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SLE news

OP0246

ATTAINMENT OF THE LUPUS LOW DISEASE ACTIVITY STATE IS ASSOCIATED WITH PROTECTION FROM DAMAGE ACCRUAL IN PATIENTS WITH ACTIVE DISEASE AT BASELINE

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Background: The recently validated Lupus Low Disease Activity State (LLDAS) definition has been shown to have utility as a treat to target endpoint in SLE, whereby LLDAS attainment is associated with reduction in permanent damage accrual. Robust evaluation is required to ensure this protective association is not simply reflective of milder disease phenotypes being over-represented among LLDAS attainers.

Objectives: To assess the effect of attainment of LLDAS on damage accrual in patients with active disease at baseline. SLEDAI-2K_{≥6} was chosen as this reflects clinical trial entry criteria.

Methods: A prospective multinational cohort study was undertaken in 13 centres between 2013-2017. Patients with SLE were recruited, SLEDAI-2k, SELENA flare index, PGA, and medication data collected at every visit, and damage score (SLICC-ACR damage index (SDI)) collected annually. Subgroup analyses were performed to assess the effect of LLDAS on damage accrual in patients who had active disease at baseline (SLEDAI-2K_{≥6}). Time-dependent hazards regression models were used to assess the association of attainment of LLDAS at any time point, and proportion of time in LLDAS at the 50% observed time cut-off, with accrual of irreversible end-organ damage.

Results: 1,735 patients were followed for (mean ± SD) 2.2 ± 0.9 years, totalling 12,717 visits. LLDAS attainment was less frequent in patients with active disease at baseline (901 of 3835 visits in LLDAS, 23.5%), compared to patients with SLEDAI-2K_{≤6} at baseline (5190 of 8845 visits in LLDAS, 58.7%), p<0.001. In contrast, compared to those with baseline SLEDAI-2K_{≤6}, patients with active disease at baseline demonstrated a stronger association of LLDAS attainment with reduction in risk of damage accrual, in visit by visit analysis (HR 0.49, 95% CI 0.28-0.86, p 0.01 vs HR 0.72, 95% CI 0.52-0.99, p 0.05), and in analysis of cumulative time spent in LLDAS (HR 0.52, 95% CI 0.33-0.83, p 0.01 vs HR 0.65, 95% CI 0.47-0.91, p 0.01).

Conclusion: Despite lower attainment of LLDAS in patients with higher disease activity at baseline, the magnitude of association of LLDAS attainment with lower damage accrual was greater in this subgroup of patients compared to those less active baseline disease. This supports the validity of LLDAS as an outcome measure, in a population similar to that typically selected into clinical trials, and further highlights the potential impact of achieving a target outcome in SLE patients with active disease.

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OP0247

EFFECT OF IMMUNOSUPPRESSIVE DRUG WITHDRAWAL ON DAMAGE PROGRESSION AND FLARE OCCURRENCE IN SLE PATIENTS IN REMISSION

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Background: Patients with Systemic Lupus Erythematosus (SLE) are often treated with prolonged maintenance therapy with immunosuppressants (ISs) after remission achievement, with the aim of avoiding disease flares and subsequent organ damage. Data on the risk of flare after IS discontinuation and the effect of IS discontinuation on damage accrual are scanty.

Objectives: Our aims were to analyze damage progression in remitted SLE patients who did or did not discontinued ISs, to assess flare rate after IS withdrawal and to compare damage accrual in patients who did or did not flare after IS discontinuation.

Methods: We considered all SLE patients included in our lupus database, diagnosed between 1990 and 2018 (ACR criteria), treated with immunosuppressants over their disease course, who discontinued IS due to remission. IS discontinuation was defined as complete withdrawal of any immunosuppressive drug, and remission as clinical SLE Disease Activity Index (SLEDAI)-2K=0. Flares were defined according to SLEDAI Flare Index, and damage according to SLICC damage Index (SDI).

Results: Eligible patients ever treated with ISs were 319 out of 456 (69.9%) currently in follow-up. Remission lasting at least 6 months was achieved by 206 patients treated with IS (64.6%) (Table 1); among them 105 (51%) discontinued ISs during the follow-up. Mean±SD follow-up after IS withdrawal was 91±71 months (range 6-372). No difference in damage accrual between remitted patients who discontinued or did not discontinue ISs was observed at the end of follow-up, after adjusting for disease duration: median (range) SDI 1 (0-6) and 0 (0-4), respectively. Accordingly, the proportion of remitted patients who accrued damage during the follow-up was similar between those who did or did not discontinue ISs (55% vs. 48%). Among patients who discontinued ISs, 26 (24.7%) experienced a flare after a median (range) of 57 (6-264) months from IS discontinuation. Flares were severe in 50% of cases (Table 2). No difference in damage progression between patients who flared and did not flare after IS withdrawal was found at the end of follow-up: median (range) SDI 1 (0-5) and 1 (0-6), respectively. Moreover, the proportion of patients with damage accrual was similar among patients with and without flare after IS discontinuation (56% vs. 54%).

