Application of lupus comprehensive disease control in newly diagnosed systemic lupus erythematosus patients: results from the Italian multicentre Early Lupus Project inception cohort

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Abstract

Objective

The concept of Comprehensive Disease Control (CDC) underlines as the control of disease activity should be associated with damage inhibition. Recently, this concept has been proposed in Systemic Lupus Erythematosus (SLE) patients (LupusCDC) with long-standing disease. In the present analysis we evaluated the incidence of LupusCDC in a cohort of newly diagnosed patients.

Methods

We analysed data from the multicentre cohort of the Early Lupus Project. Disease activity was evaluated by ECLAM and chronic damage by SDI. At each available time point, the presence of remission condition was assessed, defined as: Complete remission in GCs (GCon): ECLAM=0, antimalarials and/or immunosuppressants, PDN ≤5 mg/day; and Complete remission without GCs (GCoff): ECLAM=0, antimalarials and/or immunosuppressants. The presence of LupusCDC was analysed, defined as remission in the absence of progression of chronic damage (LupusCDC-GCon and LupusCDC-GCoff).

Results

We included 239 patients [205F; mean±DS age 45.8±14.6 years] with a follow-up of 36 months. During this period, 33.08% of patients achieved LupusCDC-GCon, while 12.03% LupusCDC-GCoff in at least one evaluation. Univariate analysis showed the association between failure to achieve LupusCDC-GCon and musculoskeletal manifestations ($p<0.001$), activity in renal and neuropsychiatric domains ($p=0.01$, $p<0.001$, respectively), association confirmed by the multivariate analysis.

Conclusion

CDC in early onset SLE is not uncommon. Indeed, one-third of patients achieved LupusCDC-GCon in at least one evaluation. More severe disease, characterised by active renal and neuropsychiatric manifestations represented a risk factor for failure to achieve LupusCDC. The lower incidence of LupusCDC-GCoff suggested the difficulty in discontinuing GC treatment in early disease phase.

Key words

systemic lupus erythematosus, disease activity, chronic damage, comprehensive disease control, outcome

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Received on November 19, 2024;
accepted in revised form on April 8, 2025.

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Competing interests: M. Mosca has received honoraria for consultancies, speakers' fees and research support from AbbVie, AstraZeneca, BMS, Eli-Lilly, Galapagos, GSK, Idorsia, Miltenyi, Novartis, Ostuka, Roche and UCB. F. Franceschini and M. Fredi have received honoraria from AstraZeneca and GSK.
The other authors have declared no competing interests.

Introduction

The control of disease activity represents one of the most important outcomes in the management of Systemic Lupus Erythematosus (SLE) patients (1). Even though several indices could be applied to assess SLE-related disease activity, the most frequently used index is definitely the SLEDAI, revised in 2002 in the SLEDAI-2k version, that was applied in different randomised controlled trials but also in a real-life setting (2, 3). Furthermore, the ECLAM was proposed in 1992 and has been applied in different studies, mainly including European SLE cohorts (4). The concept of remission in SLE patients is extremely complex due to clinical and laboratory heterogeneity. Thus, several definitions have been proposed, generally including SLEDAI-2k, but also the dosage of glucocorticoids (GCs), the treatment with immunosuppressant drugs and the evaluation of Physician Global Assessment (5). The most stringent definition is certainly that of complete remission (CR), requiring a SLEDAI-2k value equal to zero and allowing only antimalarials treatment (6). In this context, the duration of remission status is another relevant parameter to consider, due to its influence on the damage accrual prevention (6).

Remission status can be reached thanks to the availability of a great number of drugs, including biological agents, and to the application of treat-to-target strategy (7, 8). This approach, now widespread in different rheumatological conditions such as rheumatoid arthritis (RA), is able to control disease activity and therefore to change the disease course in terms of chronic damage (9).

