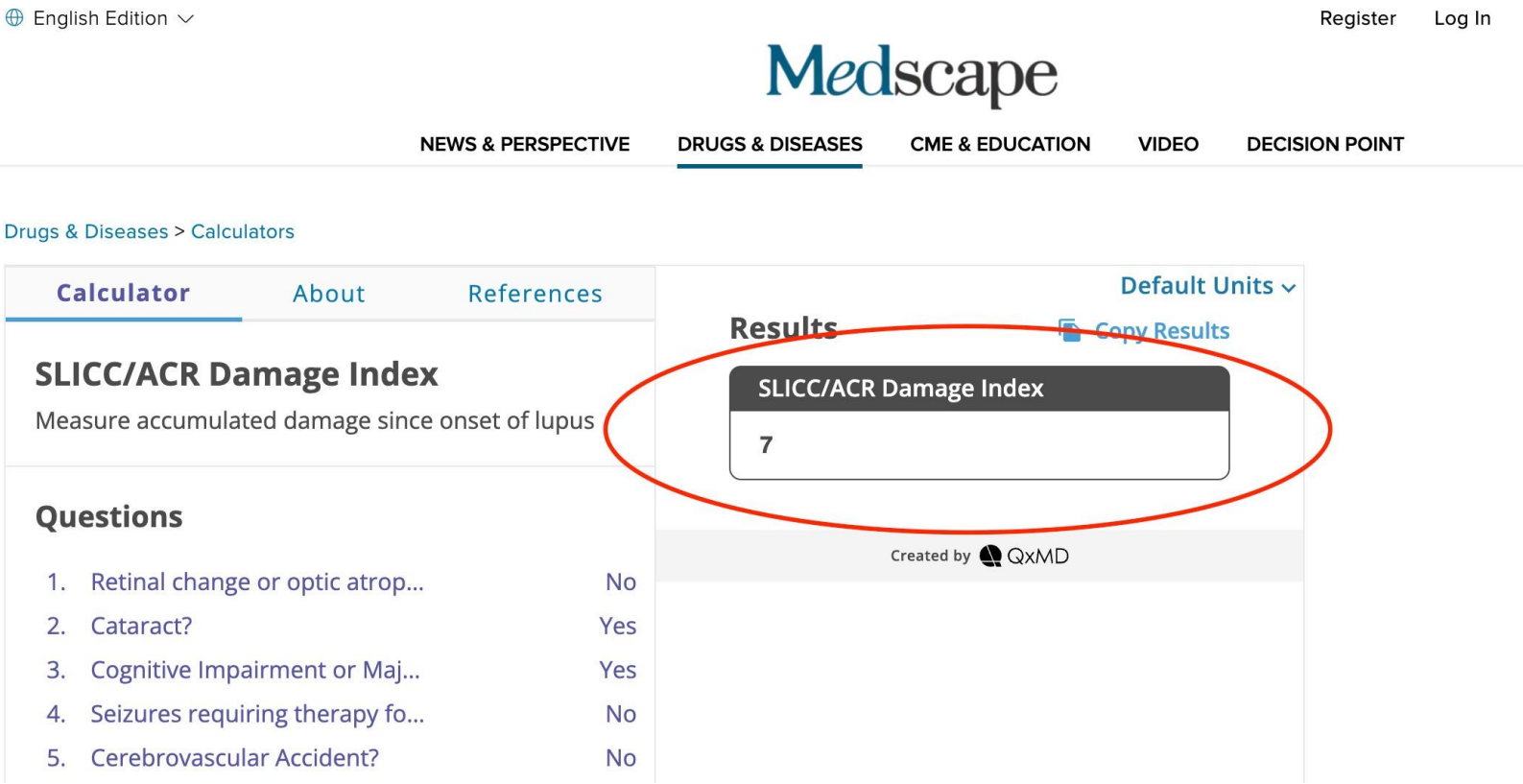
CASE #1…

- 06/2020
- Σημαντική βελτίωση στα πέλματα ! Λιγότερο σε κορμό και άκρα
- Κόπωση (+), αρθρίτιδα (+), μυϊκή ατροφία
- Μεθυλπρεδνιζολόνη 2mg/d, λοιπή αγωγή ίδια
- Σημαντική επιδείνωση διαλείπουσας χωλότητας!!!
- Triplex➔70% απόφραξη στις μηριαίες αρτηρίες
- (προσθήκη ➔κλοπιδρογέλη75mg, εζετιμίμπη/ατορβαστατίνη 10/20mg)
- Σύσταση για διακοπή καπνίσματος !!!

Πραγματικά προφίλ ασθενών από προσωπικό αρχείο

CASE #1…

- Για δύο έτη ➔ Πορεία νόσου με υφέσεις και εξάρσεις

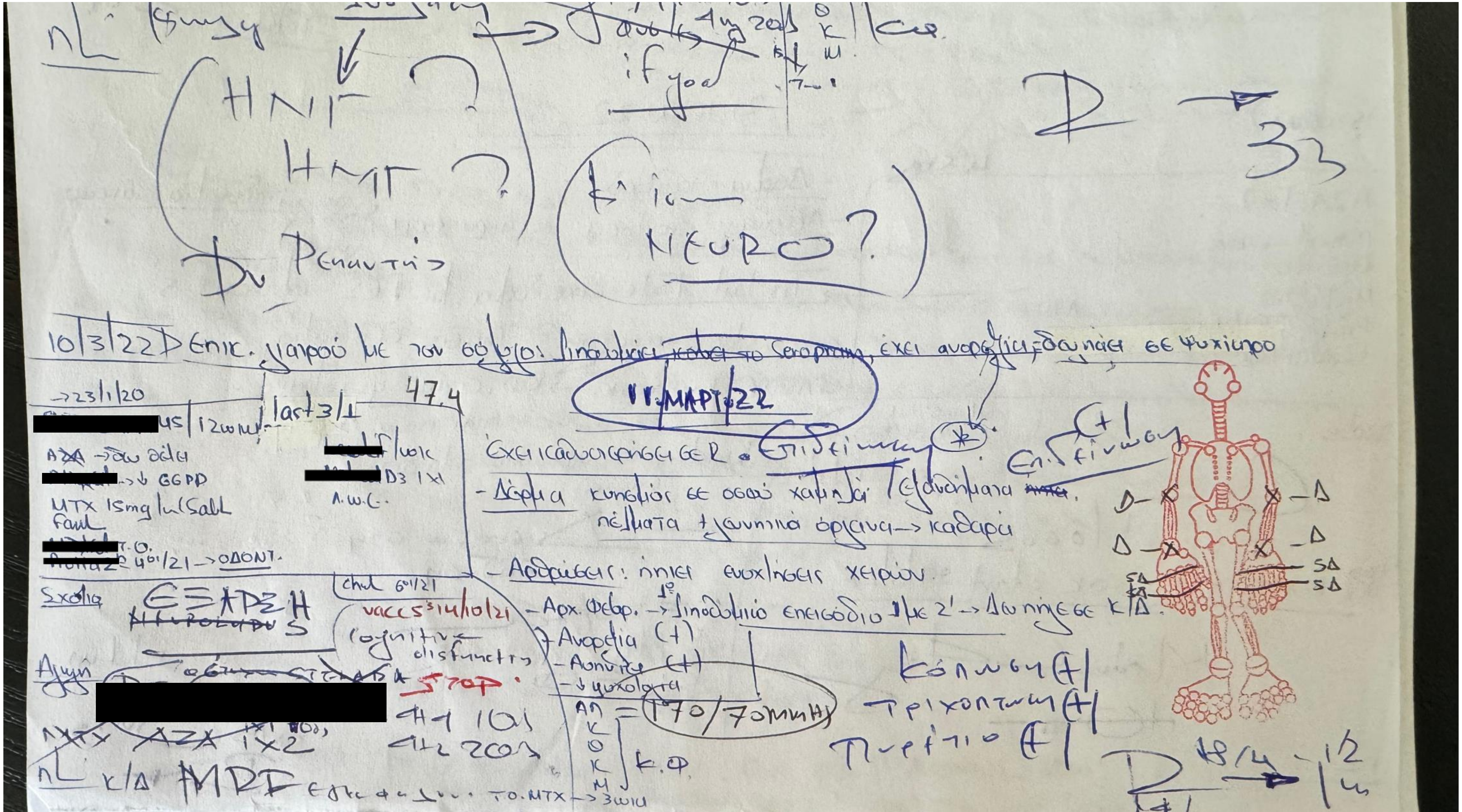


CASE #1…

- …2 χρόνια αργότερα (03/2022)
- Νέα ΕΞΑΡΣΗ ΝΟΣΟΥ με αθρίτιδα(+), εξάνθημα γενικευμένο SCLE(+), έντονη κόπωση(+), τριχόπτωση(+), πυρέτιο(+), κεφαλαλγία(+)
- SLEDAI**20**
- Διακοπή MTX, ustekinumab και έναρξη AZA 100mg/d και Μεθυλπρεδνιζολόνης **24** mg/d
- ΣΗΠ για Belimumab 200mg/wk – και έναρξη αγωγής 06/2022