Table 1. Characteristics of remitted patients according to the discontinuation of ISs. Data are expressed as mean±SD or number (%).

	Remitted patients		P value
	IS discontinued (105)	IS not discontinued (101)	
Female, N (%)	93 (88.6)	85 (84.1)	n.s.
Age at 2018, years	44±11	40±12	0.035
SLE duration at 2018, years	19.5±9.2	12.3±8.7	0.027
SLE duration at remission, years	5.2±6.1	6.3±4.2	n.s.
Remission lasting at IS discontinuation > 2 consecutive years, N (%)	66 (63)	36 (35.6)	0.001
Reason for IS therapy, N (%)			
Lupus Nephritis	68 (64.8)	57 (56.4)	n.s.
Skin involvement	6 (5.7)	7 (6.9)	
Arthritis	12 (11.4)	15 (14.4)	
Haematological involvement	5 (4.7)	8 (7.9)	
Neuropsychiatric involvement	3 (2.9)	2 (1.9)	
Vasculitis	3 (2.9)	1 (0.9)	
Multisystemic involvement	8 (7.6)	11 (11)	
Type of last IS*, N (%)			
Mycophenolate	48 (45.7)	73 (72.2)	0.001
Azathioprine	30 (28.6)	18 (17.8)	0.04
Methotrexate	14 (13.3)	5 (4.9)	0.008
Cyclosporine	7 (6.7)	4(3.9)	n.s.
Cyclophosphamide	6 (5.7)	1 (0.9)	0.001

* last IS used before withdrawal or at last visit. Multisystemic: involvement of more than 2 organs requiring IS therapy.

Table 2. Type of flare after IS discontinuation in 105 SLE remitted patients.

Type of flare	Number (%)	Severe flare, number (% of all flares)
Arthritis	5 (19.2)	2 (7.7)
Skin manifestations	6 (23.1)	1 (3.9)
Serosal involvement	2 (7.7)	0
Haematological involvement	5 (19.2)	2 (7.7)
Lupus nephritis	8 (30.8)	8 (30.8)
Total	26	13 (50)

Conclusion: In our SLE cohort, the withdrawal of IS therapy in remitted patients did not seem to influence damage progression in the medium-term.

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OP0248

THE IMPACT OF EXERCISE ON HAND FUNCTION AND QUALITY OF LIFE OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A RANDOMIZED CONTROLLED TRIAL

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Background: Systemic Lupus Erythematosus (SLE) has a significant impact on the ability to perform daily activities and patients' quality of life. To date, no studies have examined the effect of exercise on hand function and quality of life of SLE patients.

Objectives: To determine the effect of exercise on hand strength, dexterity and performance of daily activities, and the quality of life of SLE patients.

Methods: A randomized, 24-week follow-up trial was designed. A total of 240 consecutive SLE patients fulfilling the SLICC classification criteria were evaluated. Sixty two patients who met the inclusion criteria [age > 18 years, upper limb arthralgias, DASH (Disabilities of the Arm, Shoulder, and Hand) score > 10 and stable drug regimen for ≥ 3 months], were randomly assigned to the exercise group (n=32) or the routine care (control) group (n=30).

Patients in the exercise group received by the hand therapist a 30 min daily program at home of strengthening and stretching upper limb exercises for 12 weeks. Performance of daily activities was evaluated with the DASH and HAQ questionnaires, the grip and pinch strength with the Jamar dynamometer and pinch gauge tools respectively, the dexterity with the Purdue pegboard test, and the quality of life with the LUPUSQoL questionnaire, at 0, 6, 12 (end of the exercise program) and 24 weeks for both groups. SLE activity and cumulative organ damage were evaluated with the SLEDAI and SLICC/ACR-DI, respectively.

Results: There were no statistically significant differences between two groups in age (p=0.062), sex (p=0.346), disease duration (p=0.065), SLEDAI (p=0.937), SLICC/ACR-DI (p=0.242), number of tender joints (p=0.703), and use of corticosteroids (p=0.640), hydroxychloroquine (p=0.985) or immunosuppressives (p=0.806). Thirty patients (93.75%) from the exercise group completed the 12-week exercise program and 28 (87.5%) were re-evaluated at 24 weeks; 30 patients (100%) of control group completed the 24-week study.