The disease activity significantly impacts the development of damage, by contributing directly, with the tissue deposition of immune complexes, and indirectly, due to the treatment adverse events. In particular, the long-term use of GCs has been associated with the chronic damage development in different systems, such as diabetes, osteoporosis, avascular necrosis, cataract. As known, these conditions are included in the SLICC Damage Index (SDI), the only validated index to assess chronic damage in SLE patients (10). Its application in large SLE cohorts confirmed the association between chronic damage and the use of GCs (11,12). On the other hand, other factors could contribute to the damage development. Among these, a genetic predisposition and the presence of anti-phospholipid antibodies (11, 13). The available evidence suggests the possible progression of chronic damage despite the control of disease activity. Into this scenario fits the concept of Comprehensive Disease Control (CDC), firstly proposed for RA, that underlines as the control of disease activity must be achieved along with the control of chronic damage progression (14). We previously proposed the application of CDC in SLE patients (the so-called LupusCDC): this new outcome includes a remission status lasting at least one year, where there is no progression in chronic damage. The evaluation of a large monocentric SLE cohort demonstrated the achievement of LupusCDC in at least one time-point in 47.7% of patients. Furthermore, the lack of LupusCDC achievement was significantly associated with GCs treatment and the presence of renal involvement during disease course (15).

Moving from this background, in the present study we evaluated the incidence of LupusCDC in a large cohort of SLE patients with early disease,

Patients and methods

Early Lupus inception cohort

The Early Lupus Project comprises Italian centres with a great deal of experience in the diagnosis and management of SLE. An inception cohort of consecutive patients who were enrolled within 12 months since recognition of four or more 1997 ACR classification criteria for SLE (16), was recruited from January 2012 to December 2017. The patients were followed up every 6 months. The study was approved by the Ethics Committee of each participating centre, and all patients provided written informed consent.

Patients and clinical assessment

Patients who were followed up for at least 6 months (*e.g.* two visits) were included in the present analysis. The

Table I. Main clinical features, recorded according the 1997 ACR classification criteria, and immunological features at the enrolment in the Early Lupus project.

Clinical manifestations according to 1997 ACR classification criteria	n=239
Malar rash, n (%)	74 (31.1)
Discoid rash, n (%)	22 (9.3)
Photosensitivity, n (%)	71 (30)
Oral ulcers, n (%)	35 (14.9)
Non-erosive arthritis, n (%)	144 (60.8)
Pleuritis or Pericarditis, n (%)	60 (25.1)
Renal disorders, n (%)	76 (32.1)
Neurologic disorders, n (%)	21 (8.9)
Haematologic disorder, n (%)	132 (55.5)
Laboratory modifications	
ANA, n (%)	236 (98.7)
Anti-dsDNA, n (%)	178 (77,7)
Anti-Ro, n (%)	90 (41.3)
Anti-La, n (%)	39 (18.2)
Anti-RNP, n (%)	48 (22.6)
Anti-Sm, n (%)	49 (23)
Anti-Cardiolipin IgG/IgM, n (%)	57 (28.9)
Anti-b2 Glycoprotein I IgG/IgM, n (%)	44 (23.2)
Lupus Anticoagulant, n (%)	46 (24.1)
C3 levels, mg/dl (mean±SD)	72.7 ± 34.3
C4 levels, mg/dl (mean±SD)	12.1 ± 11.4

only exclusion criterion was more than 12 months elapsed since recognition of four or more 1997 ACR classification criteria for SLE (16). Demographic features, including age, gender, ethnicity, years of school education and socioeconomic status (*e.g.* low, intermediate or high), were recorded. The time elapsed since the onset of the first symptom related to SLE was also noted at baseline. Disease biomarkers including anti-dsDNA, anti-Ro/SSA, anti-La/SSB, anti-Sm, anti-RNP, aCL (IgM and IgG), anti-B2-glycoprotein I (IgM and IgG), Lupus Anticoagulant (LA), 24-h proteinuria, and C3 and C4 complement fractions were tested in the local laboratories at each centre. Ongoing treatment with GCs, antimalarials (AMs), immunosuppressants (IS), including biologic agents, or a combination of these agents was recorded at each visit, together with the cumulative prednisone equivalent dose. Disease activity based on the validated ECLAM (4) and cumulative damage according to the SDI (10) were measured every 6 months. Clinical manifestations defined according to items and domains of the validated BILAG-2004 index glossary were recorded (17).

Lupus Comprehensive Disease Control (LupusCDC)

According to ECLAM values and to current treatment, we defined two types of remission:

- Complete Remission GCon (CR-GCon): ECLAM = 0, treatment with AMs and/or IS and/or biological drugs, PDN ≤5 mg/die;
- Complete Remission GCoff (CR-GCoff): ECLAM = 0, treatment with AMs and/or IS and/or biological drugs, no treatment with GCs.

