1. Title: Physicians' attitudes in serologically active clinically quiescent systemic lupus. Results from the Portuguese registry Reuma.pt/LES

2. Background

Monitoring and controlling disease activity is of utmost importance in the management of patients with systemic lupus erythematosus (SLE) in order to prevent irreversible damage. The treat to target (T2T) approach applied to SLE is a hot topic nowadays. However, the unpredictable disease course together with measurement instruments that are not consensual and the absence of a globally accepted therapeutic goal makes its applicability in clinical practice challenging.

Remission definition is still a matter of debate in lupus and the discordance between clinical manifestations and laboratory tests is a well known phenomenon [1, 2]. In 6 to 15% of the patients serologic tests remain persistently abnormal despite the absence of clinical manifestations attributable to SLE disease activity [3]. The significance of persistently high anti-dsDNA antibodies and/or complement consumption in the absence of clinically active disease is still unclear and the outcome of these patients differ one from another. While some patients remain in clinical remission for long periods, a significant proportion flare up after some time[4]. Additionally, there is some evidence that serologically active clinically quiescent (SACQ) lupus patients may accrue damage, though at a much lower rate than clinically active patients[5]. So far, no predictors of flare have been identified in this particular patients group [4, 6] and there is no consensus regarding the best approach neither what medication (if any) is the most appropriated in SACQ lupus.

3. Objectives:

Our aim is to understand the physicians' attitudes with respect to use of medication in serologically active clinically quiescent lupus patients. Additionally we will explore what conditions predict the use of corticosteroids and immunosuppressant drugs in SACQ SLE.

4. Methodology:

a) *Study design* - observational, cross-sectional

b) *Population* - patients registered in Reuma.pt/LES that fulfill the inclusion/exclusion criteria.

Inclusion criteria

1. Having the diagnosis of SLE according to the ACR revised criteria

2. Clinically quiescent for ≥ 2 consecutive visits, with a minimum interval of 3 months between visits, according to the following definition: no clinical manifestations attributable to SLE disease activity captured by the SLEDAI 2K or BILAG (information available in Reuma.pt/LES)

3. Having anti-dsDNA antibody titers in the abnormal range for the laboratory and/or decreased C3 or C4 for ≥ 2 consecutive visits (SLEDAI 2K of 2 or 4 due to hypocomplementemia and/or positive anti-dsDNA antibody titers at each visit)

Exclusion criteria

1. The presence of other systemic rheumatic diseases except secondary antiphospholipid syndrome or secondary Sjögren's syndrome

2. SLE patients with <2 visits registered in Reuma.pt/LES

3. SLE patients without information on disease activity

c) *Outcome measures*:
   Primary outcome: therapy for SLE at the last visit of SACQ period, namely the use of antimalarials, corticosteroids and immunosuppressants (azathioprine, cyclophosphamide, mycophenolate mofetil, cyclosporine, methotrexate, leflunomide, rituximab, belimumab)
   Secondary outcome: duration of the SACQ period in SLE patients registered in Reuma.pt/LES

d) *Covariates* - Demographic characteristics: age, gender, ethnicity, education; disease characteristics: age at disease diagnosis, disease duration, cumulative organ involvement depicted by the ACR criteria; autoantibody

profile; previous medication for SLE (corticosteroids and immunosupressants); current damage measured by the SLICC-DI; co-morbidity: diabetes, osteoporosis, ischemic heart disease, impaired renal function, obesity (BMI>30 Kg/m2) and depression.

e) *Analysis* - Continuous variables will be presented as means ± standard deviations, if normally distributed, or median plus interquartile range, if not normally distributed. Categorical variables will be presented as frequencies.

SACQ patients will be divided according to the medication use (steroids and/or immunosuppressants versus antimalarials or no medication) and unadjusted comparisons between groups will be performed using chi-square or Fisher exact tests for categorical data and t-student or Mann-Whitney tests for continuous data, as appropriate.

Logistic regression analyses will be used to identify the best predictive model of the effect of covariates on the medication options in SACQ lupus patients. Covariates for the multiple modeling will be chosen on the basis of univariate analyses and clinical experience.

All the analyses will be performed using SPSS, version 17 and p value <0.05 will be considered statistically significant.

f) *Sample size and power analysis* - Taking in account the number of SLE patients registered in Reuma.pt/LES and the prevalence of SACQ lupus reported by others we expect that 100 - 150 patients fulfill the inclusion/exclusion criteria. The lack of data (ours or from the literature) about treatment of SACQ patients does not allow a power analysis.

5. Expected results and limitations:

We expect to improve understanding of SACQ SLE and identify the reasons behind physician's decisions with respect to medications. These findings will be important to incorporate in future treatment strategies for SLE patients.

Possible limitations of this study are a potential selection bias in the inclusion of the patients in the registry and the analysis may not be entirely representative of the patient population. Furthermore, the possible absence of disease activity measurement at each visit might impair the identification of SACQ patients. In

order to circumvent this and minimize lost of data, all participating centers will be encourage to actively search for missing information in all hospital records.

6. Timeline:

Start of the project - as soon as dataset can be obtained

Expected analysis

January 2014 - data cleaning and statistical analysis

January 2014 - abstract submission to the EULAR meeting and Congresso Português de Reumatologia

April, June 2014 - preparation of the manuscript to be submitted by the end of August 2014

7. Proponentes and involved institutions:

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The participation is open to all Portuguese centers interested in participating in the project. Co-authorship will be granted to a maximum of 2 co-authors per center, actively collaborating in the project.

8. Funding and conflict of interests:

None

9. References:

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