Background: The MIG network (“MIG” is a shortening for “Mid i git”) which means “In the middle of Reumatism” as well as mid-life. MIG also means “ME” in Danish

The existing offers and activities in the Danish Rheumatism Association are primarily targeted towards the age group above 60 years. Often, younger members find it difficult to feel at home and see themselves as part of that particular age group. They miss activities where they can meet up with their peers, who are going through the same challenges in life.

Objectives: The objectives of the MIG network is to create a forum for people with rheumatism, who are roughly between 35 and 55 years old. The network focuses on life with rheumatism and how to keep the balance between job, family life and the disease. The ultimate goal was to create a community based on networking, shared experiences and relevant knowledge from both each other and health professionals.

Methods: First of all, the age group needed to be involved right from the start, so we initially made a series of interviews to learn about their needs and wishes. Then we gathered a group of five volunteers, who agreed to participate in defining the objectives and activities and to start up the network.

The network consists of the following:

I) an online based network with monthly webinars on the platform Zoom, where different health professionals talks about relevant subjects. The obvious advantage being, that people could participate from all over the country, from their sofa, not needing to dress up and travel after a long day of obligations.

II) The Danish Rheumatism Association have created an App for their volunteer community. In this app we offered the members of MIG “a room of resources”, where they can find news on the latest research and other relevant news. The members can also ask questions and share written advice and good ideas with each other.

III) Last, but not least it was important for the volunteers to offer physical meetings where they can find news on the latest research and other relevant news. The ultimate goal was to create a community based on networking, shared experiences and relevant knowledge from both each other and health professionals.

Conclusion: The MIG network makes sense! And it has met a need for people with chronic disease activity and evolution of several autoimmune conditions. To date, a limited number of evidences is available on the specific role of IFN activation in antiphospholipid antibodies (aPL) positive patients, including aPL carriers, primary antiphospholipid syndrome (PAPS) and those APS subjects who presented with an associated autoimmune disease (secondary APS, SAPS), such as systemic lupus erythematosus (SLE).

Objectives: The aim of this study was to evaluate the differential expression of IFN stimulated genes (ISG) among different subsets of aPL positive subjects and SLE patients.

Methods: For the purpose of the study, a total of 112 patients attending the San Giovanni Bosco Hospital (Turin, Italy) were enrolled, including 31 PAPS, 25 SAPS, 27 SLE patients without aPL, 29 aPL carriers (mean age 48.3±13.3 years, 76% female)1-2. Nineteen subjects were also recruited as healthy controls (HCs). Complete demographic, clinical, and laboratory data were collected at the time of the inclusion. Gene expression was evaluated by RT-PCR in whole blood for the following genes: IFI6, IFI44, IFI44L, MX1, IFI27, OAS1 and RSAD2. Normalized gene expression levels (Z-scores) were averaged into a global IFN signature (IFN score). Differences were measured by Kruskal-Wallis tests and associations among genes were studied by cluster and correspondence analyses. Correlations among genes were plotted by network analyses.

Results: An overall activation of ISG was noted across APS subsets, but certain differences were noted among genes. Whereas some ISG were already upregulated in the aPL positive group compared to HC (IFI44, IFI44L, MX1, IFI27, OAS1 and RSAD2, all p<0.050), other ISG were only in increased SLE (IFI6), MX1 differed between SLE and SAPS, and IFI27 and OAS1 showed differences between PAPS and SAPS. The composite IFN score revealed quantitative differences in the IFN pathway activation across APS subsets, being elevated in aPL carriers/PAPS groups compared to HCs (both p<0.050) and increasing in SAPs (p<0.010) and SLE (p<0.001) groups. Network analyses (Figure 1A) revealed qualitative differences in the gene-gene correlation networks: (i) weaker structures were found in HC and aPL carriers, compared to stronger and higher-degree networks in SAPS and SLE groups; and (ii) the influence of each node was different across groups. Unsupervised cluster analysis identified 3 clusters (I to III) based on ISG patterns (Figure 1B). Clusters usage differed among APS subsets, thus correlating clinical status (Figure 1C). Distinct groups of ISG positively correlated to aPS/PT IgG titre in aPL carriers and PAPS groups (all rho>0.500), whereas no associations were retrieved in SLE or SLE. No associations with previous thrombotic events were observed in any subset, although IFN composite score and several ISG correlate with the number of thrombotic recurrences under anticoagulation (all rho>0.400). No associations with GAPSS were observed.
Conclusion: An overall IFN pathway activation has been observed in aPL positive patients and across all APS subsets. Qualitative and quantitative differences across the APS spectrum can be identified, leading to the identification of distinct IFN signatures with different clinical value.

