Objectives: The aim of this study is to evaluate the efficacy and the safety of HCQ as co-treatment in the standard therapy of SLE.
Methods: SLE patients (n=30) under the maintenance therapy were enrolled in this study. Dose of PSL, titer of anti-DNA antibody, WBC count, serum complement and SLE disease activity index (SLEDAI) were examined retrospectively at 0 and 12 months after administration of HCQ.
Results: Baseline patient-characteristics are as follows (mean±S.E); the age of patients was 54.4±3.2 years old, 21 patients (70%) were female, the disease duration was 108.5±25.2 months, SLEDAI was 4.0±0.9, the dose of PSL was 10.3±1.7 mg/day, the titer of anti-DNA antibody was 7.3±1.8 IU/ml, C3 was 85±4.3 mg/dl and C4 was 18±1.6 mg/dl.
The mean dose of PSL was reduced with statistically significance (pre-administration of HCQ:10.3±1.7 mg/day, 24 months after administration of HCQ:2.2±0.3 mg/day, *p<0.0001*). Furthermore, in this observation period, 6 patients could achieve the cessation of PSL.
SLEDAI was also significantly reduced (4.0±0.9 vs 1.0±0.3, *p<0.01*).
There was no statistical significance between before treatment by HCQ and after treatment in the titer of anti-DNA antibody (7.3±1.8 vs 2.8±1.6 IU/ml, *p=0.06*), WBC count (6208±4.9 vs 5096±3.3 /μl, *p=0.06*) and serum complement level (C3 85±4.3 mg/dl vs 89±4.0 mg/dl, *p=0.52*, C4 18±1.6 mg/dl vs 19±1.4 mg/dl, *p=0.45*). Relapse of SLE was clarified in only one patient.
As for adverse events (AEs), Severe bacterial infection (n=4), herpes zoster (n=1) and patellar tendon rupture (n=1) were revealed. All cases of the AEs were fully recovered.
Conclusion: Our study suggested that co-treatment with HCQ on standard SLE therapy could be enable to prevent the flare of SLE and reduce the dose of PSL with statistical significance. In some cases, we could achieve the cessation of PSL treatment.
References: None.
Disclosure of Interests: None declared
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AB0382 A RITUXIMAB AND BELIMUMAB COMBINATION THERAPY IN SLE PATIENTS.

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Background: Various mechanisms of action of RTM and BLM, in particular their interaction with defined subpopulations of B cells, can contribute to more effective suppression of autoreactive B cells and achieve a therapeutic effect.
Objectives: To assess the efficacy of a rituximab and belimumab combination therapy in pts with active SLE.
Methods: The study included 10 SLE pts (1M/9F) with high (SLEDAI2K≥10 – 8pts.) and moderate (SLEDAI2K<10- 2pts.) disease activity; out of them 2 patients had lupus nephritis, 2- vasculitis. 1 pts both (nephritis and vasculitis), and remaining 5 had predominantly mucocutaneous and articular manifestations of SLE. The dose of oral GCs at baseline did not exceed 20 mg/day in 9 pts, two pts were treated with prednisone 5 mg/day and only 1 received 60 mg. Rituximab (RTM) was administered at 500-2000 mg, with subsequent adding of Belimumab (BLM) 1-6 months later at a standard dosing regimen 10 mg/kg once a month. CD19+ B- lymphocytes counts were obtained before initiation RTM (0), and subsequently after 3 (N=10), 6 (N=10), 9 (N=7), and 12month (N=7). Depletion of CD19+ B- lymphocytes after RTM was assessed as the decrease of B-cell counts < 0,01 10*9/l, where 0 10*9/l was categorized as complete depletion, from 0,001 to 0,01 10*9/l – partial depletion, and >0,011 10*9/l – absence of depletion. The comparison group included 20 pts receiving a sing=ъ500-2000mg dose of RTM with high (SLEDAI2K≥10 – 16pts.) and moderate (SLEDAI2K<10- 4pts.) disease activity (SLEDAI Me 14[10;16])
Results: 6 pts demonstrated the decrease in clinical and laboratory SLE activity, starting from 3mo of follow-up, and by the 6th month the decrease in the activity of the disease was observed in 9 patients (SLEDAI-2K 0 mo–Me 12[10;16], 3mo-Me 8[6;10], 6mo–Me 4[2;6], 9mo–Me 6[4;10], 12mo–Me 2[2;6]) with RTM + BLM combination therapy. The oral GCs dose was reduced to 6,9 [5;10]mg/day by 6mo. One patient managed to completely eliminate glucocorticoids; he continued to receive cytostatic therapy (mycophenolate mofetil). None of the patient required prednisone dose escalation during follow-up. There were no cases of severe infection. The damage index did not increase by 6 and12mo. The combination therapy reduced the absolute counts of CD19+. B-cells. RTM therapy resulted in complete depletion in 3 pts, in partial depletion - in 4. Addition of BLM resulted in slowing down of CD19+ B-cell repopulation (Fig.1) (0mo–Me 0,11x10^9/l[0,08;0,5], 12mo -Me 0,01x10^9/l[0,01; 0,03]) vs pts receiving RTM monotherapy (0mo–Me 0,1x10^9/l[0,08;0,2], 12mo -Me 0,03x10^9/l[0,008; 0,08]). RTM and BLM combination failure, as well as failure of standard GCS and cytostatic based therapy, was documented in one patient with cutaneous, articular and hematological SLE.
Conclusion: Combination therapy allows to gain control over disease activity in short time, due to the effect of RTM, while added BLM provides further prolongation of the effect achieved, minimizing the risk of exacerbation. This combination may be used as a method of choice in pts with severe SLE involving vital organs, and in persistent cutaneous-articular disease and high immunological activity. In these patients there were no signs of infection.