Πραγματικά προφίλ ασθενών από προσωπικό αρχείο

CASE #1…



HNP?
HMT?
NEURO?
10/3/22
→23/1/20
[redacted]
last 3/1
47.4
MTX 15mg
A.W.C.
11/ΜΑΡΤ/22
- Δέρμα
- Αρθρώσεις
Σχόλια
ΕΞΑΡΣΗ
vaccs 14/10/21
cognitive dysfunction
STOP
- Ανορεξία (+)
- Αϋπνία (+)
ΑΠ = 170/70 mmHg
Κόπωση (+)
Τριχόπτωση (+)
Πυρέτιο (+)
ΑΖΑ 1x2
MRI

CASE #1…

- 4 μήνες αργότερα(10/2022)
- Μεγάλη βελτίωση κλινικά !!!
- Υπό Belimumab 200mg/wk, AZA 100mg/d, Μεθυλπρεδνιζολόνη 8mg/d
- SLEDAI 4
- Σοβαρές συννοσηρότητες (αορτολαγόνια παράκαμψη χειρουργικά 10/2022 λόγω σοβαρής αθηρωματικής νόσου)
- Λοιπή αγωγή: Δενοσουμάμπη, Σιταλοπράμη 1x2, Καντεσαρτάνη 8, εζετιμίμπη/ατορβαστατίνη 10/40, Κλοπιδογρέλη 75, ανθρακικό ασβέστιο/βιταμίνη D3 1χ1

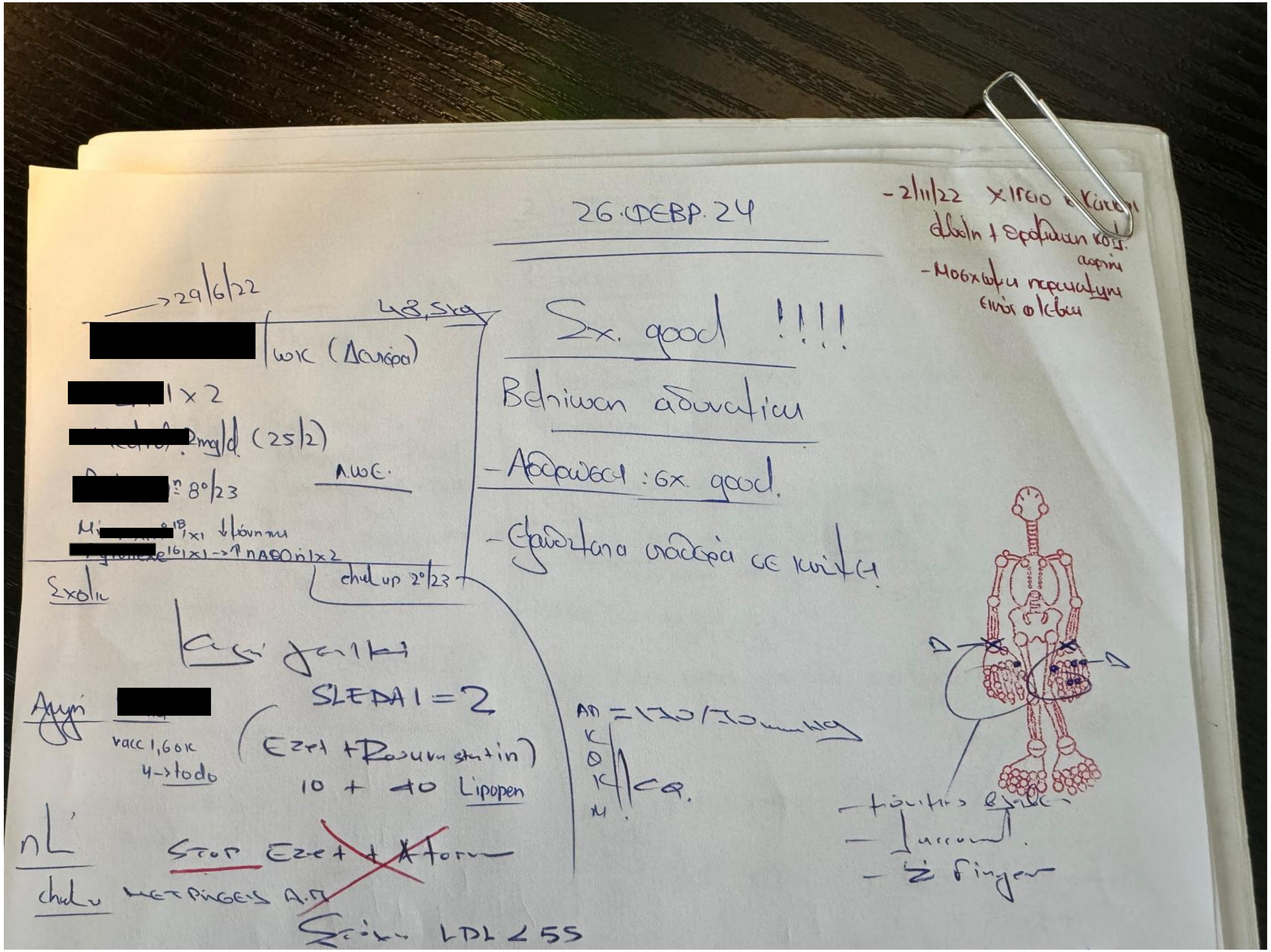
Πραγματικά προφίλ ασθενών από προσωπικό αρχείο

CASE #1…

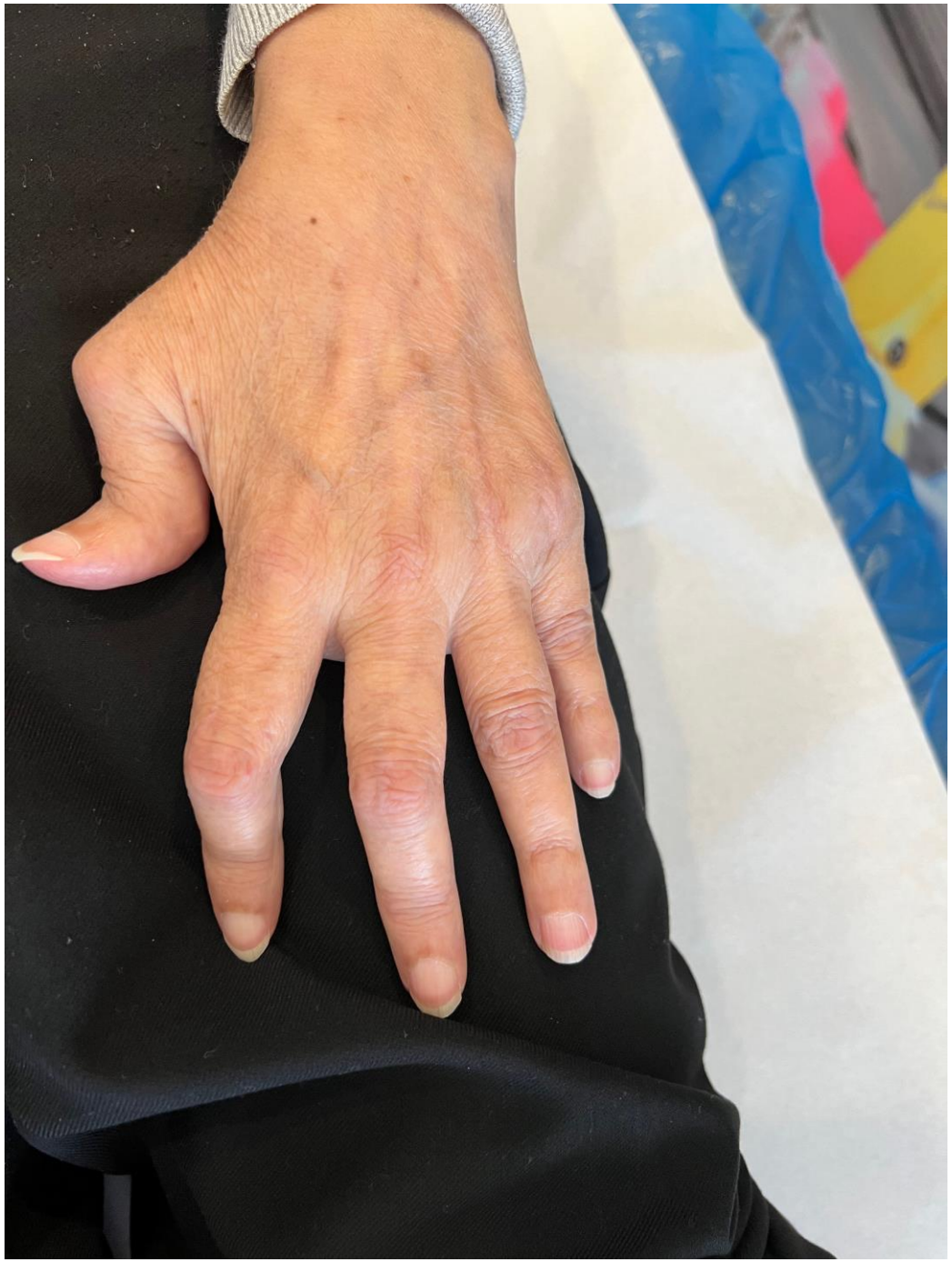
- 14 μήνες αργότερα… σε πρόσφατο πρό 3μήνου ραντεβού (02/2024)
- Αγωγή ως έχει από έναρξης Belimumab ➔ Αλλά… Μεθυλπρεδνιζολόνη μόνο 2mg/d (με προοπτική διακοπής)
- ΟΧΙ εξάνθημα, ΟΧΙαρθρίτιδα !!!
- Βελτίωση κόπωσης, ανάκτηση μυϊκής μάζας, βελτίωση ψυχολογίας, βελτίωση γνωσιακής ικανότητας
- SLEDAI 2, clinical SLEDAI 0
- όμως…**SDI 7**

