PP43

Plasma calprotectin in SpA patients: a biomarker for peripheral arthritis

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Background: Spondyloarthritis (SpA) comprises a group of rheumatic diseases involving axial and peripheral inflammatory arthritis. Inflammatory biomarkers such as ESR and CRP are weakly correlated with disease activity. Calprotectin, mainly secreted by neutrophils, is elevated in sites of active inflammation. Plasma calprotectin (p-calprotectin) is elevated in RA, SLE, and IBD.

Objectives: To investigate p-calprotectin in SpA patients from Rana, Norway: to determine whether p-calprotectin is elevated in SpA patients, whether calprotectin differs with age and gender, and whether calprotectin is correlated to BMI, inflammatory markers, or disease manifestations.

Method: SpA patients were recruited from hospital registers, family doctors, and by local newspaper advertisement. We collected clinical data and blood samples. Patients fulfilling the European Spondyloarthropathy Study Group (ESSG) criteria were included. First-degree relatives were asked about symptoms of synovitis or inflammatory back pain by questionnaire. Symptomatic relatives were investigated, and included if they fulfilled the ESSG criteria. A total of 387 SpA patients were included. Of these, 273 patients with inflammatory back pain had X-ray and MRI of SI joints. Tests for p-calprotectin were carried out in 235 patients, 51 symptomatic relatives, and 74 healthy relatives. Statistical tests were carried out with SPSS.

Results: Calprotectin levels are not significantly different in men and women, in SpA patients, relatives with symptoms, and healthy relatives of SpA patients. In SpA patients there was no difference in calprotectin levels with regard to inflammatory back pain, radiological sacroiliitis, MRI sacroiliitis, psoriasis, IBD, acute uveitis, reactive arthritis, and HLA-B27 positivity. Calprotectin levels were correlated to other inflammatory markers: ESR, CRP, Hb, and TRC; the best correlation was with CRP. Calprotectin was correlated to BMI and swollen joint count but not to BASDAI, BASFI, or MHAQ scores.

Conclusions: Plasma calprotectin could be a valuable biomarker in SpA with polyarthritis.

Table 1. Calprotectin in SpA patients.

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Calprotectin (ng/mL)</th>
<th>T-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy relatives/SpA patients</td>
<td>74/235</td>
<td>460/719</td>
<td>0.308</td>
</tr>
<tr>
<td>Symptomatic relatives/SpA patients</td>
<td>61/235</td>
<td>520/719</td>
<td>0.515</td>
</tr>
<tr>
<td>Males</td>
<td>158</td>
<td>812</td>
<td>0.097</td>
</tr>
<tr>
<td>Females</td>
<td>202</td>
<td>501</td>
<td></td>
</tr>
</tbody>
</table>

Correlations with calprotectin in SpA patients (n = 235)

<table>
<thead>
<tr>
<th>Metric</th>
<th>Spearman’s rho</th>
<th>χ² test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass index (BMI)</td>
<td>0.164</td>
<td>0.013</td>
</tr>
<tr>
<td>Age</td>
<td>−0.105</td>
<td>0.111</td>
</tr>
<tr>
<td>Disease duration</td>
<td>0.050</td>
<td>0.480</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate (ESR)</td>
<td>0.421</td>
<td>0.000</td>
</tr>
<tr>
<td>C-reactive protein (CRP)</td>
<td>0.725</td>
<td>0.000</td>
</tr>
<tr>
<td>Haemoglobin (Hb)</td>
<td>−0.249</td>
<td>0.000</td>
</tr>
<tr>
<td>Thromocyte count</td>
<td>0.545</td>
<td>0.000</td>
</tr>
<tr>
<td>Leukocytes count</td>
<td>0.050</td>
<td>0.457</td>
</tr>
<tr>
<td>Tender joint count</td>
<td>0.057</td>
<td>0.437</td>
</tr>
<tr>
<td>Swollen joint count</td>
<td>0.250</td>
<td>0.002</td>
</tr>
<tr>
<td>BASDAI</td>
<td>−0.044</td>
<td>0.504</td>
</tr>
<tr>
<td>BASFI</td>
<td>0.003</td>
<td>0.962</td>
</tr>
<tr>
<td>MHAQ</td>
<td>0.024</td>
<td>0.745</td>
</tr>
</tbody>
</table>

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; MHAQ, Modified Health Assessment Questionnaire.

