SLE, Sjögren's and APS – treatment

AB0278

OFF-LABEL RITUXIMAB FOR SYSTEMIC AUTOIMMUNE DISEASES: A CASE SERIES FROM A THIRD LEVEL HOSPITAL DURING A 5 YEAR- PERIOD

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Background: Rituximab (RTX) is a drug composed of chimeric monoclonal antibodies against the CD20 protein that leads to B cell lymphocyte depletion and is currently licensed for rheumatoid arthritis. There is growing evidence of off-label use of rituximab for severe and refractory systemic autoimmune diseases (SAD). **Objectives:** Analysing the clinical effectiveness of RTX for SADs such as vasculitis (VS), systemic lupus erythematosus (SLE), systemic sclerosis (SS), primary sjögren syndrome (pSS), necrotizing myopathy (NM) and dermatomyositis (DM) in a rheumatology outpatient clinic in a third level hospital during a 5 year-period (2015–2020).

Methods: We conducted a retrospective analysis of patients with SAD treated with RTX in the last 5 years. We evaluated demographic and clinical data, indication for RXT, previous treatments, cumulative dose of rituximab and corticosteroids, clinical response, and the presence of adverse events. We considered follow-up period between the first and the last clinical evaluation. Clinical response was considered complete with symptom and analytical remission; incomplete with partial symptom or analytical response and no response if there was no symptom or analytical response.

Results: 35 patients were included (54% women, mean age 60.16 ±17 years). The diagnosis were: pSS (31.4%), SS (17%), SLE (17%), VS (20%), NM (8.8%) and DM (5.8%). Indications for treatment were pulmonary disease in 37% of cases, renal disease in 17%, articular manifestations in 11.4%, haematological manifestations in 14.3%, skin involvement in 8.8%, neurologic manifestations in 5.7% and myopathy in 5.8%. RTX was used after therapeutic failure with previous treatments in 80% (20% of which had receiving treatment with biological disease-modifying antirheumatic drugs) and as first line treatment in only 20% of the cases. After rituximab, 60% of patients had complete response, 17% partial response, and 20% nonresponding. Mean corticosteroid dose post-rituximab was significantly reduced by 60% in pSS (p 0.02), 65% in VS (p 0.03), 50% in SS (p 0.04) and NM (p 0.046). Five patients (14%) had infectious complications, 2 of which needed hospitalization. 7 patients (17%) discontinued therapy, 5 due to ineffectiveness (2 SLE, 1 NM, 1 DM and 1 SS) and 2 patients (14%) due to infectious complications (1 pSS and 1 VS). Patients underwent a median of 2 treatment cycle. The median follow-up after starting RTX was 48.5 (IQR 25.9-74.4) months.

Table 1. Clinical characteristics

	pSS	VS	SLE	SS	NM	DM
%	31.4%	20%	17%	17%	8.8%	5.8%
Age (years)	63.8 (19-73)	63.5 (43-82)	59.2 (43-78)	65.8 (56-78)	58.5 (54-63)	48.5 (26-52)
Female	100%	71%	50%	66%	50%	50%
Duration of disease (months)	80.5 (24-108)	39 (12-60)	38.4 (36-90)	56.4 (14-96)	69 (48-90)	60 (25-82)
Cumulative RTM dose (g/m2)	2.5 (0.75-6)	3.2 (0.5-8)	1.4 (0.75-5)	2.8 (0.5 – 7)	1.2 (0.5 – 5)	0.56 (0.38-0.75)
Complete clinical response	63%	86%	33%	71%	33%	0%
Incomplete response	18%	14%	33%	14%	0%	50%
No response	18%	0%	33%	14%	66%	50%
Glucocorticoid dose (mg/day)	12.5	21.3	9	9	15	15
Before RTMX	(5-20)	(5-30)	(0-15)	(5-15)	(7.5 – 25)	(7.5 – 25)
Glucocorticoid dose (mg/day)	5	7.5	5	4.5	10	12.5
After RTX	(2.5-15)	(5-15)	(2.5-15)	(2.5-10)	(7.5-25)	(8 – 20)
Immunosuppressants	81%	71%	90%	50%	33%	50%
Before RTX						
Immunosuppressants	54%	28%	57%	66%	67%	50%
After RTX						
Severe infusion-related side effects including need for admission	0%	14%	16%	0%	0%	0%
Other infusion-related side effects	9%	29%	17%	17%	0%	0%