Πραγματικά προφίλ ασθενών από προσωπικό αρχείο

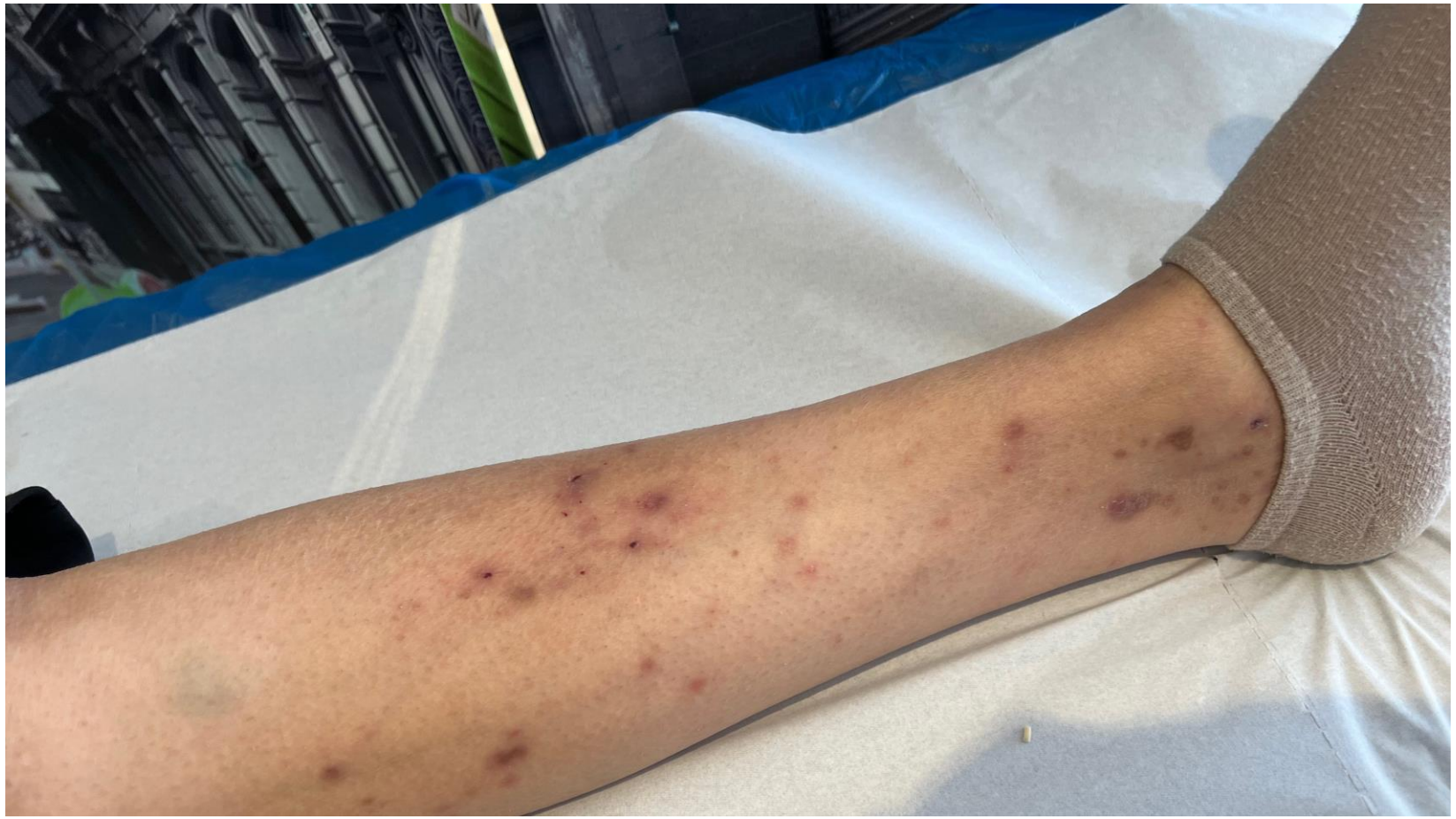
CASE # 1…



CASE #1

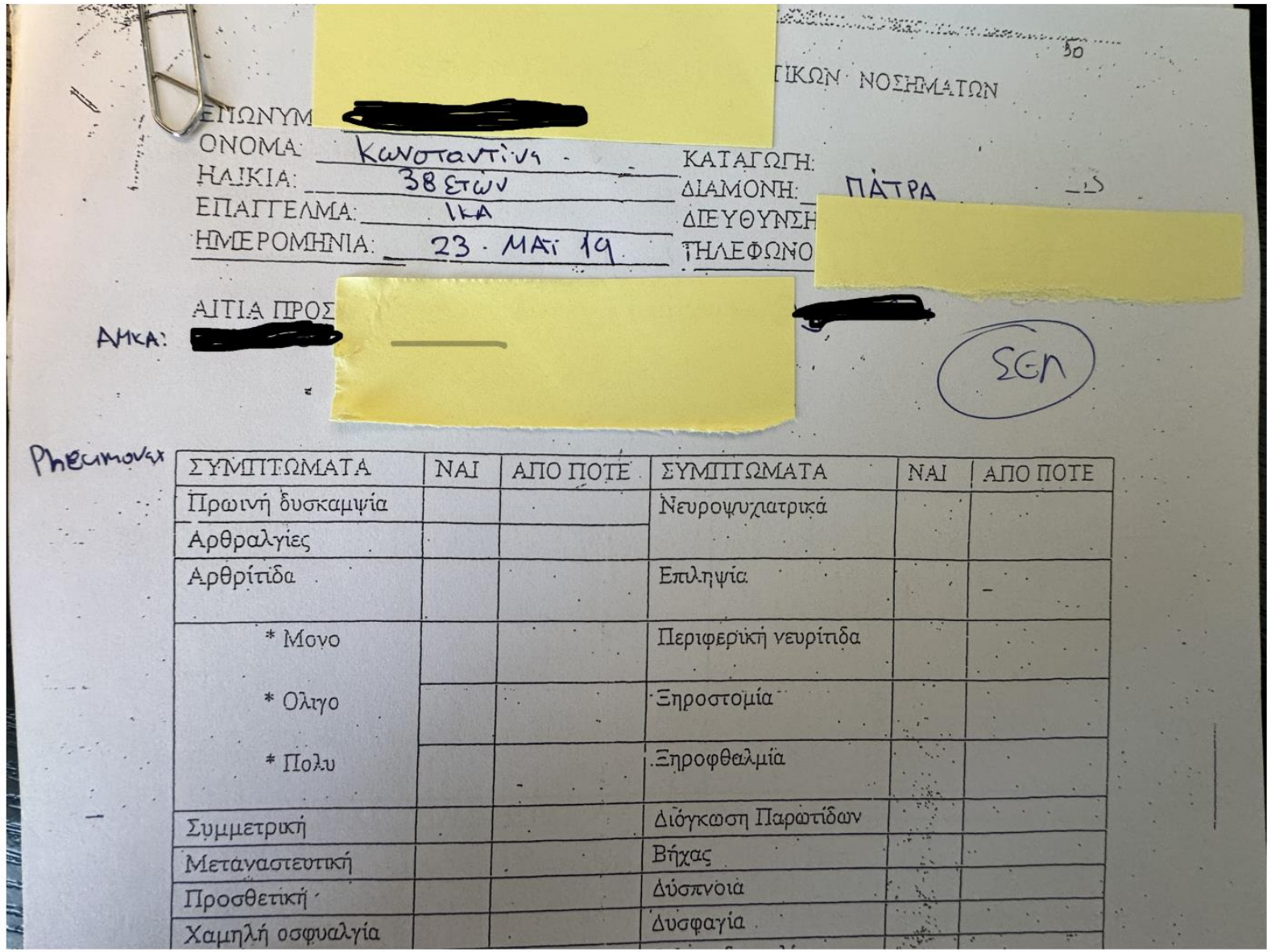


CASE #1…



SYSTEMIC LUPUS ERYTHEMATOSUS

CASE #2



50

ΤΙΚΩΝ ΝΟΣΗΜΑΤΩΝ

ΕΠΩΝΥΜ [redacted]
ΟΝΟΜΑ: Κωνσταντίνα
ΗΛΙΚΙΑ: 38 ετών
ΕΠΑΓΓΕΛΜΑ: ΙΚΑ
ΗΜΕΡΟΜΗΝΙΑ: 23 · ΜΑΪ 19

ΚΑΤΑΓΩΓΗ:
ΔΙΑΜΟΝΗ: ΠΑΤΡΑ
ΔΙΕΥΘΥΝΣΗ [redacted]
ΤΗΛΕΦΩΝΟ [redacted]

ΑΙΤΙΑ ΠΡΟΣ
ΑΜΚΑ: [redacted]