Accordingly, we defined two types of LupusCDC:

- LupusCDC-GCon: CR-GCon + ΔSDI = 0 (no increase in SDI values from the previous assessment);
- LupusCDC-GCoff*:* CR-GCoff + ΔSDI = 0 (no increase in SDI values from the previous assessment).

Statistical analysis

Demographic and clinical characteristics of SLE patients were described with means (± SD) or median (interquartile range) for continuous variables, and frequencies (%) for categorical variables. Differences between groups were assessed by using the Student's t-test, Mann-Whitney U-test and the Pearson chi-squared or Fisher's exact test for categorical variables. A paired Wilcoxon sign-rank test was used when group samples were not independently distributed.

Univariable and multivariable time-dependent Cox proportional hazards models were used to assess the impact of patient's demographic and clinical characteristics – accounting for changes over time – on the likelihood of reaching the CDC-GC-on/off outcome. In the multivariable models we employed a stepwise selection approach by including sex and age as fixed variables, while among the clinical ones mildly significant at univariable analysis (α=0.20) were included. The results were expressed as hazard ratio (HR) with 95% confidence intervals (95%CI).

All statistical analyses were performed using R v. 4.0.5 (the R Foundation for Statistical Computing, Vienna, Austria).

Results

For the present study we analysed 239 SLE patients [205 females (86.5%); mean age ±SD 45.8±14.6 years; Caucasian ethnicity 214 (89.9%)]. Eighteen patients (7.7%) reported a family history of SLE. The main clinical features, recorded according the 1997 ACR classification criteria, and immunological features are summarised in Table I. Non-erosive arthritis, involving ≥2 peripheral joints according to 1997 ACR criteria, was the most frequent manifestation in the present cohort, observed in 60.8% of patients, followed by hematologic disorders, identified in 55.5% of subjects. Furthermore, we registered data on requiring treatment comorbidities; in detail, diabetes was observed in 3.4% of patients, arterial hypertension in 17.2%, dyslipidaemia in 14.3%, osteoporosis in 2.5% and cancer in 2.5%. Regarding treatments, at baseline we observed a mean cumulative PDN dosage of 1907.1 mg (SD 3273.1).

At the time of enrolment, we observed a mean ECLAM value equal to 2.9 (SD 2.3). Furthermore, we registered data about the activity in the different domains according to BILAG index, which are summarised in Table II. As reported in this table, at the study entry, the enrolled patients showed an active involvement more frequently at level of musculoskeletal domain (59.7%), followed by mucocutaneous (48.3%), constitutional (34.6%) and renal (31.5%).

A mean SDI equal to 0.2 (SD 0.5) was registered in patients with more than 6 months disease duration at study entry.

Table II. Activity in the different domains evaluated according to the BILAG (*British Isles Lupus Assessment Group*) index.

BILAG manifestations	n (%)
Constitutional manifestations	82 (34.6)
Mucocutaneous manifestations	115 (48.3)
Neuropsychiatric manifestations	17 (7.1)
Musculoskeletal manifestations	142 (59.7)
Cardiorespiratory manifestations	47 (19.7)
Gastrointestinal manifestations	11 (4.6)
Ophtalmic manifestations	4 (1.7)
Renal manifestations	75 (31.5)
Haematological manifestations	99 (41.6)

The present SLE cohort was prospectively followed for a period of 36 months. Figure 1A-B reports the modifications of ECLAM and SDI values during this observational period. We found a significant decrease of ECLAM values at 6 months follow-up ($p<0.001$; conversely; SDI values significantly increased after 6 months ($p<0.001$).

Thus, we evaluated the incidence of LupusCDC in the Early Lupus Cohort during a 36-months follow-up. In detail we evaluated LupusCDC-GCon in 216 SLE patients [186 females, mean age 46.9 years (SD 14.8)], and LupusCDC-GCoff in 221 subjects [191 females, mean age 46.9 years (SD 14.5)]. For these patients all data needed to define LupusCDC outcome were available; furthermore, we exclude from the analysis those patients showing a LupusCDC condition already at baseline. Data on these subgroups are reported in the online Supplementary files (Suppl. Table S1).

