AB0472

PRIMARY SJOGREN SYNDROME ASSOCIATED INTERSTITIAL LUNG DISEASE: FEATURES, TREATMENT AND OUTCOME OF A MONOCENTRIC COHORT

Andreina Manfredi¹, Marco Sebastiani¹, Caterina Vacchi¹, Fabrizio Luppi², Stefania Cerri¹, Giulia Cassone^{1,3}, Carlo Salvarani^{1,3}. ¹University of Modena and Reggio Emilia, Azienda Ospedaliero-Universitaria Policlinico di Modena, Modena, Italy; ²University of Milan-Bicocca, San Gerardo Hospital, Monza, Italy; ³IRCCS Arcispedale Santa Maria Nuova, Azienda Unità Sanitaria Locale-IRCCS di Reggio Emilia, Reggio Emilia, Italy

Background: Primary Sjögren's syndrome (pSS) is an autoimmune systemic disease characterized by lymphocytic infiltration of exocrine glands, mainly resulting in dysfunction of salivary and lacrimal glands and symptomatic xerostomia and xerophthalmia. About one third of patients also present extra-glandular manifestations and, among them, interstitial lung disease (ILD) is one the most frequent, occurring in about 10–20% of patients. ILD is associated with an impaired quality of life and physical capacity and to a reduced 10-year survival. Despite it seems to be more frequently detected in late stages of the disease, some authors suggest that ILD can be diagnosed before pSS in 20% of cases. Main predictive factors of progression of pSS-ILD have not been clearly investigated in previous studies and no evidence-based treatment is defined for these patients.

Objectives: To describe the clinical and serologic features and the outcome of a monocentric cohort of pSS-ILD and the possible differences between patients treated or not with immunosuppressive treatment

Methods: We retrospectively evaluated the 37 pSS-ILD patients followed at our Rheumatology Unit (male/female ratio 1/6.4, mean age 69.6±11.3 years, mean disease duration of pSS 5±5.2 years).

Among them, 18 patients (48.6%; group 1) underwent immunosuppressive treatment because of lung disease, namely mycophenolate mofetil (9 patients, 50%), cyclophosphamide (3, 16.7%), azathioprine (5, 27.8%), high dose steroids (1, 5.6%), while 19 patients were not treated (group 2).

Results: No significant differences were observed in regard of age, male/female ratio, and disease duration of ILD and pSS, while a significant difference was observed regarding the lung function of the 2 groups; the forced vital capacity (FVC) and the diffusion lung capacity of CO (DLCO) at baseline were significantly lower in the group 1 (FVC 78.6% vs 99.4% $p=0.008$; DLCO 45.7% vs 56.9%, $p=0.025$; in group 1 and group 2, respectively). No significant difference was observed between baseline and follow-up for FVC and DLCO in both groups, regardless the immunosuppressive drug (fig. 1). At the end of follow-up FVC increased, decreased and remained stable in 5.3/10.5/84.2% and 16.7/27.8/55.6%, in group 1 and group 2, respectively; DLCO increased, decreased and remained stable in 10.5/21.1/68.4% of group 1, while remained stable or decreased in 61.1 and 38.9 of treated patients, respectively (figure 1).

Figure 1. Evolution of lung function pSS patients treated (group 1) or not (group 2) with immunosuppressive drugs

Figure 1

Conclusion: At our knowledge, few studies have investigated the features of pSS-ILD and the role of immunosuppressive drugs in these patients. Our data suggest that the decline of lung function is one of the most significant parameters to guide the prescription of immunosuppressive drugs, but no differences can be observed according to the treatment in

term of effectiveness. However, no studies have investigated the correctness of this approach or the efficacy of the MMF or CFX in pSS-ILD. Our study is strongly limited by the retrospective design and the low number of patients evaluated, but these data set attention on this unmet need. Further prospective studies are mandatory to clarify the impact of ILD in pSS patients and the correct therapeutic approach.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.6953