REFERENCES:

Disclosure of Interests: None declared


POS0093

ASSESSMENT OF HISTOLOGICAL FEATURES OF CHRONICITY OF MINOR SALVARY GLAND BIOPSY IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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Background: The origin of the histological chronic inflammation of the salivary gland in patients with primary Sjögren’s Syndrome (pSS) is questionable. It is probably a consequence of both, the evolution of the disease itself and aging.

Objectives: This study aims to evaluate histological data of chronicity of minor salivary gland biopsy with clinical characteristics and time of evolution in a series of patients with pSS.

Methods: A cross-sectional study including 98 subjects fulfilling the ACR-EULAR 2017 classification criteria for pSS. All patients underwent a minor salivary gland biopsy requested as part of clinical practice. We collected the age at diagnosis and at biopsy, xerostomia and xerophthalmia evolution time, and stimulated and unstimulated salivary flow as a clinical data. We informed the following features in the minor salivary gland biopsy: the focus score (positive if ≥ 1), atrophy, fibrosis and adiposity all graded in negative, mild, moderate, and severe stages according to pathological criteria.

Results: This study included 98 patients with pSS. The median of all recruited parameters are shown in Table 1. Only 2 patients presented severe fibrosis and adiposity, so we did not consider them for the analysis. Both, the age at diagnosis and at biopsy are significantly higher between none, mild and moderate stages in the three biopsy parameters. The age at biopsy increased in negative, mild, and moderate stages, in median, 10, 9 and 6 years in atrophy, fibrosis and adiposity respectively. Although more evolution time is observed in atrophy and fibrosis regarding classification categories, it does not reach statistical significance. Focus score is associated with atrophy as a high percentage in severe stage shows negative biopsy (78% vs 22%, p = 0.048) while in negative, mild, and moderate atrophy display a positive biopsy (61%, 73% and 64%, respectively). Furthermore, we observe a significant OR of 8.75 [1.7-68] for negative, 6 [1.25-30] in mild and 9.92 [1.8-80] in moderate compared to severe atrophy. Fibrosis and adiposity are not related to focus score. A low unstimulated salivary flow is observed in the atrophy and fibrosis stages, although differences are explained when compared negative with mild and moderate (3.5 vs 2 and 1.4 for atrophy and 3 vs 2 and 1.75 for fibrosis). Regarding adiposity, a linear statistically significant association is observed for every stage (3.5, 1.65 and 0.7, p<0.001). No differences in the stimulated salivary flow are shown.

Table 1. Description of variables included in the study.

<table>
<thead>
<tr>
<th>Categories</th>
<th>N(%)</th>
<th>Median(IQR)</th>
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<tbody>
<tr>
<td>Age at diagnosis(years)</td>
<td>55.220 (51.097, 58.407)</td>
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</tr>
<tr>
<td>Age at biopsy (years)</td>
<td>57.719 (53.851, 61.333)</td>
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<tr>
<td>Xerostomia (months)</td>
<td>19.614 (10.480, 35.121)</td>
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</tr>
<tr>
<td>Xerophthalmia (months)</td>
<td>21.487 (8.148, 38.735)</td>
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<tr>
<td>Focus score (positive)</td>
<td>63 (64.3%)</td>
<td></td>
</tr>
<tr>
<td>USF (ml/15min)</td>
<td>2.000 (1.400, 3.000)</td>
<td></td>
</tr>
<tr>
<td>SSF (ml/5min)</td>
<td>4.500 (3.000, 5.000)</td>
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Atrophy
- Negative: 28 (38.7%)
- Mild: 37 (31.8%)
- Moderate: 23 (23.7%)
- Severe: 9 (9.3%)

Fibrosis
- Negative: 29 (30.5%)
- Mild: 40 (42.1%)
- Moderate: 26 (27.4%)

Adiposity
- Negative: 39 (41.1%)
- Mild: 38 (40%)
- Moderate: 18 (18.9%)

Conclusion: An older age both, at diagnosis and at biopsy are associated with a severe stage of atrophy, fibrosis, and adiposity. Patient with severe atrophy shows less positive focus score, which might be noticed for biopsy interpretation.