PP44

Reduction in fatigue in patients with active ankylosing spondylitis: results of two phase 3 studies of secukinumab

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1Diakonhjemmet Hospital, Norway, 2University of Leeds, UK, 3Oregon Health & Science University, USA, 4Paris 06 University, France, 5Copenhagen Centre for Arthritis Research (COPE-CARE), Denmark, 6Hospital Clinic de Barcelona e IDIBAPS, Spain, 7Novartis Pharmaceuticals Corporation, USA, 8Novartis Pharma AG, Switzerland, 9RTI Health Solutions, USA

Background: Patients with active ankylosing spondylitis (AS) experience fatigue which frequently leads to reduced health-related quality of life (HRQoL).

Table 1. Calprotectin in SpA patients.
Secukinumab (SEC) treatment was found to result in rapid improvement in signs and symptoms, physical functioning, and HRQoL in patients with active AS in the phase 3 studies MEASURE1 and MEASURE2.

Objectives: To assess the impact of SEC on fatigue in patients with AS, and to investigate correlations between fatigue and clinical endpoints.

Method: Patients with active AS (MEASURE1, n = 371; MEASURE2, n = 219) were randomized to receive SEC 150 mg or 75 mg or PBO administered every 4 weeks after initiating therapy. Fatigue was assessed using the FACIT-F scale. A change in FACIT-F score of ≥ 4 from baseline defined the fatigue response. Possible correlations between the FACIT-F score and clinical parameters were investigated using a logistical regression model.

Results: At week 16, 66.4% (MEASURE1) and 77.6% (MEASURE2) of patients receiving SEC 150 mg achieved a fatigue response, compared with 47.7% (MEASURE1) and 50.0% (MEASURE2) for PBO (p < 0.05 for both comparisons). Responses were sustained at week 52 in both studies (MEASURE1, 73.6%; MEASURE2, 80.6%) and at week 104 in MEASURE1 (71.3%). A fatigue response was strongly positively correlated at weeks 16 and 52 with clinical response (ASAS20, 40, 5/6 responses, ASAS partial remission, ASDAS-CRP major improvement, and BASDAI 50 response).

Conclusions: SEC 150 mg provides rapid improvement in fatigue, and the response was sustained for up to 104 weeks. Fatigue response shows a strong correlation with improvement in clinical response criteria, indicating a relationship between fatigue and disease activity in AS.

### Systemic lupus erythematosus

**PP45**

The value of multidisciplinary reassessment in the attribution of neuropsychiatric symptoms to SLE: data from the Leiden NPSLE cohort

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3Department of Cardiology, Rigshospitalet, Denmark

Objectives: To determine the contribution of reassessment of SLE patients presenting with neuropsychiatric (NP) complaints in the attribution to SLE as the cause of these complaints in a large, prospective and multidisciplinary assessed NPSLE cohort.

Method: A total of 304 SLE patients with NP symptoms were evaluated in the Leiden NPSLE clinic. All subjects underwent standardized multidisciplinary medical, neuropsychological, laboratory, and radiological examination during a 1-day admission. The assignment process was made by consensus in a 2-weekly scheduled meeting. Every NP event was attributed to one of the following: (i) NPSLE: related to SLE; (ii) non-NPSLE: explained by other aetiology; (iii) undefined NPSLE: unable to establish a final attribution. All subjects were reassessed by the same multidisciplinary evaluation 3–18 months later. The following factors were taken into account: (i) improvement/worsening over time and (ii) onset of new NP events or other symptoms related and non-related to SLE contributing to new and previous NP events.

