Figure 1. Hemodynamic changes during immunosuppressive therapy

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AB0286 EFFICACY OF MYCOPHENOLATE MOFETIL PLUS RITUXIMAB COMPARED WITH INTRAVENOUS CYCLOPHOSPHAMIDE PLUS RITUXIMAB IN PATIENTS WITH RELAPSING LUPUS NEPHRITIS

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Background: Lupus nephritis (LN) remaining as one of the most devastating manifestations of systemic lupus erythematosus (SLE). Only 60% of patients with LN achieve a complete (CR) or partial remission (PR) with mycophenolate mofetil (MMF) or intravenous (iv) cyclophosphamide (CY) plus corticosteroids. Of those nearly one-half will have a relapse following maintenance therapy [1]. Rituximab (RTX) is considered a treatment of relapsing LN [2]. Although potential benefits have been revealed in descriptive studies, efficacy has not been established in randomized trials [3,4].

Objectives: This study compares the efficacy achieving a CR or PR with MMF+RTX versus iv CY+RTX in patients with relapsing LN.

Methods: Mexican SLE patients classified by SLICC 2012 criteria were recruited from 2013 to 2019 with LN diagnosed by renal biopsy who previously having achieved a CR with MMF or iv CY followed by the maintenance therapy with azathioprine (AZA) or MMF and subsequently present relapsing LN consisting of a new active urinary sediment (US), worsening proteinuria and renal function. Demographic, renal clinical and paraclinical variables were examined. All patients received oral prednisone (1 mg/kg/d) accompanying MMF 3g/d or CY 0.5–1 g/m² monthly plus RTX 1 g at 0 and 14 days. The data were evaluated at 0, 6, 12 and 24 month(s) after the start both treatments. CR was defined as normal serum creatinine (SCr), inactive US, plus 24-Hour Urine Protein (24hUP) <50mg/d and PC was established as 50 percent

improvement in renal parameters. Fisher's exact and Student's-t tests were performed by univariate analysis.

Results: Of nine SLE patients with relapsing LN, seven were women. The mean age [standard deviation (SD)] was 25.1 (6.4) years. The mean time at the onset of SLE (SD) was 3.44 (1.12) years ago. Four and five patients had class IV and IV/V LN respectively. Time of relapsing LN after of CR (SD) was 21.2 (7.17) months. Seven patients used CY followed by AZA and two employed MMF previously of relapsing LN. The mean of basal SLEDAI and SLICC (SD) were 19.11(3.2) and 1.22 (0.44) respectively. The mean of basal 24hUP (SD) was 4.67 (2.6) g/d and sCr (SD) was 2.0 (0.84) mg/dl. Five patients used MMF+RTX and four patients utilized CY+RTX. No statistically significant differences were found for CR, PR, 24hUP, sCr, US, anti-dsDNA and complement between both groups. At 6 months one patient achieved a CR and six reached a PR. At 12 months four patients fulfilled a CR and seven had a PR. Finally, at 24 months seven patients showed a CR and a CP. Only two patients did not achieve a CR or PR at 24 months.

Conclusion: This study suggests that the most of SLE patients with relapsing LN treated with CY or MMF plus RTX achieved CR or PR at 24 months, although were no found differences between both treatments. However, these observations must be confirmed in larger and prospective studies.

REFERENCES:

- [1] Ann Rheum Dis 2020;79(6):713;
- [2] Nephrol Dial Transplant 2019;34(1):22;
- [3] Clin J Am Soc Nephrol 2009;4(3):579;
- [4] Arthritis Rheum 2012;64(4):1215

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AB0287 EFFECTS OF HYDROXYCHLOROQUINE ON PERIPHERAL BLOOD CYTOKINE EXPRESSION ASSOCIATED WITH ATHEROSCLEROSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: In systemic lupus erythematosus(SLE), a higher frequency of atherosclerotic lesions is associated with a poor life prognosis (1). Hydroxychloroquine (HCQ) has been reported to improve the prognosis of life and dyslipidemia in SLE (2), and the mechanism has been unclear.

Objectives: To determine the effect of HCQ treatment on serum cytokines associated with atherosclerosis in SLE.

Methods: SLE patients who received additional HCQ and maintained low disease activity between January 2016 and September 2020 were included in this study. Disease activity was assessed by SLEDAI, CLASI and LLDAS, and serum complement titers, anti-ds-DNA antibodies, serum insulin and serum cytokines (adiponectin, resistin and leptin) were analyzed before and after HCQ treatment.

Results: Fifty-four patients (3 males, 51 females, mean age 41.9±12.8 years) were included (Table 1). Thirty-two patients achieved LLDAS at baseline. Serum adiponectin and insulin levels were significantly increased after 3 months of HCQ treatment compared to baseline, and serum resistin levels were significantly lower (Figure 1). Patients with a history of renal disease had greater degree of changes in serum adiponectin and resistin levels. Among SLE patients who did not achieve LLDAS at baseline, those who still did not achieve LLDAS after 3 months had significantly lower serum leptin levels before HCQ treatment than those who achieved it after 3 months.

The change of serum resistin levels correlated with those of serum S100A8 levels ($r=0.5$, $p=0.0001$).

Conclusion: Additional HCQ treatment in SLE patients improves lipid abnormalities. HCQ may improve prognosis by controlling disease activity in SLE and reducing risk factors for atherosclerosis.

