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