and aggressive immunosuppressive therapy. Nevertheless, therapy for TM in the context remains insufficient and should be assessed in a controlled clinical trial setting.

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AB0284

COMBINATION THERAPY WITH RITUXIMAB AND BELIMUMAB IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Objectives: To assess the efficacy of combined therapy with rituximab (RTM) and belimumab (BLM) in patients with active systemic lupus erythematosus (SLE).

Methods: The study included 12 SLE pts (1M/11F) with severe (SLEDAI2K_≥10 – 8pts.) and moderate (SLEDAI2K<10- 4pts.) disease activity; out of them 5 patients had lupus nephritis, vasculitis and 7 had predominantly mucocutaneous and articular manifestations of SLE. The dose of oral GC was: 60mg in one patient with vasculitis, LN, cerebrovasculitis; in 9 patients from 10 to 5mg; in 2 patients without oral glucocorticoids. All patients with SLE with kidney damage, CNS, and vasculitis received cytostatics. All patients with vasculitis, LN, etc. received mycophenolate mofetil or cyclophosphamide. Rituximab (RTM) was administered at 500-2000mg, with subsequent adding of Belimumab (BLM) 1-6 months later at a standard dosing regimen 10mg/kg once a month a total of 7 infusions. The following parameters were evaluated: the effectiveness of therapy, the concentration of autoantibodies, the dose of oral corticosteroids initially at the time of RTM administration and then every 3 months after the initiation of BLM therapy.

Results: 8 pts demonstrated the decrease in clinical and laboratory SLE activity, starting from 3mo of follow-up. After the start of BLM infusions, a decrease in SLE activity was observed in all patients. Among them, 9 had SLEDAI-2K activity of less than 4 points (SLEDAI-2K Me 12 [9.5;17], after treatment of RTM and BLM 4[2;4]). Only one patient (№4) had a relapse of SLE, due to the omission of the BLM infusion. He was receiving standard GC doses. In dynamics, a decrease anti-double DNA titres (Me 101 [39;250]U/ml vs 19 [9;70] U/ml), C3 (0.44 [0.39;0.59]g/l vs 0.81 [0.72;0.87] g/l), C4 (0.06 [0.031;0.1] g/l vs 0.14 [0.13;0.14] g/l) was registered. The GC dose was reduced in most patients (tab. 1), but the previously prescribed immunosuppressive therapy continued. There were no cases of severe infection.

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 flare. The use of such therapy contributes to a rapid and effective reduction in the activity of the disease, normalization of laboratory markers of SLE (at to ds-DNA, C3, C4), the use of lower doses of oral GCs. 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.

Table 1. Dose of oral glucocorticoids (prednisone), mg

№ patient	Before the introduction of RTM, mg	1st 7th injection of BLM, mg	7th injection of BLM, mg	
1	20	20	15	↓
2	7.5	5	5	↓
3	5	5	5	=
4	10	10	10	↓
5	5	5	5	↓
6	60	7.5	2.5	↓↓↓
7	10	2.5	0	↓↓↓
8	10	10	5	↓
9	2.5	2.5	2.5	=
10	10	10	5	↓
11	0	0	0	=
12	0	0	0	=

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AB0285

EFFECTIVENESS OF IMMUNOSUPPRESSIVE THERAPY FOR CONNECTIVE TISSUE DISEASE-ASSOCIATED PULMONARY ARTERIAL HYPERTENSION

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Background: Connective tissue disease (CTD) associated pulmonary arterial hypertension (PAH) is considered to be an indication for immunosuppressive therapy (IT) except scleroderma associated PAH. However, the response rate defined by improvement of WHO functional class and hemodynamic parameters is reported to be around 50% [1]. Since CTDs are systemic diseases, it may be difficult to evaluate the efficacy of IT by subjective symptoms. Although there are previous studies reporting that the combined use of IT and pulmonary vasodilators significantly improved hemodynamics [2], response to IT without titration of pulmonary vasodilators remains to be elucidated.

Objectives: To examine whether IT is effective for CTD-PAH.

Methods: We retrospectively examined the medical records of consecutive 13 patients with CTD-PAH (female 13, mean age 47 ± 15 years) treated with methylprednisolone (1mg/kg/day, oral) and intravenous bolus cyclophosphamide (IVCY) (500mg/m²) every four weeks for six times. Patient characteristics are described in Table 1. Right heart catheterization (RHC) was done at prior to IT, before adding PAH specific agents, and at the fifth or sixth course of IVCY. In treated cases, the previous vasodilators remained unchanged during the first term of IT.

Results: At the first follow up RHC, decrease of mean pulmonary arterial pressure over 5 mmHg was observed in all patients, and decrease of pulmonary vascular resistance (PVR) was observed in twelve out of 13 patients (Figure 1). Over 20% of PVR reduction was observed more in the patients of pulmonary vasodilator naïve and started IT within one year from symptoms than others (6/7 vs 1/6, p=0.03). Although six-minutes walk distance (6MWD) tended to be prolonged between first and second RHC (298 ± 70 m vs 382 ± 81 m; p=0.054; n = 9), 6MWD was shortened in some cases with good hemodynamic improvement (2/5). All patients were prescribed oral PAH specific agents finally, but no one needed parenteral prostanooids. Two patients (15%) died during maintenance therapy for causes other than PAH. Three-year and five-year survival rates were 91.7% and 81.5%, respectively.

Conclusion: IT without titration of pulmonary vasodilators significantly improved hemodynamic parameters despite of less improvement in 6MWD in CTD-PAH patients. Considering that CTDs itself might affect the exercise tolerance regardless of PAH, these hemodynamic changes may contribute to better prognosis and IT might be considered especially for patients early in clinical courses and treatment naïve.

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Table 1. Characteristics of patients

Patient	Age, yr	Connective Tissue Disease	Years from symptom to immunosuppressive therapy	Previous vasodilators	vasodilators at final visit
1	47	SS	1.5	PGI2	ERA
2	62	SS, RA	2	none	PDE5
3	32	SS	1	none	ERA
4	57	SS, SSc	0.5	none	PDE5
5	26	SS, MCTD, SLE, SSc	0.5	none	PDE5
6	70	SSc, SS s/o	13	sGC, ERA	sGC, ERA
7	32	SS s/o, SLE	0.1	none	PDE5
8	31	MCTD	3	ERA, PDE5, PGI2	ERA, PDE5, PGI2
9	43	SSc, SLE	0.6	ERA, PDE5	ERA, PDE5, PGI2
10	67	MCTD, PM	0	none	sGC
11	41	SS	0.1	none	ERA, PDE5
12	69	SS	0.3	none	PDE5
13	44	SS, MCTD s/o, SLE s/o	0.1	none	ERA, sGC

N.A., not acquired; s/o, suspect of; SS, Sjögren's syndrome; RA, rheumatoid arthritis; SSc systemic sclerosis; SLE, systemic lupus erythematosus; MCTD, mixed connective tissue disease; PM, Polymyositis; PGI2, prostacyclin derivative; sGC, soluble guanylate cyclase stimulator; ERA, endothelin receptor antagonist; PDE5, phosphodiesterase type 5 inhibitor.

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.

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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.

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