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.