SGN

Rheumatic

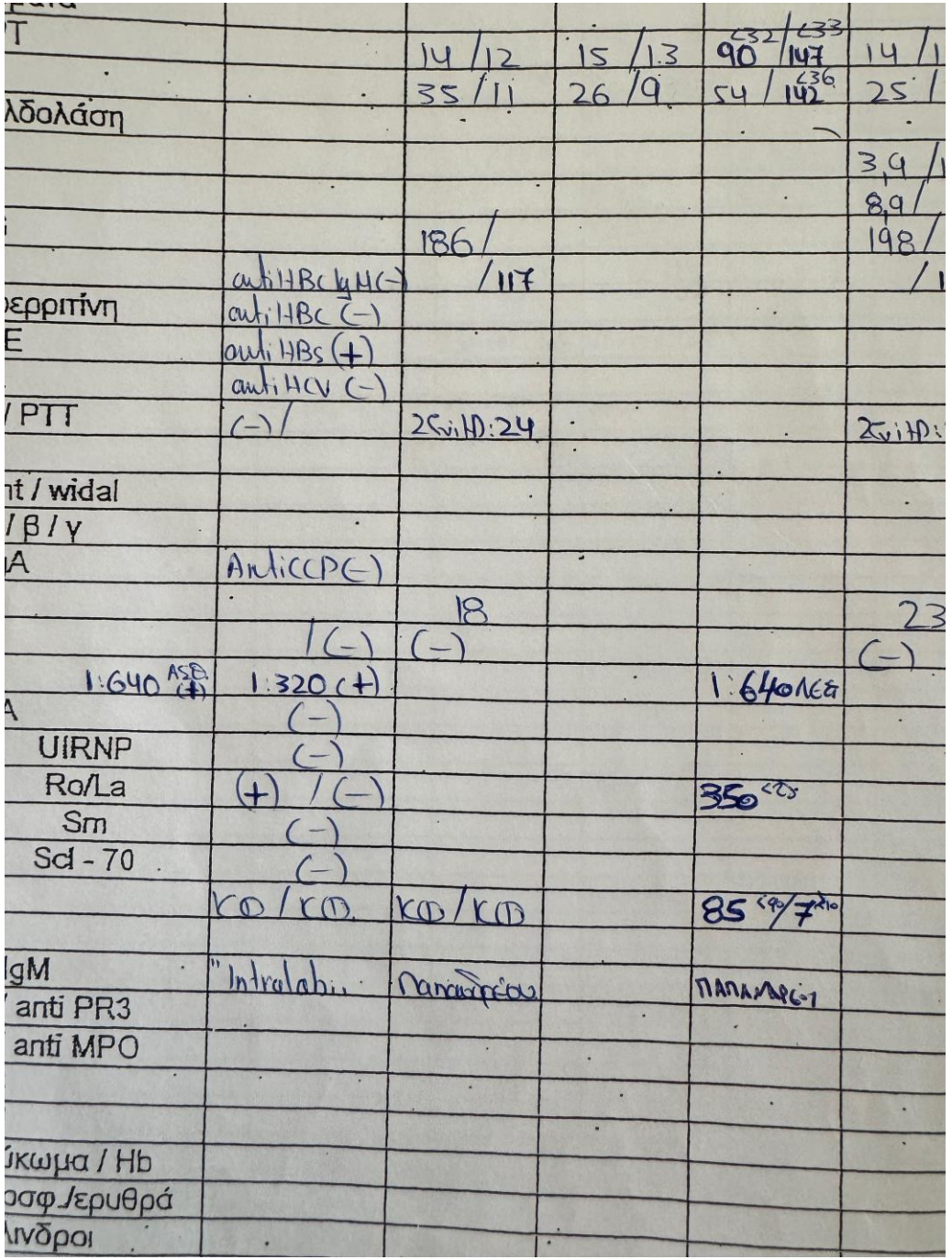
ΣΥΜΠΤΩΜΑΤΑ	ΝΑΙ	ΑΠΟ ΠΟΤΕ	ΣΥΜΠΤΩΜΑΤΑ	ΝΑΙ	ΑΠΟ ΠΟΤΕ
Πρωινή δυσκαμψία			Νευροψυχιατρικά		
Αρθραλγίες					
Αρθρίτιδα			Επιληψία		
* Μονο			Περιφερική νευρίτιδα		
* Ολιγο			Ξηροστομία		
* Πολυ			Ξηροφθαλμία		
Συμμετρική			Διόγκωση Παρωτίδων		
Μεταναστευτική			Βήχας		
Προσθετική			Δύσπνοια		
Χαμηλή οσφυαλγία			Δυσφαγία		

CASE#2

- 05/2019 στο ιατρείο
- Γυναίκα 38 ετών με διάγνωση ΣΕΛ από έτους
- Εκτεταμένο κηλιδοβλατιδώδες εξάνθημα ➔ Δερματολόγοι, Αλλεργιολόγοι ➔ θετικός ανοσολογικός έλεγχος ➔ Ρευματολόγος
  ➔ΣΕΛ=>Υδροξυχλωροκίνη 400mg/d (ΒΣ=82kg) και GCs IM και per os
  υψηλές δόσεις
- ANA 1: 320 λεπτός στικτός, anti-Ro/SSA (+)

Πραγματικά προφίλ ασθενών από προσωπικό αρχείο

CASE#2



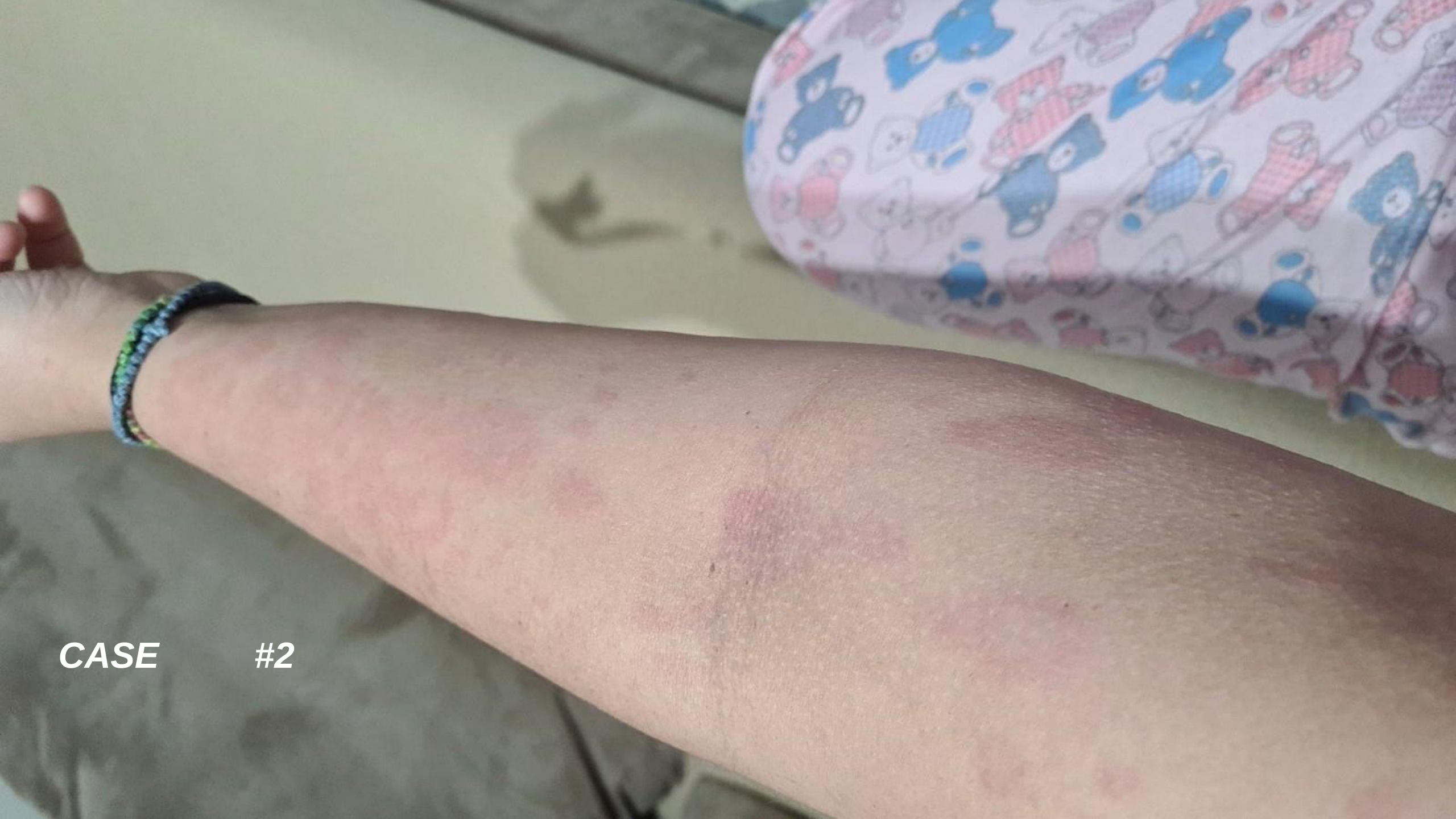
T		14 / 12	15 / 13	90 (32) / 147 (33)	14 / 1
		35 / 11	26 / 9	54 / 142 (36)	25 /
λδολάση					
					3,9 /
					8,9 /
		186 /			198 /
	anti HBc IgM (-)	/ 117			/ 1
ερριτίνη	anti HBc (-)				
E	anti HBs (+)				
	anti HCV (-)				
/ PTT	(-) /	25 νι ND: 24			25 νι ND:
nt / widal					
/ β / γ					
A	Anti CCP (-)				
		18			23
	/ (-)	(-)			(-)
1:640 ASO (+)	1:320 (+)			1:640 ΛΕΑ	
A	(-)				
UIRNP	(-)				
Ro/La	(+) / (-)			350 <20	
Sm	(-)				
Scl - 70	(-)				
	KD / KD	KD / KD		85 <90 / 7 x10	
IgM	"Intralab...	Παγκρέας		ΠΑΠΛΜΡΘ-1	
anti PR3					
anti MPO					
ύκωμα / Hb					
ασφ./ερυθρά					
Λινδροι					