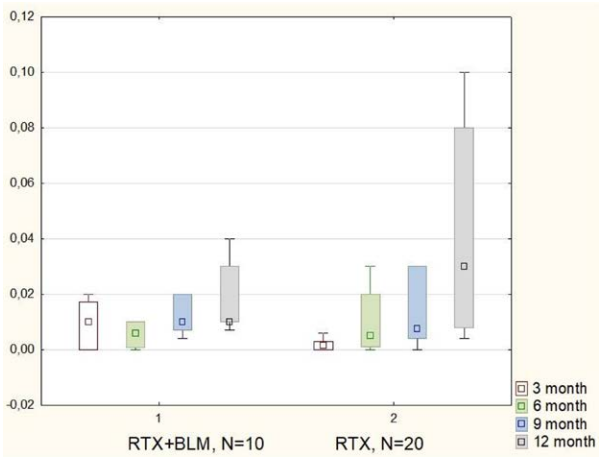

Figure 1.

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AB0383 EXTREME FATIGUE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND NEUROPSYCHIATRIC SYMPTOMS

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Background: Fatigue is commonly described in chronic illnesses, especially auto-immune disorders such as systemic lupus erythematosus (SLE).
Objectives: We aim to study the prevalence of fatigue in SLE patients with NP symptoms and compare fatigue in SLE patients with NP symptoms attributed to major organ involvement due to SLE (NPSLE) with SLE patients with NP symptoms not caused by major nervous system involvement (non-NPSLE).
Methods: All patients visiting the tertiary referral center for NPSLE in the LUMC between 2007-2019 with the clinical diagnosis of SLE and age >18 years that signed informed consent were included in this study. Patients underwent a standardized multidisciplinary assessment, including two questionnaires: SF-36 (2007-2019) and multidimensional fatigue index (MFI, 2011-2019). Patients were classified as NPSLE in this study if NP symptoms were attributed to SLE and immunosuppressive or anticoagulant therapy was initiated, otherwise patients were classified as non-NPSLE. The vitality (VT) domain of the SF-36 domain was used to assess fatigue, which generates a score from 0-100, 100 representing the complete absence of fatigue. Patients with a score more than 1 standard deviation (SD) removed from age-related controls of the Dutch general population were classified as fatigued; patients more than 2 SD removed were classified as extremely fatigued[1]. The MFI was also used, which consists of 5 subdomain scores between 0-20, leading to a total score between 0-100, 100 representing the most extreme fatigue. All scores are presented as mean and standard deviation.
Results: 373 patients fulfilled the inclusion criteria and SF-36 questionnaires of 328 patients were available (88%). The majority of these patients was female (87%) and 98 were classified as NPSLE (30%). In NPSLE patients, average age was 41 ± 13 years and in non-NPSLE the average age was 45 ± 14 years. The average score of the SF-36 vitality domain was 36.0 ± 20.7 in NPSLE vs 33.9 ± 18.8. in non-NPSLE. Overall, 73.5% of the patients were fatigued and 46.9% extremely fatigued in NPSLE vs 77.8% fatigued and 45.7% extremely fatigued in non-NPSLE.
The MFI questionnaire and VAS score were available for 222 patients, of which 65 patients were classified as NPSLE (29.3%). Table 1 depicts the scores of NPSLE and non-NPSLE patients on the MFI subdomains and the VAS score.

Table 1. Fatigue in NPSLE and non-NPSLE patients (N = 222)

	NPSLE (N = 65)	Non-NPSLE (N = 157)
MFI (mean, sd)		
General Fatigue	10.8 (1.8)	11.1 (1.5)
Physical Fatigue	11.4 (2.4)	12.3 (1.9)
Reduced Activity	9.6 (2.9)	10.7 (2.2)
Reduced Motivation	10.7 (2.6)	11.1 (1.9)
Mental Fatigue	9.5 (3.0)	9.8 (2.7)
Total score	51.8 (9.9)	54.9 (6.9)
SF-36 Vitality (mean, sd)	35 (20.7)	32.7 (18.2)

Table 1.