Disclosure of Interests: None declared


POS0094

ALP-303, AN ENGINEERED DUAL BAFF/APRIL ANTAGONIST, POTENTLY INHIBITS PATHOGENIC LYMPHOCYTE SUBSETS AND FUNCTION IN B-CELL- AND ANTIBODY-RELATED PRECLINICAL MODELS

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Background: B-cell activating factor (BAFF) and a proliferation-inducing ligand (APRIL) are tumor necrosis factor (TNF) superfamily members that bind TACI (transmembrane activator and CAML interactor), BCMA (B-cell maturation antigen), and/or BAFF-R on B cells and together support B cell development, differentiation, and survival. ALP-303 is an Fc fusion protein of a human TACI variant TNFR domain engineered by directed evolution. It mediates significantly improved combined BAFF and APRIL inhibition in vitro and enhanced pharmacokinetic and immunomodulatory properties in preclinical studies, as compared to wild-type (WT) TACI-Fc molecules. B-cell targeting therapies like the WT TACI-Fc fusions atacicept and telitacicept have demonstrated promising clinical potential in B cell-related diseases like systemic lupus erythematosus (SLE). ALP-303, with enhanced inhibitory activity against BAFF and APRIL, has previously been shown to demonstrate promising efficacy in an NZB/NZW F1 mouse model of lupus, and may therefore further improve clinical outcomes in such diseases.

Objectives: To further characterize the comparative activity of ALP-303 versus an Fc matched control, a WT TACI-Fc comparator (telitacicept), and/or a B cell-depleting therapy (anti-mouse CD20 [anti-mCD20] monoclonal antibody [mAb]), in antibody-related preclinical models.

Methods: The functional activity of ALP-303, as compared to telitacicept or a depleting anti-mCD20 mAb, was evaluated in a sheep red blood cell (SRBC) immunization mouse model. Mice immunized intraperitoneally with SRBC on Study Day 0 were administered 200 µg ALP-303 or a molar-matched amount (240 µg) of telitacicept on Days 1 and 6 or were treated with 200 µg anti-mCD20 (rat IgG2b) on Day 1. At study termination on Day 15, serum was collected to measure levels of test article and anti-SRBC immunoglobulin (Ig) titers, and spleens and bone marrow (BM) were collected for immunophenotyping by flow cytometry. A study in the inducible bm12 mouse model of lupus was also conducted, with mice treated twice weekly with 200 µg ALP-303 or a molar-matched dose of Fc control, starting on Day 5 after splenocyte transfer and containing through Week 13.

Results: ALP-303 administration rapidly and potently reduced BM plasma cells, splenic germinal center B cells, follicular T helper cells, and plasmablasts in SRBC-immunized mice, often significantly more so than telitacicept and/or anti-mCD20 mAb. ALP-303 also significantly reduced serum titers of anti-SRBC IgM, IgG1, IgG2a, and IgG2b as compared to all other treatment groups. In the bm12 model, ALP-303 treatment significantly impacted the same key lymphocyte subsets affected in the SRBC model, and significantly reduced circulating anti-dsDNA antibodies (Figure 1) and total IgG, IgM, IgG1, IgG2b, and IgG3, and inhibited renal IgG deposits (Figure 1).

Figure 1. ALP-303 treatment significantly reduces serum autoantibody titers and renal immune complex deposition in the inducible bm12 mouse model of lupus. *p<0.05, **p<0.01, ***p<0.001 by the Kruskal-Wallis test.

Conclusion: ALP-303 is an engineered, potent BAFF/APRIL antagonist that continues to consistently demonstrate encouraging immunomodulatory activity and efficacy in vivo and in vitro, as further demonstrated in the SRBC immunization and bm12 lupus models, with superiority to WT TACI-Fc and anti-CD20 comparators. ALP-303 may thus be an attractive development candidate for