In these cohorts, the incidence of LupusCDC-GCon was 33.1% (95%CI 25.17–41.77) and of LupusCDC-GCoff 12.0% (95%CI 7.04–18.8). Accordingly, the incidence of LupusCDC-GCon was significantly higher than LupusCDC-GCoff ($p=0.006$).

Furthermore, incidence rates were 10.22 years per 100 person years (95%CI 8.1–12.7) for LupusCDC-GCon and 2.85 years per 100 person years (95%CI 1.88–4.15) for LupusCDC-GCoff. We evaluated the time spent in a condition of LupusCDC: we observed a median time equal to 12 months (IQR 12.0–19.5) for LupusCDC-GCon and equal to 12 months (IQR 12.0–18.0) for LupusCDC-GCoff.

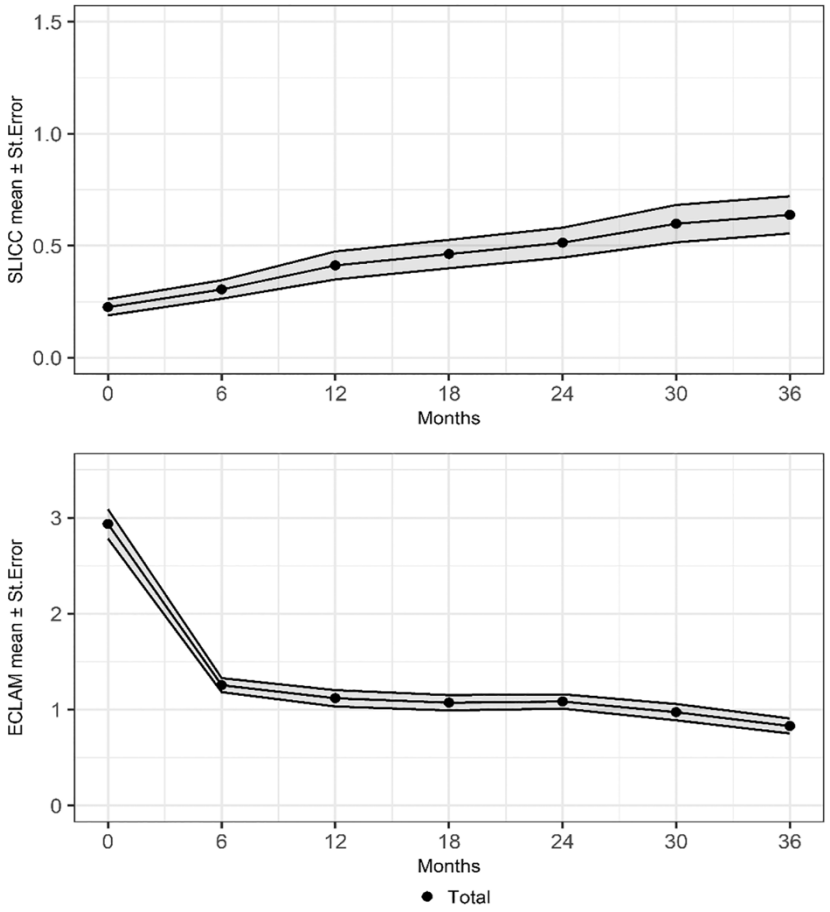


Fig. 1. Modification of SDI and ECLAM values during the follow-up period.

Furthermore, we provided data about the proportion of SLE patients not achieving LupusCDC due to persistent active disease or due to damage progression. In detail, in the LupusCDC-GCon cohort, among patients never reaching the outcome, 41 patients (18.9%) showed the progression of chronic damage (ΔSDI >0), while 109 (50.4%) experienced a persistently active disease; 38 patients (17.6%) have both conditions. Similar proportions were observed in LupusCDC-GCoff cohort: indeed, 22.1% (49 patients) did not reach the outcome for damage progression, 75.1% (166 patients) for active disease and 20.8% (46 patients) for concomitant active disease and damage progression.