Conclusion: Treatment with RTX was very effective in SADs, particularly in VS, SS and pSS. Further studies are needed to clarify RTX efficacy and safety in SADs, as well as indications and optimal RTX regimens.

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AB0279

THE IMPACT OF HYDROXYCHLOROQUINE DAILY DOSE IN THE PREVENTION OF FLARES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN REMISSION

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Background: The EULAR recommendations for the management of systemic lupus erythematosus (SLE) suggest a hydroxychloroquine (HCQ) dose of ≤5.0 mg/kg/day instead of 6.5 mg/kg/day to reduce the risk of HCQ-induced retinopathy (1). This change in HCQ dose may potentially lead to undertreatment with blood levels below the presumed therapeutic range.

Objectives: The aim of this study was to compare flare rates and HCQ blood levels between the two different oral dosages in patients with SLE in remission.

Methods: Eligible patients were SLE patients in clinical remission according to the preliminary Definitions of Remission in SLE (DORIS) criteria for at least one year and treatment with stable dose of HCQ for at least six months and stable dose of glucocorticoids and/or immunosuppressants (2). Flares were defined by SELENA-SLEDAI Flare Index (3). A venous blood sample was collected on two different occasions from all patients, reflecting actual therapeutic adherence. The biosamples were analyzed in a UPLC-MS/MS system composed of a Nexera chromatograph (Shimadzu) coupled with a Q-trap 6500 spectrometer (AB Sciex). A mean [HCQ] value ([HCQm]) for each patient was then calculated. Predictors of flares were analyzed by Cox regression.

Results: We selected 66 patients who were stratified according to HCQ oral dose in two groups (Table 1). We observed 23 (35%) flares that developed in mean 26,0 (±15,1) months: 8/32 (25%) patients taking HCQ 5 mg/kg/day; 15/34 (44%) in the other group. No statistically significant difference was observed between the two group in number of flares (p=0,106), mean time of occurrence (p=0,904) and median [HCQm] (p=0,983). At regression analysis, older age at baseline was protective against flare occurrence (HR 0,93), while concomitant immunosuppressive therapy showed significant positive association (HR 3,66).

Conclusion: Our study suggests that low dosage of HCQ (5 mg/kg/day) may safely be prescribed in SLE patients in remission, without significant differences in terms of blood concentration and impact on the clinical course of SLE.

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Table 1. Demographic, clinical and therapeutic features of the cohort and follow up data.