The percent changes of DASH and HAQ scores were significantly lower (improvement) in the exercise group compared to control group at all-time points. Moreover, all percent changes of grip strength, pinch strength hand dexterity and the LupusQoL score were significantly higher in the exercise group compared to control group at all-time points (Table 1).

Table 1. Comparison between groups of percent changes from baseline to 6, 12 and 24 weeks for all parameters.

	Evaluation time (weeks)	Exercise Group	Control Group	P-value
DASH score	6	-33.7 (28.4)	-1.3 (33.8)	<0.001
	12	-43.4 (31.5)	-11.2 (34.5)	<0.001
	24	-51.9 (47.8)	-7.1 (54.1)	<0.001
HAQ score	6	-20 (49.8)	49.7 (39.9)	0.013
	12	-55 (70.4)	-9.72 (42.2)	<0.001
	24	-69.8 (56.3)	-9.13 (60.4)	<0.001
Grip strength (DH)	6	9.9 (32.8)	2.39 (35.5)	0.044
	12	20.9 (43.4)	4.10 (30.2)	<0.001
	24	23.1 (41)	13.51 (36.8)	0.020

Pinch strength (JAW)	6	17.2 (50)	5.98 (37.4)	0.049
	12	27.1 (55.8)	0 (48.5)	0.002
Dexterity (COM)	24	34.2 (57.6)	2.04 (56.7)	<0.001
	6	17.4 (19.4)	0 (18.6)	<0.001
LUPUSQoL score (PH)	12	23.6 (32)	3.13 (31.1)	0.004
	24	22.2 (30.3)	9.55 (22.5)	0.003
	6	9.5 (49.9)	-5.62 (30.5)	0.010
	12	32.5 (53.8)	5.59 (28.4)	<0.001
	24	28.6 (74.8)	2.38 (48.8)	0.002

All values are presented as median (interquartile range). DASH=Disabilities of the Arm, Shoulder, and Hand, HAQ=Health Assessment Questionnaire, LUPUS-QoL=Lupus Quality of Life, PH=physical health domain, DH=dominant hand, JAW=tripoid pinch, COM=combination.

Conclusion: Upper limb exercise, significantly improves hand function and quality of life in SLE patients.

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OP0249

ANTIPHOSPHOLIPID SYNDROME (APS) IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) LEADS TO A MORE SEVERE DISEASE

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Background: Antiphospholipid antibodies (aPL) have been associated with organ damage and certain features in SLE patients.

Objectives: Our aim was to investigate the differences between SLE patients according to the presence of aPL and/or clinical antiphospholipid syndrome.

Methods: Patients from the RELESSER-T registry were included. RELESSER-T is a multicenter, hospital-based registry, with retrospective cross-sectional collection of data from a large representative sample of adult non-selected patients with SLE attending Spanish rheumatology services from the public national health system.

Results: We included 3651 SLE patients and 1368 were positive for aPL (44.9% of patients were positive for anticardiolipin antibodies, 27.3% showed positivity for anti b2glycoprotein I and 24% for lupus anticoagulant). Overall 2283 patients were classified as SLE no aPL, 528 as SLE-APS and 840 as SLE-aPL. Demographic data, clinical and laboratory features in the different groups are showed in **Table 1**. Regarding cardiovascular risk factors, SLE-APS patients had higher rates of hypertension, dyslipidemia and diabetes than SLE-aPL and SLE no aPL patients ($p < 0.001$, $p < 0.001$ and $p = 0.022$, respectively). SLE-APS patients showed a lower prevalence of photosensitivity and higher frequencies of serositis, proteinuria (>0.5 grs), urinary cell casts, seizures and psychosis ($p \leq 0.001$). Overall, SLE-APS patients showed a lower rate of cutaneous manifestations and higher rates of neuropsychiatric, cardiac, pulmonary, renal, joint and ophthalmological manifestations (**Table 1**). In accordance with a more severe clinical profile, higher frequency of anti-DNA antibodies and hypocomplementemia were observed in the SLE-APS group ($p < 0.001$). In addition to a higher disease activity (SLEDAI), SLE APS patients presented more damage accrual with higher values in SLICC (1.9±2.2 in SLE APS, 0.9±1.4 in SLE aPL and 1.1±1.6, $p < 0.001$) and Katz indexes (3±1.8 in SLE APS, 2.7±1.7 in SLE aPL and 2.6±1.6 in SLE no aPL, $p < 0.001$).