Moving on to the treatments taken during this time, LupusCDC-GCon was achieved by 40 patients (49.4%) treated only by anti-malarials drugs, 14 (17.3%) treated only by immunosuppressant drugs (including one patient treated by belimumab), while the remaining 27 patients were treated by antimalarials plus immunosuppressant drugs (including 2 patients treated by biological drugs). Considering the LupusCDC-GCoff condition, 15 patients (55.5%) were taking only antimalarials, 3 patients (11.1%) only immunosuppressant and the remaining 9 patients by the combination of antimalarials and immunosuppressant drugs (2 of them were treated by biological drugs). The univariate analysis demonstrated a significant association between the failure to achieve LupusCDC-GCon and the presence of arthritis, as defined in the 1997 ACR revised criteria ($p<0.001$), and the presence of renal and neurological activity, as defined in the BILAG ($p=0.01$ and $p<0.001$, respectively). As reported in Table III, the multivariate analysis confirmed the results from the univariate analysis, also showing as the positivity for anti-dsDNA at the baseline was identified as a risk factor for failure to achieve LupusCDC-GCon ($p=0.032$, HR 0.6).

Table III. Multivariate analysis for risk factors affecting the achievement of LupusCDC-GCon.

Features	HR	HR IC 2.5%	HR IC 97.5%	*p*-value
Age	0.991	0.974	1.008	0.28
Sex (male)	1.444	0.803	2.6	0.22
Anti-dsDNA	0.609	0.387	0.959	0.032
BILAG Mucocutaneous manifestations	0.298	0.115	0.774	0.013
BILAG Neuropsychiatric manifestations	0.000	0.000	0.000	<0.001
Arthritis (1997 ACR criteria)	0.3	0.171	0.524	<0.001
BILAG Cardiorespiratory manifestations	0.000	0.000	0.000	<0.001
BILAG Renal manifestations	0.201	0.067	0.609	0.005
BILAG Haematological manifestations	0.081	0.011	0.597	0.014

Discussion

In the present study, we evaluated the achievement of comprehensive disease control in a large cohort of SLE patients with early disease. These patients have been enrolled within the inception cohort included in the Early Lupus Project, that aims to provide information on the main clinical and serological characteristics at the beginning of the disease and the evolution of disease (18, 19).

The early diagnosis is essential to promptly introduce the most appropriate treatment and thus to obtain the best possible outcome. In the last years we have observed a radical change in the SLE evolution, thanks to the improvement of patient management and the introduction of new treatments, in particular biological drugs. This change has led clinicians to strive for more ambitious outcomes, such as prolonged remission and control of damage progression.

As mentioned above, a strict correlation between disease activity and chronic damage was generally found in SLE patients, confirming as the activity represents a major driver in damage progression. Nevertheless, other factors could influence the development of damage, including demographic factors, positivity for anti-phospholipid antibodies, genetic background (11). Thus, it is conceivable the progression of damage in patients with inactive disease. From this evidence, comes the suggestion of an outcome including disease activity and chronic damage, the so-called Lupus Comprehensive Disease Control (LupusCDC). This outcome has been previously evaluated in a cohort of SLE patients with established disease, as demonstrated by a median disease duration equal to 180 months (15). Herein in the present study we tested LupusCDC in a cohort of patients with early disease, defined as the enrolment in the analysis within 12 months since disease classification (16).

Our results demonstrated as the achievement of a LupusCDC status in patients with early SLE is possible since almost a third of patients reached a LupusCDC-GCon condition. The lower prevalence of LupusCDC-GCoff status could suggest a difficulty in withdrawing GC at an early stage of disease. Nonetheless, the condition of LupusCDC-GCon includes only patients treated with a PDN dosage ≤5 mg/die.

Floris and colleagues have previously evaluated the GC tapering in the same early SLE cohort, demonstrating as the PDN tapering up to PDN <5 mg/day was achieved and maintained in half of newly diagnosed SLE patients. These results could represent a good balance between the need to prevent damage accrual and the risk of disease relapse (20). Piga and colleagues previously reported a lower proportion of GC-related damage in the present early SLE cohort in comparison with data previously reported by other authors. This difference could be attributable to the shorter disease duration and to the lower daily PDN dosage recorded in the present early SLE cohort. Thus, this limited use could reduce the impact of GCs as determinant of chronic damage, as demonstrated by the lack of association in multivariable models (21). The importance of achieving a PDN dosage ≤5 mg/day has also been clearly reflected in the most recent EULAR recommendations, going so far as to consider the possibility of withdrawing GCs when possible (22).