REFERENCES:

- [1] Gregory Katz, et al. Systemic Lupus Erythematosus and Increased Prevalence of Atherosclerotic Cardiovascular Disease in Hospitalized Patients. Mayo Clin Proc. 2019; 94:1436-1443.
- [2] Laura Durcan, et al. Longitudinal Evaluation of Lipoprotein Parameters in Systemic Lupus Erythematosus Reveals Adverse Changes with Disease Activity and Prednisone and More Favorable Profiles with Hydroxychloroquine Therapy. J Rheumatol. 2016; 43: 745–750.

Table 1. Characteristics of SLE patients enrolled in this study

Characteristics	n=54, no.(%)
Female, no(%)	51(94)
Age, years, mean±SD	41.9±12.8
Disease duration, years, mean±SD	15.1±11.1
Past involvement	
Renal involvement	23 (43)
NPSLE	5 (9)
Complication	
APS	10 (19)
Dyslipidemia	2 (4)
Diabetes	1 (2)
Concomitant immunosuppressive treatments	
Prednisone	
No.(%)	46 (85)
Median Dosage, mg/day (range)	5.0 (1-10)
Disease activity	
SLENA-SLEDAI score	3.9±2.0
Current skin involvement	30 (56)
anti-dsDNA positive, no(%)	21 (39)
low complement, no(%)	29 (54)

Anti-dsDNA positive means anti ds-DNA titer increases over 12 IU/mlLow complement means any of C3, C4 and CH50 decreases to less 68mg/dl, less 12mg/dl, 30U/ml.APS: Anti-phospholipid antibody syndrome, NPSLE: neuropsychiatric SLE,

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AB0288

SAFETY OF BELIMUMAB IN PATIENTS WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS: YEAR 2 FOLLOW-UP OF A LARGE PHASE 4, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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Background: Belimumab (BEL), a recombinant human monoclonal antibody that inhibits B-lymphocyte stimulator (BLyS), is approved for the treatment of systemic lupus erythematosus (SLE). Clinical studies have yielded varying incidence rates of mortality and adverse events of special interest, such as malignancies, thereby necessitating large-scale, long-term assessment following BEL exposure.

Objectives: To assess all-cause mortality and new primary malignancies during post-treatment Year 2 follow-up in adult patients with active, autoantibody-positive SLE who received intravenous (IV) BEL or placebo (PBO), plus standard therapy in the 52-week double-blind treatment period of the ongoing BASE trial.¹

Methods: This was a post-treatment follow-up of the Phase 4, double-blind study (BASE¹; GSK Study BEL115467; NCT01705977), which randomised 4019 adults with active SLE and receiving standard therapy to BEL (10mg/kg IV) or PBO on Days 0, 14, 28, and monthly thereafter until Week 48. All patients (including those who discontinued BEL before the end-of-treatment phase) were contacted by phone annually (+/-30-day time window). Rates of mortality and new primary malignancy are summarised for Year 2 follow-up, presented by the treatment received during the 52-week double-blind treatment period (Year 1).

Results: Baseline patient characteristics and disease activity collected at the start of the study, evaluated in patients with Year 2 follow-up were similar to the overall Year 1 study population. Cumulatively by Year 2 follow-up, 10.7% and 9.5% of patients had been exposed to commercial BEL in the BEL and PBO groups, respectively. Cumulative follow-up adjusted mortality and malignancy rates (per 100 patient years) were lower in the BEL vs PBO Year 1 treatment group (Table 1).

Conclusion: Year 2 follow-up results of BASE, the largest clinical trial of SLE to date,¹ provide continued support for the BEL safety profile. No new BEL safety concerns were identified in patients with active, autoantibody-positive SLE receiving standard therapy.

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REFERENCES:

[1] Sheikh SZ, et al. *Lancet Rheum*. 2020 (ePub ahead of print) doi.org/10.1016/S2665-9913(20)30355-6

	BEL	PBO	Total
Year 1 as-treated population	N=2002	N=2001	N=4003
Year 1 deaths, n (%)	13 (0.65)	22 (1.10)	35 (0.87)
Year 1 new primary malignancies, n (%)	9 (0.45)	10 (0.50)	19 (0.47)
Year 2 (as-treated in Year 1) population	N=1681	N=1666	N=3347
Year 2 deaths by MedDRA SOC, n (%)	9 (0.54)	21 (1.26)	30 (0.90)
Cardiac disorders	2 (0.12)	6 (0.36)	8 (0.24)
Infections and infestations	4 (0.24)	2 (0.12)	6 (0.18)
Uncoded	1 (0.06)	3 (0.18)	4 (0.12)
General disorders/administration site conditions	1 (0.06)	2 (0.12)	3 (0.09)
Gastrointestinal disorders	1 (0.06)	1 (0.06)	2 (0.06)
Neoplasms	0	2 (0.12)	2 (0.06)
Other	0	5 (0.30) [†]	5 (0.15)
Cumulative deaths by Year 2 follow-up, n (%)	22 (1.10)	43 (2.15)	65 (1.62)
Incidence rate per 100 patient years	0.60	1.18	0.89
Year 2 new primary malignancies by MedDRA SOC, n (%)	3 (0.18)	4 (0.24)	7 (0.21)
Neoplasms	2 (0.12)	4 (0.24)	6 (0.18)
Hepatobiliary disorders	1 (0.06)	0	1 (0.03)
Cumulative malignancies by Year 2 follow-up, n (%)	12 (0.60)	14 (0.70)	26 (0.65)
Patient incidence rate per 100 patient years	0.34	0.40	0.37

*Patients in the post-treatment follow-up period are no longer receiving study treatment; [†]1 event/patient: blood/lymphatic system, musculoskeletal/connective tissue, nervous system, psychiatric, and renal/urinary disorders.MedDRA, Medical Dictionary for Regulatory Activities; SOC, system organ class.

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