Results: The number of NP events established was 463. Of these, 275 (59.4%) were classified as non-NPSLE, 152 (32.8%) as NPSLE, and 36 (7.8%) as undefined NPSLE. After reassessment, in 130 NP events the diagnosis of NPSLE was confirmed while 22 were recategorized as non-NPSLE. Furthermore, of the 275 non-NPSLE events, six were recategorized as NPSLE. All 36 NP events initially categorized as undefined NPSLE were recategorized into NPSLE (nine NP events) and non-NPSLE (27 NP events). In total, attribution to SLE was discordant after reassessment in 64 (13.8%) NP events.

Conclusions: Reassessment of NPSLE patients is important in the attribution process of NP events to SLE.

**PP46**

Cutaneous lupus erythematosus and systemic lupus erythematosus are associated with clinically significant cardiovascular risk: a Danish nationwide cohort study

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Background: Systemic lupus erythematosus (SLE) is a well-known cardiovascular risk factor. Less is known
about cutaneous lupus erythematosus (CLE) and the risk of developing cardiovascular disease (CVD). Therefore, we investigated the risk of mortality and adverse cardiovascular events in patients diagnosed with SLE and CLE.

**Method:** We conducted a cohort study of the entire Danish population aged ≥18 and ≤100 years, followed from 1997 to 2011 by individual-level linkage of nationwide registers. Multivariable adjusted Cox regression models were used to estimate hazard ratios (HRs) for a composite cardiovascular endpoint and all-cause mortality for patients with SLE and CLE.

**Results:**
A total of 3282 patients with CLE and 3747 patients with SLE were identified and compared with 5,513,739 controls. The overall HR for the composite CVD endpoint was 1.31 (95% CI 1.16–1.49) for CLE and 2.05 (95% CI 1.83–2.30) for SLE. The corresponding HRs for all-cause mortality were 1.32 (95% CI 1.20–1.45) for CLE and 2.21 (95% CI 2.03–2.41) for SLE.

**Conclusions:** CLE and SLE were associated with significantly increased risk of CVD and all-cause mortality. Local and chronic inflammation may be the driver of low-grade systemic inflammation.

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**Table 1.** Hazard ratios (HRs)* and 95% confidence intervals (CIs) for the composite cardiovascular disease (CVD) endpoint and all-cause mortality for patients diagnosed with cutaneous lupus erythematosus (CLE) and systemic lupus erythematosus (SLE) divided into age groups and adjusted for age, calendar year, concomitant medication, comorbidity, socioeconomic status, and gender.

<table>
<thead>
<tr>
<th></th>
<th>CLE</th>
<th>SLE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall ≤ 50 years &gt; 50 years</td>
<td>Overall ≤ 50 years &gt; 50 years</td>
</tr>
<tr>
<td>Composite CVD endpoint HR (95% CI)</td>
<td>1.31 (1.16–1.49) 1.54 (1.18–2.00) 1.25 (1.08–1.44)</td>
<td>2.05 (1.83–2.30) 2.78 (1.15–3.44)</td>
</tr>
<tr>
<td>p-value</td>
<td>&lt; 0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>All-cause mortality HR (95% CI)</td>
<td>1.32 (1.20–1.45) 1.61 (1.30–2.00) 1.26 (1.13–1.40)</td>
<td>2.21 (2.03–2.41) 2.51 (2.09–3.01)</td>
</tr>
<tr>
<td>p-value</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Composite CVD endpoint: stroke, acute myocardial infarction, and cardiovascular death.

*HR calculated by comparing CLE and SLE patients with the general population.
respectively. These risks were higher among subjects < 40 years of age and in patients with LN. For the latter, the corresponding HRs were 10.91, 3.67, and 5.78.

**Conclusions**: Patients with SLE had an increased risk of CVD and CVM compared with controls; especially in the subsets of patients with LN and younger age. In particular, the risk of MI was increased among patients with LN.