Furthermore, our analysis suggests that more severe disease-related manifestations represent a risk factor for the failure to reach LupusCDC condition. In fact, the failure to achieve LupusCDC-GCon was associated with the presence of renal and neurological activity, as defined in the BILAG index. This result is not surprising since the presence of renal and neuropsychiatric involvement has always been considered an expression of more severe disease, requiring a more intensive treatment, including the possibility of using high-dose GCs.

Moreover, the presence of arthritis could negatively impact on the achievement of LupusCDC. In this view, it should be considered that arthritis was defined according to the 1997 ACR revised criteria, considering only patients with the involvement of at least 2 peripheral joints, with tenderness and swelling (16). These criteria could determine the evaluation of SLE patients with a more severe phenotype in terms of joint involvement. As known, the most recent 2019 EULAR/ACR classification criteria have significantly changed the definition of joint involvement, allowing also the inclusion of patients with tenderness in at least two joints (23).

In conclusion, our data suggest the possibility to achieve ambitious outcomes in SLE patients with early disease, in agreement with the most recent suggestions (24). A condition of LupusCDc, defined for the remission plus no damage progression, could be reached in almost one third of evaluated patients. The application of more recent classification criteria, including different definition of disease related manifestations and allowing an earlier classification, could improve the possibility to reach this condition. Furthermore, the extension of the longitudinal evaluation of our cohort may also allow the inclusion of the duration of remission in the LupusCDC definition, as well as assessing its persistence.