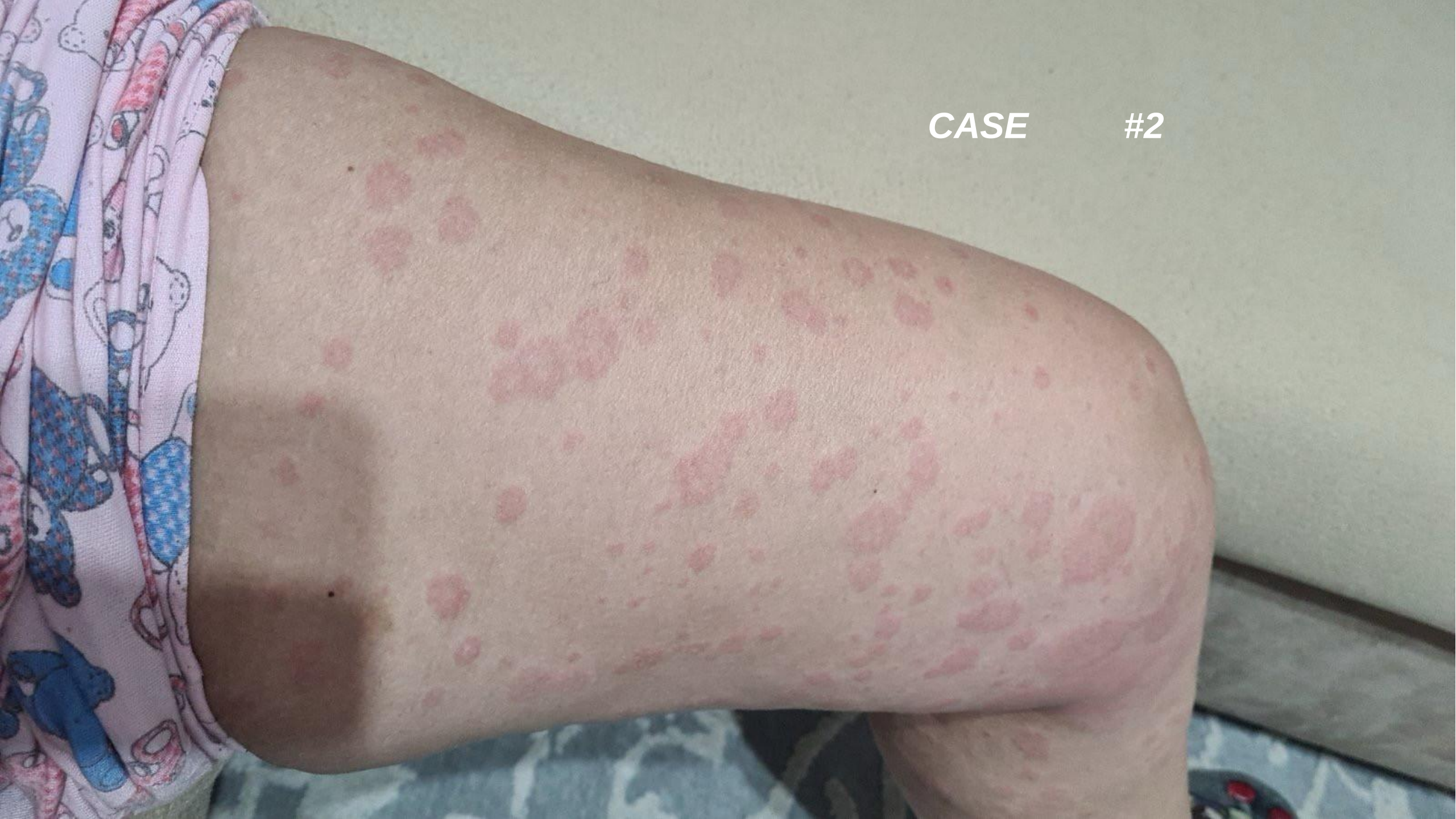
CASE#2

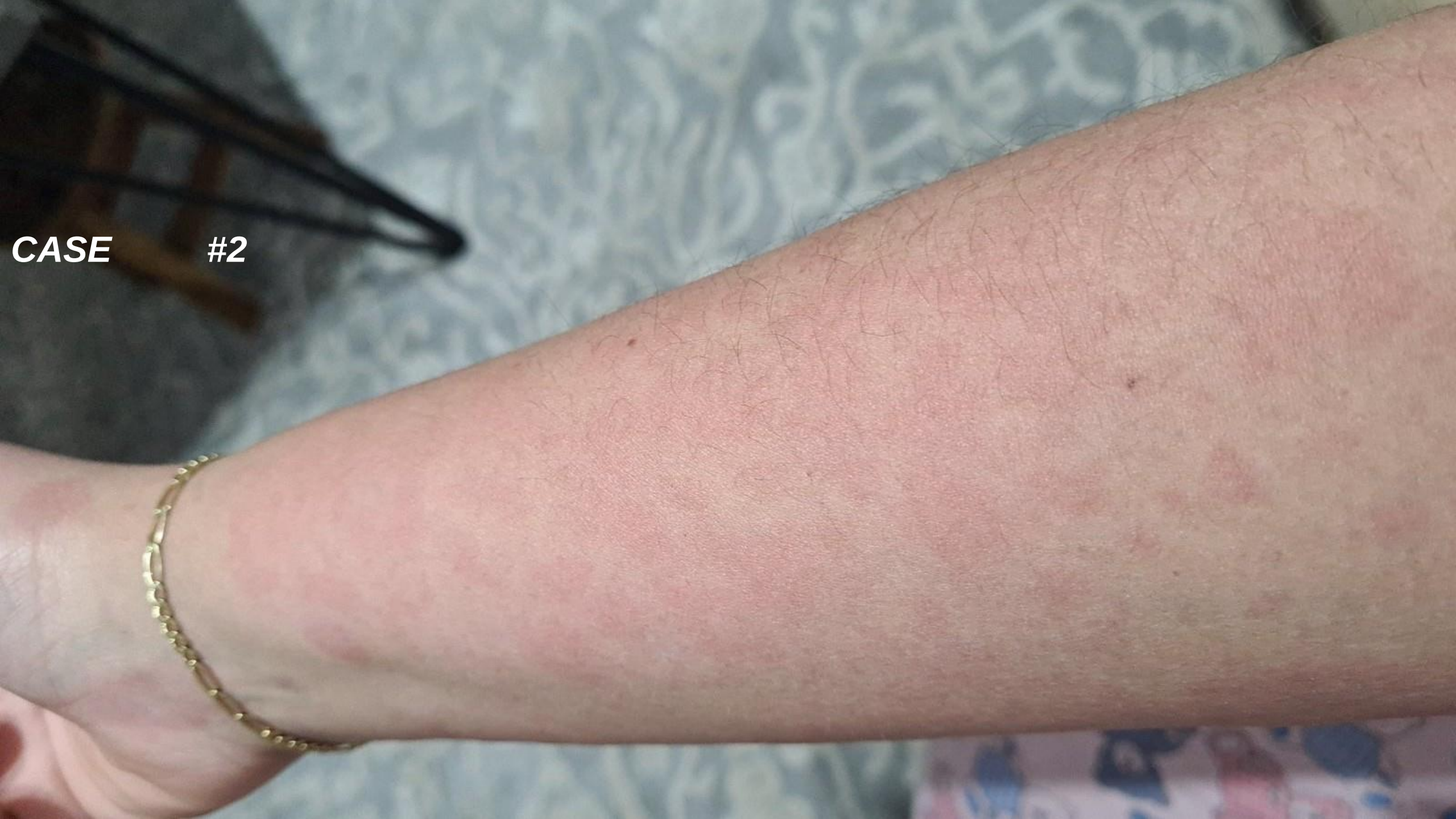
- Ήταν καλά για 2 χρόνια (πλην ήπιων αρθραλγιών και εύκολης κόπωσης)
- Υπό Υδροξυχλωροκίνη 400/200mg ΕΠΗ