**PP48**

**Microparticles bind to circulating phagocytes and erythrocytes: a possible clearance mechanism relevant to the pathogenesis of systemic lupus erythematosus**

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**Introduction**: The pathogenesis of systemic lupus erythematosus (SLE) is unknown, but impaired clearance of apoptotic cell material that leads to tissue deposition of pro-inflammatory microparticle-derived immune complexes may be of importance. We examined surface characteristics of microparticles and their capacity to bind to circulating phagocytes and erythrocytes from SLE patients and healthy individuals.

**Method**: Surface characteristics of microparticles from 17 SLE patients and 10 healthy individuals were assessed by flow cytometry using leucocyte subtype surface markers and antibodies against C3b/iC3b/C3d complement fragments. The ability of microparticles labelled with 5 (and 6)-carboxyfluorescein diacetate succinimidyl ester to bind to autologous phagocytes and erythrocytes was also assessed by flow cytometry.

**Results**: Microparticles from SLE patients carried more total C3 (p = 0.031) but fewer opsonizing C3b and iC3b molecules (p = 0.006) on their surface than healthy individuals. The C3b/iC3b level correlated with that of plasma C3 (r = 0.52, p = 0.0499). Overall, microparticles were capable of binding to phagocytes and erythrocytes (p < 0.0001), and granulocytes from SLE patients bound more microparticles than granulocytes from healthy individuals (p = 0.047). The binding of microparticles to phagocytes was inhibited by the presence of erythrocytes.

**Conclusions**: The reduced carriage of opsonizing C3 fragments, despite the increased total number of C3, on microparticles from SLE patients supports the hypothesis of defective clearance of apoptotic material in SLE. Our findings also indicate other potential clearance deficiencies including competitive binding of microparticles to various blood cells. Increased binding of microparticles to SLE granulocytes supports the emerging role of granulocytes as important effector cells in SLE.

**PP49**

**Increased levels of microvesicles containing nuclear molecules and immunoglobulins in patients with systemic lupus erythematosus**

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**Background**: Enhanced apoptosis, activation of immune cells, and defective clearance are suggested, but not proven, pathogenic mechanisms in systemic lupus erythematosus (SLE). During apoptosis and cell activation, microvesicles (MVs) are released into the circulation. MVs are phospholipid vesicles that expose transmembrane proteins and receptors and enclose cytosolic components. We quantified the surface expression of immunoglobulins and the content of nuclear molecules in MVs from SLE patients and controls.

**Method**: Plasma samples from 280 well-characterized SLE patients and 282 matched controls were investigated. MVs

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Table 1. Fully adjusted* hazard ratios (HRs) and 95% confidence intervals (CIs) for myocardial infarction (MI), stroke, and cardiovascular mortality (CVM) in SLE.

<table>
<thead>
<tr>
<th>MI</th>
<th>Stroke</th>
<th>CVM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>SLE, all</td>
<td>2.38 (1.56–3.62)</td>
<td>2.21 (1.64–2.98)</td>
</tr>
<tr>
<td>SLE, women</td>
<td>1.89 (1.15–3.09)</td>
<td>2.32 (1.68–3.18)</td>
</tr>
<tr>
<td>SLE, men</td>
<td>4.59 (2.06–10.24)</td>
<td>1.56 (0.68–3.61)</td>
</tr>
<tr>
<td>SLE &lt; 40 years</td>
<td>3.74 (1.02–13.70)</td>
<td>5.26 (2.32–11.94)</td>
</tr>
<tr>
<td>SLE 40–55 years</td>
<td>2.62 (1.41–5.63)</td>
<td>3.21 (1.91–5.38)</td>
</tr>
<tr>
<td>SLE &gt; 55 years</td>
<td>1.92 (1.10–3.35)</td>
<td>1.50 (1.00–2.24)</td>
</tr>
<tr>
<td>SLE without LN</td>
<td>1.93 (1.22–3.05)</td>
<td>2.07 (1.30–2.84)</td>
</tr>
<tr>
<td>SLE with LN</td>
<td>10.91 (3.26–36.55)</td>
<td>3.67 (1.63–9.29)</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex, Charlson’s comorbidity index, baseline cardioprotective therapy, socioeconomic index, previous events of stroke, and myocardial infarction.
were analysed by flow cytometry as vesicles less than 1.0 μm in size and positive for SYTO 13 (binds to DNA/RNA). We also measured the expression of HMGB1, IgG, and IgM on MVs. In addition, we investigated whether immunoglobulins from MV-depleted SLE plasma could bind to MVs from healthy volunteers (n = 5).

