ONLINE SUPPLEMENTARY MATERIAL

PATIENTS AND METHODS

Definition of flares

The presence of a lupus flare and its characterisation in severe or mild/moderate flare was recorded according to the SELENA-SLEDAI Flare index (SFI) [1, 2]:

Mild or moderate flares were defined as 1 or more of the following: a) change in SELENA-SLEDAI instrument score of 3 points or more (but not to more than 12); b) new or worsening discoid, photosensitive, or other rash attributable to lupus (including lupus profundus, cutaneous vasculitis, or bullous lupus), nasopharyngeal ulcers, pleuritis, pericarditis, arthritis, or fever not attributable to infection; c) increase in prednisone, but not to >0.5 mg/kg/day; d) Added NSAID or hydroxychloroquine for SLE activity; and e) ≥1.0 increase in physician's global assessment (PGA) score, but not to more than 2.5.

Severe flares were defined as 1 or more of the following: a) Change in SELENA-SLEDAI instrument score to greater than 12; b) new or worsening central nervous system involvement, vasculitis, nephritis, myositis, thrombocytopenia (platelet count < $60x10^9$ cells/L), or hemolytic anemia (hemoglobin level < 70 g/L or decrease in hemoglobin level > 30 g/L over a 2-week period), each requiring doubling of corticosteroid dosage to a final dosage greater than 0.5 mg/kg per day or hospitalization; c) any SLE manifestation requiring an increase in dosage of prednisone or equivalent drug to greater than 0.5 mg/kg per day, or initiation of therapy with cyclophosphamide, azathioprine, mycophenolate mofetil, or methotrexate; d) hospitalisation for lupus activity; and e) Increase in PGA score to >2.5.

An isolated change in anti-dsDNA or C3 or an increase in SLE treatment, in the absence of clinical manifestations, were not indicative of a flare.

Mathian A, *et al. Ann Rheum Dis* 2020; 79:339–346. doi: 10.1136/annrheumdis-2019-216303

Alternatively, flares were assessed with the BILAG 2004 index: *severe flares* were defined as a patient with an A score in any system due to items that are new or worse, *moderate flare* as a patient with two or more B scores due to items that are new or worse, and *mild flare* as a patient with a single B score or at least 3 C scores due to items that are new or worse.[3-6] Anyone without one of these criteria would be categorised as no flare.

Follow-up

At each visit, outcomes and adverse effects were ascertained according to a history of current symptoms and medications. Complete physical examination, treatment regimen, SELENA-SLEDAI, SFI, SLEDAI-2K[7] and BILAG 2004 scores, SDI, adverse events (AEs), not-related to disease activity, and laboratory testing, including complete blood cell count, serum creatinine assay, urinalysis, C3 levels by nephelometry (cut-off value: 0.78g/L) and anti-dsDNA Abs measurement by Farr assay (Trinity Biotech®, provided by InGen®; cut-off value: 9.0 IU/mL) were recorded. HbA1c, lipid profile and bone mineral density (measured by dual-energy X-ray absorptiometry, Hologic® Discovery™ W (S/N 84030) were collected at Day 0 and Month 12. In a post-hoc analysis, the changes in glucocorticoid toxicity index (GTI) were calculated for each patient between Day 0 and Month 12.[8] AEs that occurred during treatment were rated, using a pre-specified list, as related or not related to treatment, including prednisone intake and antimalarial and/or immunosuppressive therapy. Only AEs related to treatment are reported. SLE flares were not considered adverse events. We had considered the possibility of the occurrence of a pregnancy during the study and had decided, due to the hypothetical increased probability of lupus flares in the withdrawal group, that the intervention would cease in the event of a pregnancy and that the patient would resume the 5 mg daily prednisone she had been taking prior to the trial (thus preventing the woman and her fetus to be exposed to an unacceptable risk).

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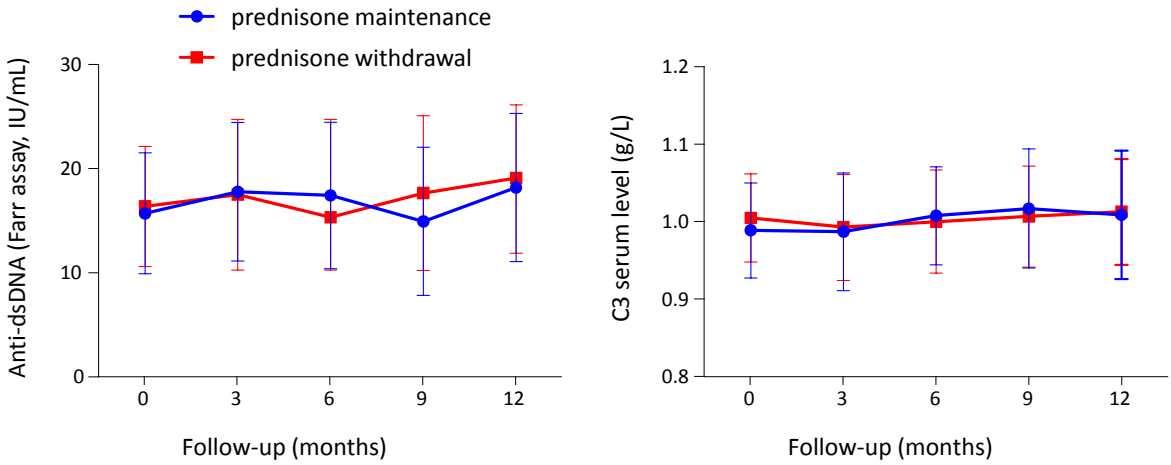
RESULTS



Online supplementary Figure S1. **Changes in immunological parameters.** Serum was analysed for the presence of anti-dsDNA Abs by Farr assay (cut-off value: 9.0 IU/mL) and for C3 levels (cut-off value: 0.78g/L) at the indicated times. Blue points and red squares represent the mean and 95% confidence interval values in each group. Using the Mann-Whitney test, anti-dsDNA and C3 levels were not significantly different between groups of patients tested at each time point. Using the Wilcoxon matched pairs test, anti-dsDNA and C3 levels were not significantly different within each group of patients tested at the different time points.

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Online supplementary table S1. **Short Synacthen responses in selected patients**

Patient#	T0 cortisol (nmol/l)	T60 cortisol (nmol/l)
59	758	1082
77	400	653
78	270	641
107	321	554

Patients received a bolus iv injection of 0.25 mg human tetracosactide (1-24-ACTH) (Synacthen). The test was carried out at 8:00 AM after an overnight fast. Plasma cortisol was measured at the time of administration of Synacthen (T0) and 60 minutes (T60) afterward. The plasma cortisol response to Synacthen was analyzed according to Sacre et al.[9] The diagnosis of adrenal insufficiency was based on the measurement of cortisol levels below 100 nmol/L at baseline (T0) or below 550 nmol/L at T60 after administration of Synacthen.

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