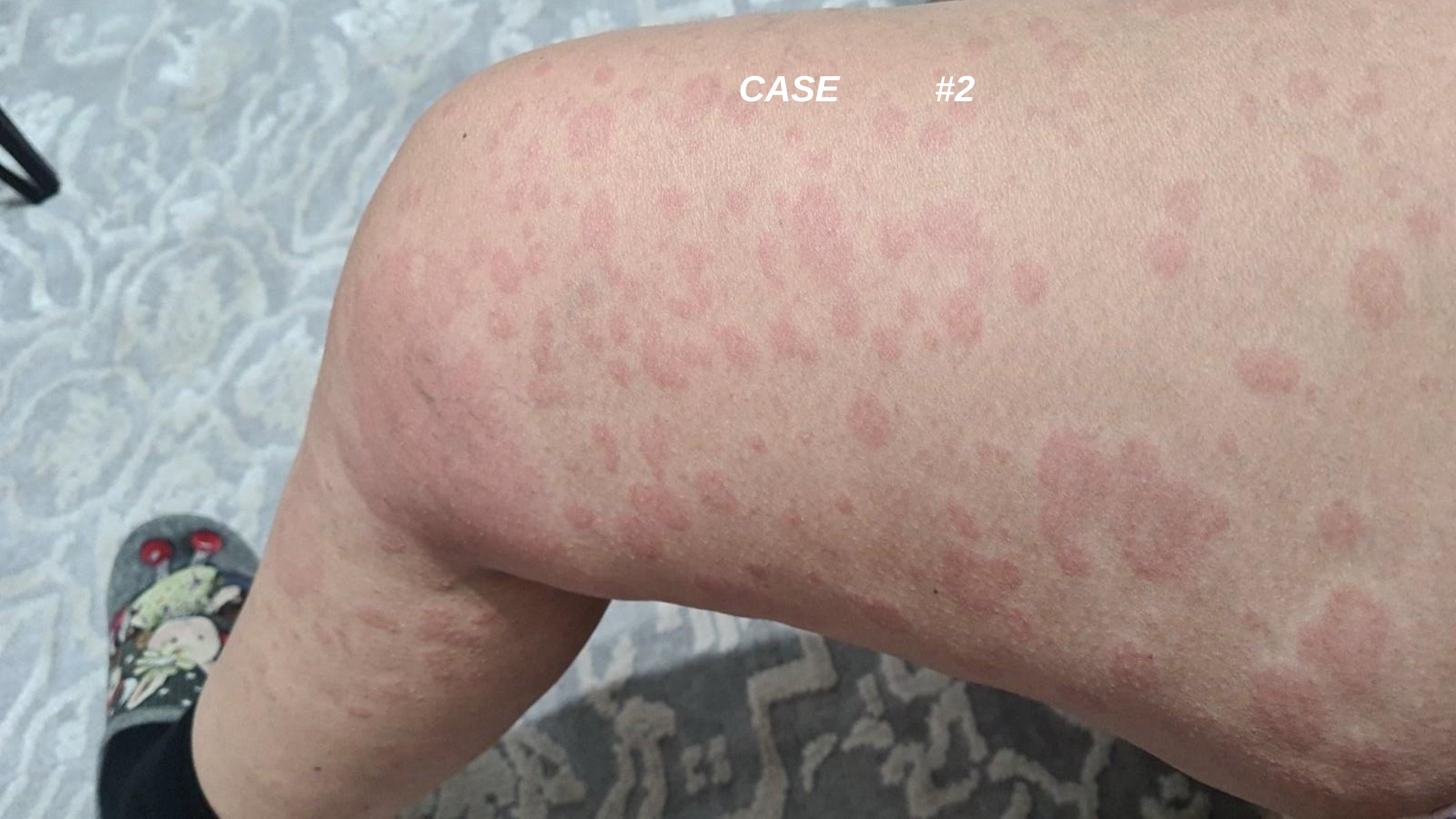
- 01/2022 (λοίμωξη COVID19 πρό 20μέρου) ➔
- ➔ εκτεταμένο κηλιδοβλατιδώδες εξάνθημα σε κορμό, άνω και κάτω άκρα, πρόσωπο και τριχωτό κεφαλής με ήπιο κνησμό, BSA=50

Πραγματικά προφίλ ασθενών από προσωπικό αρχείο


CASE #2


CASE #2

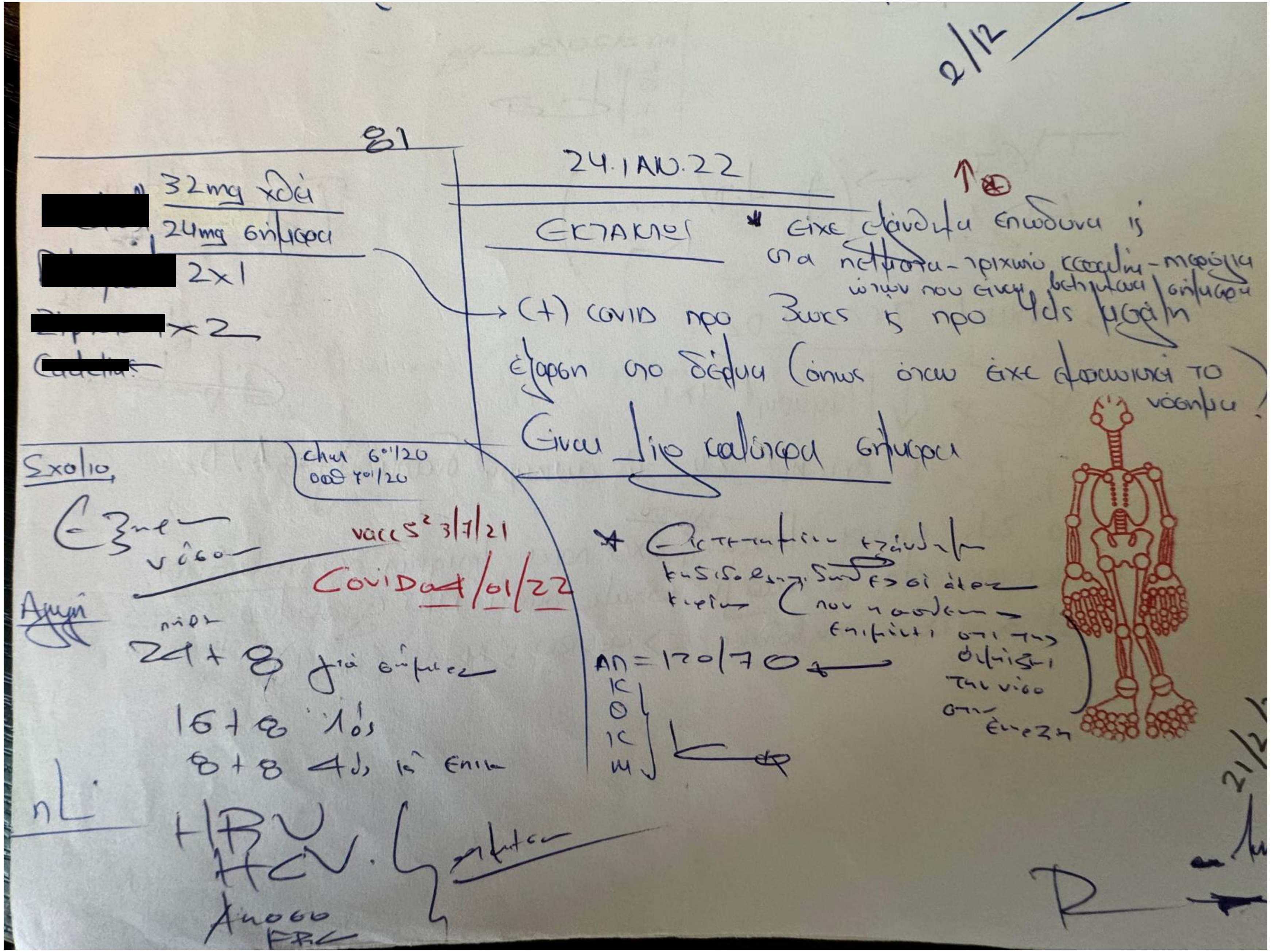

CASE #2


CASE #2

CASE #2

- Έναρξη Μεθυλπρεδνιζολόνης 32mg/d (με σταδιακή μείωση)
- Υδροξυχλωροκίνη 400mg/d
- Έλεγχος για HBV,HCV,TB,
- ΚΑΙ μοριακός έλεγχος για πολυμορφισμό γονιδίων μεθυλοτρανσφεράσης της θειοπουρίνης(Thiopurine-S-methyltransferase TPMT):
- Συγκεκριμένοι πολυμορφισμοί του γονιδίου οδηγούν σε μείωση ή πλήρη απουσία της ενεργότητας του ενζύμου σε 10-12% των Καυκάσιων ➔ Τοξικότητα στο μυελό των οστών