	GC	AM	IS					
			MPh	MPhA	AZA	MTX	CyA	LEF
Overall med survival, days to 25% discontinuation (95%CI)	1048 (938, 1197)	1267 (1113, 1428)	175 (175, 182)	387 (252, 756)	409 (350, 476)	525 (219, 686)	268 (182, 350)	329 (190, 524)
Univariable associations,HR (95% CI) p-value								
Disease activity								
≤4	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
>4 & <10	0.69 (0.56, 0.84) p<0.001	1.15 (0.92, 1.44) 0.2	0.92 (0.80, 1.05) 0.2	1.37 (0.78, 2.42) 0.3	1.16 (0.97, 1.39) 0.11	1.11 (0.72, 1.71) 0.6	1.26 (0.90, 1.77) 0.18	1.88 (1.07, 3.30) 0.03
≥10	0.65 (0.35, 1.21) 0.18	1.56 (0.94, 2.59) 0.08	0.84 (0.45, 1.57) 0.6	1.92 (0.80, 4.63) 0.14	2.69 (1.86, 3.91) p<0.001	1.85 (0.92, 3.71) 0.08	2.66 (1.36, 5.21) 0.004	1.62 (1.13, 2.32) 0.009
LLDAS								
<50%	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
≥50%	1.30 (1.09, 1.55) 0.003	0.67 (0.54, 0.84) <0.001	1.22 (1.08, 1.40) 0.002	0.83 (0.44, 1.57) 0.6	0.83 (0.69, 1.00) 0.054	0.70 (0.46, 1.07) 0.10	1.29 (0.92, 1.83) 0.14	0.43 (1.5, 1.25) 0.12

Conclusion: Nearly half of patients with SLE and NP symptoms are as extremely fatigued as only 2.5% of the general Dutch population. Extreme fatigue is not influenced by major nervous system involvement.

References:

[1] Aaronson *et al.* J Clin Epidemiol. Vol. 51, No. 11, pp. 1055–1068, 1998

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AB0384

MEDICATION USE IN SYSTEMIC LUPUS ERYTHEMATOSUS – DATA FROM A MULTICENTRE COHORT STUDY

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Background: In the absence of evidence-based treatment guidelines, medication use in SLE is highly variable. Low rates of remission and lupus low disease activity state (LLDAS) suggest that suboptimal responses to standard medications, which include glucocorticoids (GC), anti-malarial (AM) drugs and immunosuppressive (IS) agents, are common. Understanding the utility of current medications will facilitate the selection of patients for advanced therapies as they emerge.

Objectives: To examine medication use patterns in a large multicentre SLE cohort.

Methods: We used 2013-18 data from the Asia Pacific Lupus Collaboration (APLC) cohort in which disease activity (SLEDAI-2K) and medication details were captured at every visit. LLDAS was defined as in Golder *et al.*, 2019 (1). We examined the use of medication (med) categories (GC &/or AM &/or IS) by SLE disease activity and LLDAS at the visit level. Additionally, we performed Cox regression analyses to determine the time-to-discontinuation of meds stratified by SLE disease activity, ranked by time-adjusted mean SLEDAI-2K, and by percent-time spent in LLDAS.

Results: We analysed data from 19,804 visits of 2,860 patients. We observed 8 med categories: no meds; GC, AM or IS only; GC+AM; GC+IS; AM+IS and GC+AM+IS (triple therapy). Triple therapy was the most frequent med pattern (32%); single agents were used in 21% of visits and biologicals in only 3%. Among visits where SLEDAI-2K was ≥10, triple therapy was used in 46%, with median [IQR] GC dose 10 [6, 24] mg/day; in contrast, among visits with SLEDAI-2K≤4 triple therapy was used in 28% (p<0.01). Patients in LLDAS received less combination therapy than those who were not in LLDAS.

Med persistence (survival analysis) varied widely, with lowest survivals for IS. Patients with time-adjusted mean SLEDAI-2K ≥10 had lower discontinuation of GC and higher discontinuation of IS including azathioprine, leflunomide and cyclosporine (Table 1). In contrast, increased time in LLDAS was associated with reduced discontinuation of AM and azathioprine.

Conclusion: In a large multicentre SLE cohort, most patients were receiving combination treatment. AM treatment survival was high and associated with low disease activity, GC survival was high and associated with high disease activity, while IS survival was low. Patients with high disease activity received more medication combinations but had reduced IS survival. These data suggest ongoing unmet need for improved medications for treatment of SLE.

Reference:

Golder, V., et al Lancet Rheum. 2019 1(2):e95-102

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