AB0473

HYPOGAMMAGLOBULINEMIA AND INFECTIONS IN RHEUMATOLOGIC PATIENTS TREATED WITH RITUXIMAB

Andres Fierro¹, Mariano Andres², Jenny de la Torre-Aboki³, Paloma Vela-Casasempere³, Maria Paz Martínez-Vidal³. ¹Universidad Miguel Hernández, Faculty of Medicine, Alicante, Spain; ²Hospital General Universitario de Alicante, Alicante, Spain; ³Hospital General Universitario de Alicante, Alicante, Spain

Background: Treatment with rituximab (RTX) for rheumatologic diseases may produce hypogammaglobulinemia (hypoglob) (1,2), and that may increase the risk to acquire certain infections (3,4). There are no established guides to evaluate and treat hypoglob in these patients. In our hospital, the percentage of patients who develop hypoglob and severe infections is unknown.

Objectives: To analyse the effect of RTX on immunoglobulin (Ig) levels and to evaluate the severe infections and hepatitis B reactivations that could be related to this treatment.

Methods: This is a descriptive, retrospective study of patients followed up in the Rheumatology Unit of the Alicante General University Hospital (HGUA) who had received at least one course of RTX. Clinical characteristics and laboratory parameters were obtained from the electronic charts: type of disease, posology and total amount of RTX, Ig levels before and after treatment with RTX, the concomitant treatment with disease-modifying drugs (DMDs), hepatitis B virus's (HBV) reactivations and infections that required hospitalization. Hypoglob was assessed when IgG < 750 mg/dL, and severe hypoglob if IgG < 450 mg/dL. The association of hypoglob with disease and treatment's aspects was studied by t-Student, U-Mann-Whitney and Chi-2. Multiple logistic regression was conducted to study the independent risk factors associated with hypoglob. The study was approved by the Hospital Ethics Committee.

Results: Finally 106 patients were included, 85 women (80.2%) and 21 men (19.8%). The more frequent conditions were rheumatoid arthritis (47.2%), Sjögren syndrome (16%), Systemic Lupus Erythematosus (13.2%), vasculitis (6.6%) and other connective tissue diseases (10.4%). Characteristics of the sample are shown in table 1. A correct follow up of the Ig levels during the treatment was shown to be undergone in 87.7% of the cases. It was found that 35.8% of the patients presented hypoglob and 13.2% presented severe infections after receiving RTX. No HBV reactivations were found. Among the patients with hypoglob, 78.9% received concomitant treatment with other immunosuppressants (methotrexate 23.6%, leflunomide 23.6%). Hypoglob was more frequent in rheumatoid arthritis (44%), lupus (42.8%) and vasculitis (28.6%). Through simple logistic regression hypoglob during treatment was associated with the presence of previous hypoglob ($p=0.025$), higher doses received ($p=0.01$) and longer treatment ($p=0.003$). In the multiple logistic regression, only low levels of Ig before treatment turned out to be an independent risk factor for hypoglob during treatment (OR 6.86; IC 1.25-37.57). The IgM and IgA levels, but no the IgG levels were significantly lower in patients who has severe infections.

Duration of treatment with RTX (months)	34.7 ± 30
Total dosage (grams)	12.7 ± 9.6
RTX posology	79 (74.5%)
Standard	10 (9.4%)
Single iv dose every 6 months	11 (10.4%)
On demand	
Ig levels followed up during treatment	YES: 93 (87.7%) NO: 13 (12.3%)

Patients with hypoglyb during RTX	38 (35.8%)
Severe hypoglyb	4 (3.8%)
Patients with severe infections which required hospitalization	14 (13.2%)
With hypoglyb	7 (6.6%)
Without hypoglyb	7 (6.6%)
Severe infections which required RTX discontinuation	2 (1.9%)
Respiratory	0
HBV reactivation	2 (1.9%)
Skin (Erysipela and celulitis)	
Exitus	0 (0%)

Conclusion: Hypogammaglobulinemia happens in a third of the patients who receive RTX, especially in those who have low previous IgG levels; therefore a follow up during the treatment should be encouraged. Low IgM and IgA levels during the treatment could also be associated with severe infections.