CASE#2



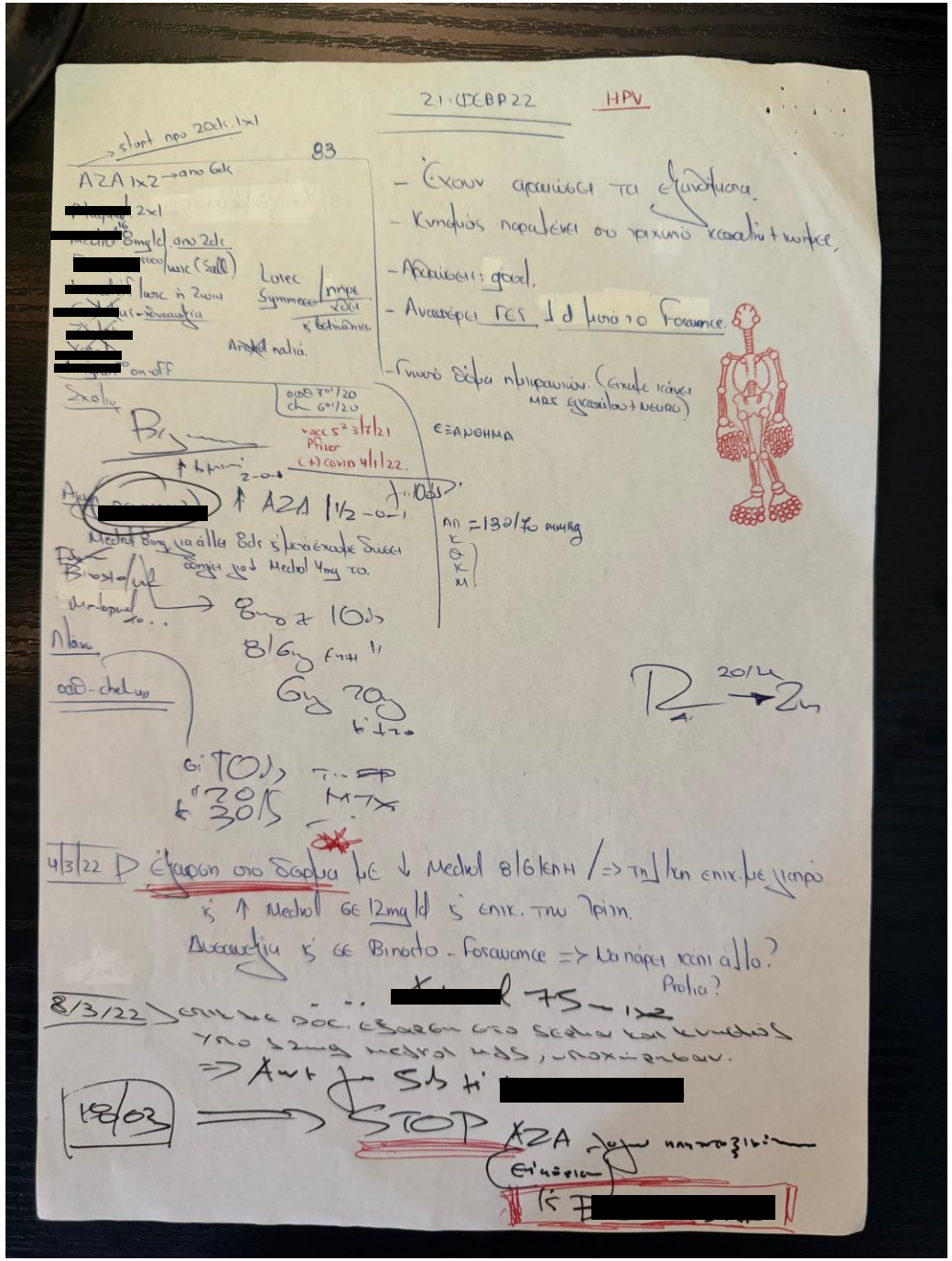
24.ΙΑΝ.22
2/12
32mg χθές
24mg σήμερα
[redacted] 2x1
[redacted] x2
[redacted]
ΕΚΤΑΚΤΟΣ
(+) COVID προ 3wks & προ 4ds μεγάλη
έξαρση στο δέρμα (όπως όταν είχε αρχικά το νόσημα)
Είναι λίγο καλύτερα σήμερα
Σχόλιο
COVID 04/01/22
ΑΠ = 120/70
HBV
HCV

CASE#2

- 02/2022
- Υπό AZA 100mg/d, Υδροξυχλωροκίνη 400mg/d, Μεθυλπρεδνιζολόνη 8mg/d
- Σχετική βελτίωση
- Αλλά… σε 2 wks νέα έξαρση και ηπατικά ένζυμα >3πλάσιο
- Διακοπή AZA , Μεθυλπρεδνιζολόνη24mg/d
- ΣΗΠ για **belimumab** 03/2022 ➔ (έναρξη…05/2022)

Πραγματικά προφίλ ασθενών από προσωπικό αρχείο

CASE #2



CASE#2

- 4μήνες αργότερα (09/2022)
- Μεγάλη βελτίωση!!!
- Ελάχιστο εξάνθημα, BSA=5
- Ήπιο σ.Cushing
- Αρθραλγίες (-), κόπωση (-)
- Διακοπή κορτιζόνης

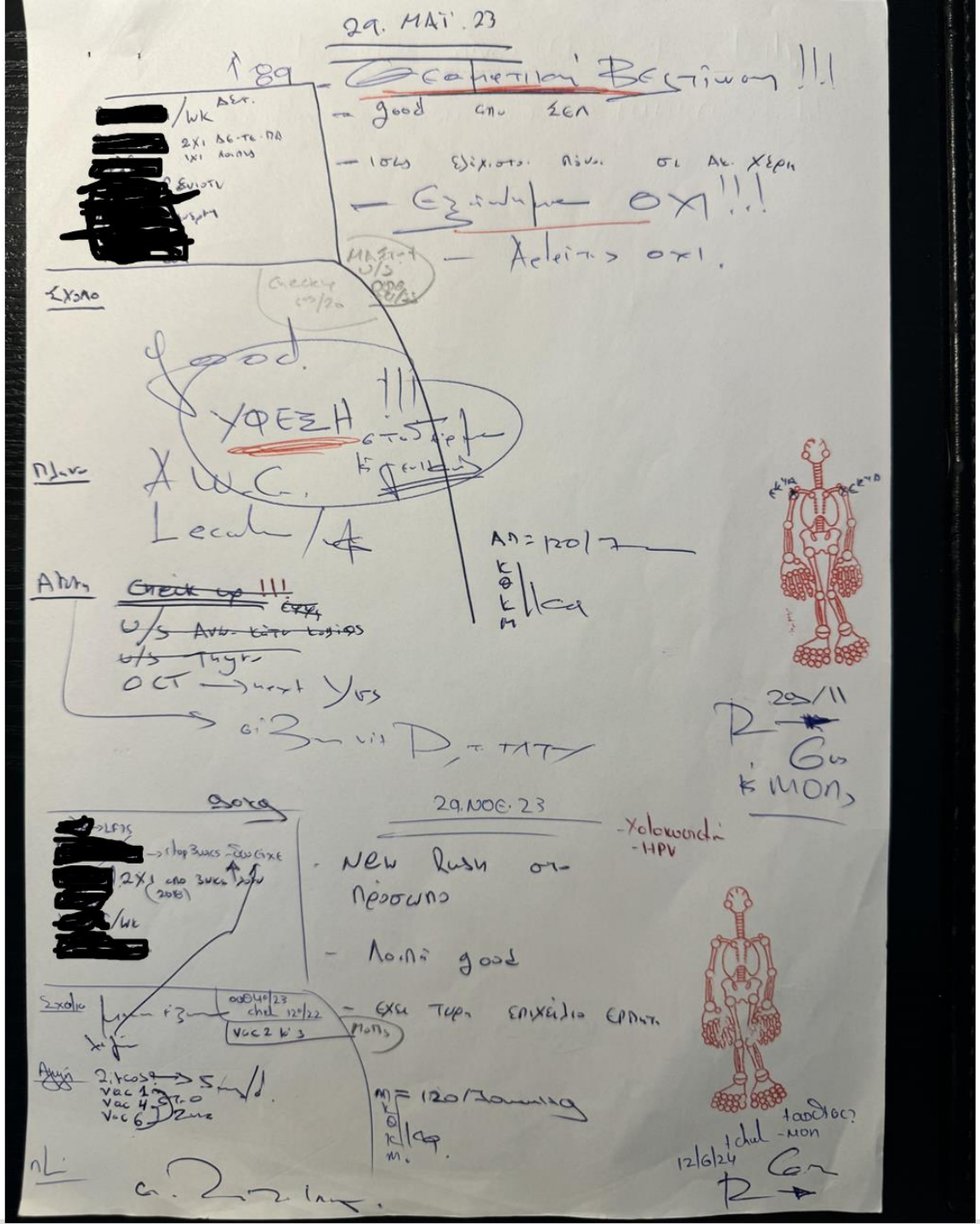
Πραγματικά προφίλ ασθενών από προσωπικό αρχείο

CASE#2

- 12μήνες αργότερα (05/2023)
- Θεαματική βελτίωση!!!
- **Απουσία εξανθήματοςαπό 6μήνου,** BSA=0
- σ.Cushing (-)
- Αρθραλγίες (-), κόπωση (-)
- **SLEDAI 0**
- **SDI 0**
- **GCs (-)**

Πραγματικά προφίλ ασθενών από προσωπικό αρχείο

CASE #2


29. ΜΑΪ. 23
good
ΧΦΕΣΗ !!!
Check up !!!
29/11
29.ΝΟΕ.23
New Rush ογ-
- Λοιπ good

Applying the Working Definition of the Disease Modification Criteria to Systemic Lupus Erythematosus Treatments From the Published Literature