	All patients (n= 66)	HCQ ≤5mg/Kg/die (n=32)	HCQ 6,5mg/Kg/die (n=34)	P
Sex, female	65 (99)	31 (97)	34 (100)	0,3026
Age, y, mean (SD)	42,00±11,27	41,80±10,25	42,10±12,30	0,9140
Disease duration, y, mean (SD)	15,70 (9,02)	17,80 (8,01)	13,67 (9,50)	0,0624
SLEDAI, median (range)	2 (0-4)	1 (0-4)	2 (0-4)	0,6480
SLICC, median (range)	0 (0-2)	0 (0-2)	0 (0-1)	0,8556
[HCQm] ng/mL, median (range)	512,60 (104,41-3105,66)	457,16 (104,41-3105,66)	538,49 (149,24-1239,15)	0,5989
[DCQ] ng/mL, median (range)	73,41 (4,16-649,84)	66,84 (4,16-649,84)	66,31 (10,75-258,41)	0,9380
Time remission, y, median (range)	2,00 (1-11)	2,96 (1-10)	2,00 (1-11)	0,6588
Previous renal involvement	31 (47)	15 (47)	16 (47)	0,9882
Time HCQ, y, median (range)	5 (0-32)	8 (0-26)	5 (1-32)	0,2391
Glucocorticoids	33 (50)	18 (56)	15 (44)	0,4700
Mycophenolate mofetil	6 (9)	2 (6)	4 (12)	0,4396
Azathioprine	7 (11)	4 (14)	3 (9)	0,6305
Methotrexate	1 (2)	0	1 (3)	0,3320
Cyclosporine	2 (3)	1 (3)	1 (3)	0,9655
Belimumab	1 (2)	0	1 (3)	0,3320
Follow up time, m, median (range)	49 (4-67)	52 (7-67)	43 (4-67)	0,1115
Number of flares	23 (35)	8 (25)	15 (44)	0,1060
Time to flare, m, mean (SD)	26,0 (±15,1)	26,6 (±16,4)	25,8 (±14,9)	0,9042
Ocular alterations	6 (9)	4 (12)	2 (6)	0,0947

	HR	95% CI	P
Age, y	0.9336	0.8947 to 0.9742	0.0016
Disease duration, y	0.9712	0.9257 to 1.0191	0.2340
SLEDAI	1.1193	0.8084 to 1.5498	0.4971
SLICC	1.5583	0.7785 to 3.1191	0.2102
[HCQm] ng/mL	0.9997	0.9987 to 1.0007	0.3983
[DCQ] ng/mL	0.9973	0.9922 to 1.0024	0.3048
Clinical remission off/on therapy	1.3702	0.6001 to 3.1282	0.4546
Complete remission off/on therapy	0.7298	0.3197 to 1.6663	0.4546
Time remission	0.7984	0.6287 to 1.0138	0.0647
Previous renal involvement	1.1207	0.4942 to 2.5416	0.7850
Time HCQ	0.9735	0.9128 to 1.0383	0.4140
Glucocorticoids	2.1489	0.8966 to 5.1502	0.0863
Immunosuppressive therapy	3.6639	1.5924 to 8.4304	0.0023
HCQ dosage	0.4995	0.2113 to 1.1805	0.1137

Figure 1. Predictors of flares analyzed by Cox regression.*Serena Fasano and Valentina Messinitti contributed equally to this abstract

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AB0280

THE INFLUENCE OF TARGET THERAPY AS WELL AS GLUCOCORTICOID TAPERING ON DISEASE FLARE IN SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM A PROSPECTIVE CHINESE COHORT

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Background: Treat-to-target in systemic lupus erythematosus (SLE) has been proposed for 7 years and several recommendations were developed [1]. In these recommendations, prevention of flares should be a realistic target. Meanwhile, 'remission' or 'low disease activity' was recommended as the treatment target and minimizing glucocorticoids (GC) dose or withdrawal if possible was suggested in the maintenance treatment. However, would target therapy and GC tapering/withdrawal influence disease flare?

Objectives: To investigate the frequency and determinants of disease flare, especially the influence of target therapy as well as GC tapering on flare in Chinese lupus patients.

Methods: The baseline and follow-up data of all consecutive patients in a prospective longitudinal lupus cohort from January 2017 to June 2020 were collected. The lupus low disease activity state (LLDAS) was defined as in Golder et al., 2019[2]. The criteria for remission were from DORIS definitions [3]. Flare was assessed using the SELENA-SLEDAI flare index [4].