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Disclosure of Interests: Andres Fierro: None declared, Mariano Andres: None declared, Jenny de la Torre-Aboki: None declared, Paloma Vela-Casasempere Grant/research support from: UCB, Abbvie, Pfizer, Roche, Bristol-Myer-Squibb (another research, not BIOBADASER related), Consultant for: UCB, Lilly, Pfizer, Roche, Bristol-Myer-Squibb, Speakers bureau: Roche, UCB, MSD, Pfizer, GSK, BMS, Lilly, Maria Paz Martínez-Vidal: None declared

DOI: 10.1136/annrheumdis-2019-eular.3767

AB0474

MORTALITY ACROSS RITUXIMAB-TREATED PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM THE BRITISH ISLES LUPUS ASSESSMENT GROUP (BILAG) REGISTRY

Aysun Aksoy^{1,2}, Stephen McDonald^{3,4}, Eoghan McCarthy⁴, Ben Parker^{3,4}, Ian N. Bruce^{3,4}, British Isles Lupus Assessment Group. ¹Marmara University Faculty of Medicine, Division of Internal Medicine, Department of Rheumatology, Istanbul, Turkey; ²University of Manchester, Division of Musculoskeletal and Dermatological Sciences, Manchester, United Kingdom; ³University of Manchester, NIHR Manchester BRC, Manchester, United Kingdom; ⁴Manchester University Foundation Trust, The Kellgren Centre, Manchester, United Kingdom

Background: Mortality in Systemic Lupus Erythematosus (SLE) is elevated in comparison to the general population. Previously we have demonstrated improved disease control in response to Rituximab (RTX) therapy in a cohort of refractory SLE patients.

Objectives: To investigate mortality in refractory SLE patients treated with RTX and identify risk factors that may be associated with death.

Methods: All patients recruited to the BILAG-BR (both RTX treated and standard of care-SOC) were included from initial study visit to death or 3 years post last treatment change. Demographics, concurrent medication use, disease activity (BILAG/SLEDAI) and damage scores (SLICC-DI) were recorded. Information regarding mortality was collected from study centres and NHS digital national death registry. Baseline demographic data are presented using descriptive statistics performed using Stata (version 14).

Results: 830 patients were included (715 RTX-treated, 115 standard therapy). RTX-treated patients tended to have longer disease duration (10 vs 6.5 years respectively) and were more likely to have active musculoskeletal disease (% BILAG A or B: 39% vs 23%). Rates of renal (11% vs 16%) and neurological disease (12% vs 9%) were comparable between groups as were baseline SLICC-DI and SLEDAI scores.

33 deaths were reported. 28 (3.9%) RTX-treated patients (1.2 deaths/100 pt yrs follow up) and 5 (4.3%) non-RTX patients (1.5 deaths/100 pt yrs follow up).

Cause of death was identifiable in 20 RTX treated patients. Infection was the commonest cause of death (10/20, 50%) followed by ischaemic heart disease (5/20, 25%) and malignancy (3/20, 15%). Median time to death for RTX-treated was 481 days.

Risk factors associated with mortality within the RTX group included male gender, older age at diagnosis, renal disease, hypogammaglobulinaemia, high SLICC-DI and higher steroid use at last review (Table 1). Median cumulative RTX dosing was 2g for deceased and alive.

Deceased RTX patients had a greater total number of co-morbidities at baseline (2.5 vs 0, $p < 0.01$) driven predominantly by the presence of hypertension (11/28, 39% vs 159/687, 25%, $p = 0.05$), ischaemic heart

disease (4/28, 14% vs 11/687, 2%, $p = 0.00$) and diabetes (7/28, 25% vs 15/687, 2%, $p = 0.00$).

Conclusion: RTX treated patients do not appear to have higher mortality rates compared to patients starting SOC treatment. Mortality is associated with cardiovascular risk factors, higher steroid doses, hypogammaglobulinaemia and renal disease. Active management of these risk factors may lead to improved mortality outcomes.