References

1. PIGA M, ARNAUD L: The main challenges in systemic lupus erythematosus: where do we stand? *J Clin Med* 2021; 10(2): 243. https://doi.org/10.3390/jcm10020243
2. GLADMAN DD, IBAÑEZ D, UROWITZ MB: Systemic lupus erythematosus disease activity index 2000. *J Rheumatol* 2002; 29(2): 288-91.
3. CECCARELLI F, PERRICONE C, MASSARO L *et al*.: Assessment of disease activity in systemic lupus erythematosus: lights and shadows. *Autoimmun Rev* 2015; 14(7): 601-8. https://doi.org/10.1016/j.autrev.2015.02.008
4. VITALI C, BENCIVELLI W, ISENBERG DA *et al*.: Disease activity in systemic lupus erythematosus: report of the Consensus Study Group of the European Workshop for Rheumatology Research. II. Identification of the variables indicative of disease activity and their use in the development of an activity score. The European Consensus Study Group for Disease Activity in SLE. *Clin Exp Rheumatol* 1992; 10(5): 541-47.
5. VAN VOLLENHOVEN RF, BERTSIAS G, DORIA A *et al*.: 2021 DORIS definition of remission in SLE: final recommendations from an international task force. *Lupus Sci Med* 2021; 8(1): e000538. https://doi.org/10.1136/lupus-2021-000538 Erratum in: *Lupus Sci Med* 2022; 9(1): e000538corr1. https://doi.org/10.1136/lupus-2021-000538corr1
6. SACCON F, ZEN M, GATTO M *et al*.: Remission in systemic lupus erythematosus: testing different definitions in a large multicentre cohort. *Ann Rheum Dis* 2020; 79(7): 943-50. https://doi.org/10.1136/annrheumdis-2020-217070
7. ASKANASE A, KHALILI L, TANG W *et al*.: New and future therapies: changes in the therapeutic armamentarium for SLE. *Best Pract Res Clin Rheumatol* 2023: 101865. https://doi.org/10.1016/j.berh.2023.101865
8. VAN VOLLENHOVEN RF, MOSCA M, BERTSIAS G *et al*.: Treat-to-target in systemic lupus erythematosus: recommendations from an international task force. *Ann Rheum Dis* 2014; 73(6): 958-67. https://doi.org/10.1136/annrheumdis-2013-205139
9. FANOURIAKIS A, TZIOLOS N, BERTSIAS G, BOUMPAS DT: Update on the diagnosis and management of systemic lupus erythematosus. *Ann Rheum Dis* 2021; 80(1): 14-25. https://doi.org/10.1136/annrheumdis-2020-218272
10. GLADMAN DD, UROWITZ MB, GOLDSMITH CH *et al*.: The reliability of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index in patients with systemic lupus erythematosus. *Arthritis Rheum* 1997; 40(5): 809-13. https://doi.org/10.1002/art.1780400506
11. CECCARELLI F, PERRICONE C, NATALUCCI F *et al*.: Organ damage in systemic lupus erythematosus patients: a multifactorial phenomenon. *Autoimmun Rev* 2023; 22(8): 103374. https://doi.org/10.1016/j.autrev.2023.103374
12. DING H, SHEN Y, HONG SM, XIANG C, SHEN N: Biomarkers for systemic lupus erythematosus - a focus on organ damage. *Expert Rev Clin Immunol* 2024; 20(1): 39-58. https://doi.org/10.1080/1744666x.2023.2260098
13. CECCARELLI F, OLIVIERI G, PIRONE C *et al*.: The impacts of the clinical and genetic factors on chronic damage in caucasian systemic lupus erythematosus patients. *J Clin Med* 2022; 11(12): 3368. https://doi.org/10.3390/jcm11123368
14. KEYSTONE EC, BREEDVELD FC, VAN DER HEIJDE D *et al*.: Achieving comprehensive disease control in patients with early and established rheumatoid arthritis treated with adalimumab plus methotrexate versus methotrexate alone. *RMD Open* 2017; 3(2): e000445. https://doi.org/10.1136/rmdopen-2017-000445
15. CECCARELLI F, OLIVIERI G, SORTINO A *et al*.: Comprehensive disease control in systemic lupus erythematosus. *Semin Arthritis Rheum* 2021; 51(2): 404-8. https://doi.org/10.1016/j.semarthrit.2021.02.005
16. HOCHBERG MC: Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1997; 40(9): 1725. https://doi.org/10.1002/art.1780400928
17. ISENBERG DA, RAHMAN A, ALLEN E *et al*.: BILAG 2004. Development and initial validation of an updated version of the British Isles Lupus Assessment Group's disease activity index for patients with systemic lupus erythematosus. *Rheumatology* (Oxford) 2005; 44(7): 902-6. https://doi.org/10.1093/rheumatology/keh624
18. SEBASTIANI GD, PREVETE I, PIGA M *et al*.: Early Lupus Project - A multicentre Italian study on systemic lupus erythematosus of recent onset. *Lupus* 2015; 24(12): 1276-82. https://doi.org/10.1177/0961203315585817
19. SEBASTIANI GD, PREVETE I, IULIANO A *et al*.: Early Lupus Project: one-year follow-up of an Italian cohort of patients with systemic lupus erythematosus of recent onset. *Lupus* 2018; 27(9): 1479-88. https://doi.org/10.1177/0961203318777112
20. FLORIS A, CHESSA E, SEBASTIANI GD *et al*.; STUDY GROUP ON EARLY SLE OF THE ITALIAN SOCIETY OF RHEUMATOLOGY (SIR): glucocorticoid tapering and associated outcome in patients with newly diagnosed systemic lupus erythematosus: the real-world GULP prospective observational study. *RMD Open* 2022; 8(2): e002701. https://doi.org/10.1136/rmdopen-2022-002701
21. PIGA M, FLORIS A, SEBASTIANI GD *et al*.: Risk factors of damage in early diagnosed systemic lupus erythematosus: results of the Italian multicentre Early Lupus Project inception cohort. *Rheumatology* (Oxford) 2020; 59(9): 2272-281. https://doi.org/10.1093/rheumatology/kez584
22. FANOURIAKIS A, KOSTOPOULOU M, ANDERSEN J *et al*.: EULAR recommendations for the management of systemic lupus erythematosus: 2023 update. *Ann Rheum Dis* 2024; 83(1): 15-29. https://doi.org/10.1136/ard-2023-224762
23. ARINGER M, COSTENBADER K, DAIKH D *et al*.: 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. *Arthritis Rheumatol* 2019; 71(9): 1400-12. https://doi.org/10.1002/art.40930
24. SCHILIRÒ D, SILVAGNI E, CIRIBÈ B *et al*.: Systemic lupus erythematosus: one year in review 2024. *Clin Exp Rheumatol* 2024; 42(3): 583-92. https://doi.org/10.55563/clinexprheumatol/mnvmvo