Results: We enrolled 185 patients with disease duration at recruitment of 2.3 (0.8–7.7) years. During the 26.2 (12.5–34.5) months of follow-up, 73 (39.5%) patients experienced 95 flares, including 70 mild/moderate and 25 severe flares. The incidence of flare per patient-year was 0.27. Kaplan-Meier analyses showed that compared with those who never achieved LLDAS or DORIS, the patients who achieved the target at least once had a higher flare free survival rate; meanwhile, the patients with prednisone withdrawn had significantly lower flare free rate compared with those with small dose of GC maintained (≤ 7.5 mg/d) (Figure 1A), but among the patients with different prednisone maintain doses (7.5–5mg, 5–2.5mg, and ≤ 2.5 mg) there was not significant difference (Figure 1B). Cox regression analysis showed that younger age at disease onset and lower Complement 3 (C3) level at recruitment were independent risk factors for flare and achieving LLDAS or DORIS $\geq 50\%$ of visits was independent protective factor (Table 1).

Conclusion: In this Chinese prospective SLE cohort, age at disease onset, C3 level at recruitment and therapeutic target achieving influenced disease flare independently and significantly. GC tapering in appropriate patients and with appropriate pace did not increase the flare rate, but prednisone withdrawal may induce more disease exacerbation, which needs to be confirmed by large prospective studies.

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Table 1. Determinants of disease flare by multivariate Cox regression analyses

	Model 1 (LLDAS) ^Δ			Model 2 (RONT) ^Δ			Model 3 (Complete RONT) ^Δ		
	HR	95%CI	P value	HR	95%CI	P value	HR	95%CI	P value
Age at disease onset (years) [†]	0.97	0.95-0.99	0.004	0.97	0.95-0.99	0.003	0.97	0.95-0.99	0.003
Anti-dsDNA positive at recruitment	1.34	0.82-2.18	0.217	1.12	0.68-1.85	0.649	1.19	0.73-1.96	0.486
C3 (mg/L) at recruitment	0.998	0.997-0.999	0.004	0.998	0.997-0.999	0.007	0.998	0.997-1.000	0.010
Minimum prednisone dose during follow-up (mg/d)	0.98	0.90-1.08	0.716	1.01	0.94-1.08	0.747	1.04	0.97-1.11	0.243
Therapeutic target achieved $\geq 50\%$ of observations ^Δ	0.60	0.39-0.94	0.001	0.54	0.34-0.87	0.011	0.68	0.51-0.92	0.011

^Δ In the three hazard models, the different target achievement status were included respectively. RONT: Clinical remission on treatment; Complete RONT: Complete remission on treatment.

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AB0281

MORTALITY PREDICTORS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A SINGLE TERTIARY CENTER REFERRAL EXPERIENCE

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Background: Systemic Lupus Erythematosus (SLE) is a heterogeneous chronic multisystemic disease that has an increased risk of requiring inpatient management with higher morbidity and mortality rates.

The most frequent causes of mortality are a high disease activity, infections, and cardiovascular diseases.

Objectives: To determine the predictors of mortality in patients diagnosed with SLE.

Methods: A longitudinal, descriptive, observational study was performed from March 2017-March 2020 at the University Hospital of the Autonomous University of Nuevo León, México, including patients with a diagnosis of SLE according to the ACR-EULAR 2012/2019 criteria.

Descriptive statistics were used for demographic variables. Associations between mortality and clinical variables were determined using binary logistic regression analysis; a p < 0.05 was considered statistically significant. The SPSS program version 20 was used.

Results: One-hundred and eighty-six patients with SLE diagnosis who fulfilled ACR-EULAR 2012/2019 criteria were included, 161 (86.6%) were women; the mean age was 35.8 (SD 15.41) years. The main chief complaints were dyspnea 31 (16.7%), fever in 28 (15.1%), renal involvement in 21 (11.29%), and arthritis in 19 (10.22%) patients.

Of the 186 patients, 34 (18.3%) had a readmission, 13 (7%) required intensive care unit management, 68 (36.6%) had some type of infection and 22 (11.8%) died. Factors associated with mortality are shown in table 1.

Patients receiving steroids and immunosuppression previous to hospitalization were 73 (39.2%) and 92 (49.5%) respectively.

Conclusion: Infections remain the leading cause of death in SLE patients. Factors that predispose to infections are a chronic use of steroids and immunosuppression as well as high activity of disease.