Table 1. Deceased and alive RTX treated patients

	Deceased (n=28)	Alive (n=687)
Gender (M: F%) (n= 708)	7:21 (25% M, 75% F)	63:617 (9.26% M, 90.74% F)
Median Age at Diagnosis in years (IQR) (n = 713)	51.5(42.5-66.5)	39(30-49)
Median Disease duration in years (IQR) (n=647)	13(11-19)	12.27(6-16)
Median Cumulative Rituximab dose in mg (IQR) (n=567)	2000 (2000-4000)	2000 (2000-4000)
Ethnicity	17:5	291:178
(Caucasian: Non-Caucasian) (n =491)	(77.27% Caucasian, 24% Non-Caucasian)	(62.05% Caucasian, 37.95% Caucasian)

Disclosure of Interests: Aysun Aksoy: None declared, Stephen McDonald: None declared, Eoghan McCarthy: None declared, Ben Parker Grant/research support from: GSK, Consultant for: AZ, UCB, GSK, Ian N. Bruce Grant/research support from: Genzyme Sanofi, GlaxoSmithKline, Consultant for: AstraZeneca, Eli Lilly, GlaxoSmithKline, ILTOO Pharma, MedImmune, Merck Serono, Speakers bureau: GlaxoSmithKline, UCB Pharma

DOI: 10.1136/annrheumdis-2019-eular.351

AB0475

BELIMUMAB: EXPERIENCE IN CLINICAL PRACTICE SETTINGS AT A RHEUMATOLOGY DEPARTMENT IN A TERTIARY HOSPITAL

Carolina Merino Argumánez¹, Olga Rusinovich¹, Consuelo Ramos Giraldez², María Espinosa³, Hilda Godoy¹, Carmen Barbadillo Mateos¹, Jose Campos Esteban¹, Mercedes Jiménez Palop¹, Jesus Sanz¹, Luis Fernando Villa Alcázar¹, Carlos Isasi Zaragoza¹, Monica Fernandez Castro¹, José Luis Andréu Sánchez¹. ¹Hospital Puerta de Hierro, Majadahonda (Madrid), Spain; ²Valme Hospital, Sevilla, Spain; ³Hospital Infanta Sofía, Madrid, Spain

Background: Belimumab is a human IgG1 monoclonal antibody directed against BAFF, a B lymphocyte survival factor. It is indicated as adjuvant treatment in adult patients with active systemic lupus erythematosus (SLE), with positive autoantibodies and with a high degree of activity of the disease despite standard treatment.

Case	Gender	Age	Indication	Start date	Withdrawal	Reason for withdrawal	Initial and final daily prednisone dose	Time in treatment
1	♀	56	thrombocytopenia	26/01/2012	Yes	Inefficiency	0 → 0	8 months
2	♀	33	arthritis	17/03/2012	No		10 → 5	6 years and 6 months
3	♀	48	arthritis	22/03/2012	Yes	Neutropenia	7.5 → 2.5	8 months
4	♀	64	thrombocytopenia	03/04/2012	Yes	Urothelial carcinoma	15 → 2.5	5 years
5	♀	45	cutaneous	07/05/2012	Yes	Inefficiency	30 → 30	4 months
6	♀	70	cutaneous thrombocytopenia	09/12/2013	No		15 → 2.5	4 years and 9 months
7	♀	54	arthritis	18/12/2014	No		15 → 2.5	3 years and 9 months
8	♀	46	arthritis	30/11/2015	No		0 → 0	2 years and 10 months
9	♀	58	arthritis	30/05/2017	No		7.5 → 5	1 year and 4 months
10	♀	31	arthritis	17/01/2018	No		10 → 5	8 months
11	♀	46	arthritis	15/02/2018	No		5 → 2.5	7 months
12	♀	49	serositis	11/04/2018	No		5 → 5	5 months

Objectives: This study aims to describe a sample of patients diagnosed with SLE who received treatment with belimumab in a tertiary hospital.