Poster No. POS1153

Anca D Askanase[1], Richard Furie[2], Maria Dall'Era[3], Andrew S Bomback[1], Andreas Schwarting[4,5], Ming-Hui Zhao[6], Ian N Bruce[7], Munther Khamashta[8], Bernie Rubin[9], Angela Carroll[9], Mark Daniels[10], Roger Abramino Levy[11], Ronald van Vollenhoven[12], Murray B Urowitz[13]

[1]Department of Medicine, Columbia University Irving Medical Center, New York, NY, USA; [2]Division of Rheumatology, Northwell Health, Great Neck, NY, USA; [3]Division of Rheumatology, University of California San Francisco School of Medicine, San Francisco, CA, USA; [illegible]

Introduction

- Systemic lupus erythematosus (SLE) is a chronic, multisystemic autoimmune disease, where 30–50% of patients develop organ damage within 5 years of diagnosis[1,2]
- Classification of available treatments for SLE as disease modifying would assist in comparing treatments and informing treatment decision-making
- Recently, criteria for disease modification in SLE have been proposed as 'minimizing disease activity with the fewest treatment-associated toxicities and slowing or preventing organ damage progression'[3]
  - Evaluation criteria at three time points were also proposed

Objective

To review the published literature of extra-renal disease lupus and apply the proposed criteria to SLE treatments at three time points

Methods

- A selection of SLE clinical trial (n=32) and clinical practice/observational (n=54) publications that contained outcomes relevant to the criteria across different treatment classes were reviewed (authors' clinical experience was also considered for inconclusive/missing data), and outcomes were matched to the proposed extra-renal disease modification criteria at three time points (1 year, 2–5 years, and >5 years)
  - Specific criteria at each time point were designated as: having been met; insufficient evidence in literature, but strong general indications of criterion met; inconclusive (unclear if data available satisfies the criterion); no data available in selected literature to support the criterion as met; or data were available in the literature, but there was a negative impact on criterion
- While safety was included in the definition of disease modification, the focus of this review was the extra-renal disease activity components of the definition

Results

Table 1. Application of the proposed matrix for extra-renal disease activity and organ damage disease modification criteria

Product	DISEASE MODIFICATION POTENTIAL		DISEASE MODIFICATION CONFIRMED (BEYOND 5 YEARS)
	Outcomes Year 1	Outcomes Years 2–5	Outcomes Year >5
	1 Significant reduction in disease activity measured using a validated tool (i.e. SELENA-SLEDAI, BILAG, SRI-4) 2 Significant reduction in severe flare measured using a validated tool (i.e. SFI or BILAG) 3 Reduction in use of steroids* and/or immunosuppressants	1 Sustained improvement in multiple organ domains/no worsening in multiple organ domains 2 Prevention of severe flares 3 Continued reduction in use of steroids* and/or immunosuppressants	No change in SDI or delayed progression
Glucocorticoids	1 green; 2 yellow; 3 red	X red; X red; 3 yellow	X red
Hydroxychloroquine†	1 green; 2 yellow; 3 red	1 green; 2 yellow; 3 yellow	§ green
Immunosuppressants			
Azathioprine	1 red; 2 red; 3 yellow	1 red; 2 red; 3 yellow	red
Cyclophosphamide	1 green; 2 red; 3 red	1 red; 2 red; 3 red	red
Leflunomide	1 green; 2 red; 3 red	1 red; 2 red; 3 red	red
Methotrexate	1 yellow; 2 red; 3 yellow	1 red; 2 red; 3 red	red
Mizoribine	1 red; 2 red; 3 red	1 red; 2 red; 3 red	red
Mycophenolate mofetil	1 green; 2 red; 3 yellow	1 yellow; 2 yellow; 3 yellow	red
Calcineurin inhibitors			
Cyclosporine	1 yellow; 2 red; 3 yellow	1 red; 2 red; 3 red	red
Tacrolimus	1 green; 2 red; 3 yellow	1 red; 2 red; 3 red	red
Biologics			
Abatacept	1 green; 2 yellow; 3 red	1 red; 2 red; 3 red	red
Anifrolumab	1 green; 2 green; 3 green	1 green; 2 green; 3 green	red
Belimumab	1 green; 2 green; 3 green	1 green; 2 green; 3 green	green
Rituximab	1 green; 2 green; 3 yellow	1 yellow; 2 red; 3 yellow	red

Green, criterion met; green (§), insufficient evidence in the literature to meet the specific criterion, but strong general indications of criterion met; yellow, inconclusive; red, data not available in the literature to support criterion met; red (X), data were available in the literature, but there was a negative impact on criterion.

*≤7.5 mg/day per 2019 EULAR SLE treatment guidelines and LLDAS (prednisolone-equivalent)[6,7]; ≤5 mg/day (prednisolone-equivalent) per DORIS remission definition;[8] †includes chloroquine diphosphate.

BILAG, British Isles Lupus Assessment Group; DORIS, definition of remission in SLE; LLDAS, Lupus Low Disease Activity State; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; SELENA-SLEDAI, Safety of Estrogens in Lupus Erythematosus National Assessment - SLE Disease Activity Index; SFI, SELENA-SLEDAI flare index; SRI-4, SLE Responder Index-4.

- **Table 1** shows which disease modification criteria were met (green), or for which data were inconclusive (yellow) or not available/indicated a negative impact (red) at each of the three time points
- Most of the SLE treatments (n=10/14) evaluated met at least one disease modification criterion across all time points (**Table 1**)
- For many SLE treatments, data relevant to the specific criteria at each time point were lacking or inconclusive according to our disease modification criteria definitions
- Hydroxychloroquine improved cumulative 15-year survival rates (0.95 versus 0.68 [p<0.001] with and without hydroxychloroquine, respectively), which is suggestive of slowed organ damage progression and long-term disease modification; however, data pertaining to the specific criterion (no change in SDI or delayed progression) are lacking[4]
- Belimumab met all of the criteria at the first two time points and was the only treatment to meet disease modification criteria at >5 years based on the current literature
  - In a post hoc propensity score matched longitudinal analysis, the change in SDI at Year 5 was significantly reduced with belimumab versus standard therapy (mean difference [95% confidence interval]: −0.434 [−0.667, −0.201]; p<0.001)[5]
- While glucocorticoids certainly decrease disease activity at early time points, doses >7.5 mg/day (prednisone-equivalent) can negatively impact damage accrual, hampering their disease modification potential >5 years

Conclusions

- The use of multiple agents in combination, differences in study designs, patient populations, and definitions of treatment response pose challenges in categorising SLE treatments as disease modifying using the recently published criteria
- Of the 14 SLE treatments evaluated, only hydroxychloroquine and belimumab met the recently published disease modification criteria at all three time points

Disclosures

[illegible]

Acknowledgements

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2. Chambers SA, et al. Rheumatology 2009;48(6):673–5.
3. van Vollenhoven R, et al. Lupus Sci Med 2022;9(1):e000634.
4. Ruiz-Irastorza G, et al. Lupus 2006;15(9):577–83.
5. Urowitz MB, et al. Ann Rheum Dis 2019;78(3):372–9.
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7. Franklyn K, et al. Ann Rheum Dis 2016;75(9):1615–21.
8. van Vollenhoven RF, et al. Lupus Sci Med 2021;8(1):e000538.

Please find the online version of this poster by scanning the QR code or via [illegible]

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Poster presented at the European Alliance of Associations for Rheumatology Congress, 31 May – 3 June 2023, Milan, Italy

the Published Literature

osed matrix for extra-renal disease activity and organ damage disease modification criteria

DISEASE MODIFICATION POTENTIAL		DISEASE MODIFICATION CONFIRMED (BEYOND 5 YEARS)
Outcomes Year 1	Outcomes Years 2–5	Outcomes Year >5
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1 2 3	X X 3	X
1 2 3	1 2 3	§

	(i.e. SFI or BILAG) 3 Reduction in use of steroids* and/or immunosuppressants	3 Continued reduction in use of steroids* and/or immunosuppressants	
Glucocorticoids	1 2 3	X X 3	X
Hydroxychloroquine†	1 2 3	1 2 3	§
Immunosuppressants			
Azathioprine	1 2 3	1 2 3	●
Cyclophosphamide	1 2 3	1 2 3	●
Leflunomide	1 2 3	1 2 3	●
Methotrexate	1 2 3	1 2 3	●
Mizoribine	1 2 3	1 2 3	●
Mycophenolate mofetil	1 2 3	1 2 3	●
Calcineurin inhibitors			
Cyclosporine	1 2 3	1 2 3	●
Tacrolimus	1 2 3	1 2 3	●
Biologics			
Abatacept	1 2 3	1 2 3	●
Anifrolumab	1 2 3	1 2 3	●
Belimumab	1 2 3	1 2 3	●
Rituximab	1 2 3	1 2 3	●

●, criterion met; §, insufficient evidence in the literature to meet the specific criterion, but strong general indications of criterion met; ●, inconclusive; ●, data not available in the literature to support criterion met; X, data were available in the literature, but there was a negative impact on criterion.

*≤7.5 mg/day per 2019 EULAR SLE treatment guidelines and LLDAS (prednisolone-equivalent)[A,T]; ≤5 mg/day (prednisolone-equivalent) per DORIS remission definition;[B] †includes chloroquine diphosphate.

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Ρωμαϊκό ΩδείοΠάτρας

- THANK