**Results:** SLE patients had significantly higher numbers of MVs containing nucleic acids and these MVs expressed more HMGB1, IgG, and IgM compared to controls (Figure 1). In vitro experiments revealed that immunoglobulins from MV-depleted SLE plasma bind to MVs from healthy volunteers (IgG: 0.3 ± 0.03 vs. 0.64 ± 0.07 mean fluorescence intensity (MFI), IgM: 0.29 ± 0.02 vs. 0.41 ± 0.08 MFI; p < 0.0001 and p < 0.05).

**Conclusions:** MVs from SLE patients exposed IgG and IgM on their surface, demonstrating that immunoglobulins can bind to antigenic sites on MVs. The abundance of MVs in SLE could thus play an important role in the pathogenesis of SLE. Together, these studies demonstrate that MVs in SLE contain nucleic acids as well as the alarmin HMGB1, which could indicate the active release of MVs by apoptosis and/or activation of immune cells.

**PP50**

The TNF-α/p-albumin ratio: a suggested biomarker for disease activity in SLE


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**Background:** Validated measures of disease activity in systemic lupus erythematosus (SLE), such as the SLE Disease Activity Index (SLEDAI) and the SLE Activity Measure (SLAM), are composite scores which are insensitive to change and have failed to differentiate treatment
Table 1. Biomarkers with the best discriminatory power between SLE patients and controls and/or strongest correlations with SLE disease activity, as measured by the SLEDAI and the SLAM.

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Mean (95% CI) Patients n = 433</th>
<th>Mean (95% CI) Controls n = 322</th>
<th>p-value</th>
<th>Patients vs. Controls</th>
<th>Spearman’s ρ</th>
<th>p-value</th>
<th>SLEDAI</th>
<th>SLAM</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNF-α (pg/mL)</td>
<td>5.6 (5.2–6.0)</td>
<td>2.6 (2.2–3.0)</td>
<td>7.0 × 10⁻⁶</td>
<td>0.32</td>
<td>6.0 × 10⁻¹²</td>
<td>0.34</td>
<td>5.0 × 10⁻¹³</td>
<td></td>
</tr>
<tr>
<td>IL-6 (pg/mL)</td>
<td>2.1 (1.9–2.4)</td>
<td>0.7 (0.4–1.0)</td>
<td>2.5 × 10⁻⁵</td>
<td>0.24</td>
<td>9.6 × 10⁻⁷</td>
<td>0.23</td>
<td>1.3 × 10⁻⁶</td>
<td></td>
</tr>
<tr>
<td>IL-15 (pg/mL)</td>
<td>3.6 (3.4–3.7)</td>
<td>2.2 (2.0–2.3)</td>
<td>3.4 × 10⁻⁴</td>
<td>0.26</td>
<td>8.6 × 10⁻⁹</td>
<td>0.28</td>
<td>4.0 × 10⁻⁹</td>
<td></td>
</tr>
<tr>
<td>MIP-1β (pg/mL)</td>
<td>91.3 (88.5–96.2)</td>
<td>48.7 (43.0–54.3)</td>
<td>3.8 × 10⁻⁹</td>
<td>0.20</td>
<td>4.2 × 10⁻⁵</td>
<td>0.16</td>
<td>0.0009</td>
<td></td>
</tr>
<tr>
<td>IL-8 (pg/mL)</td>
<td>8.6 (7.6–9.7)</td>
<td>3.6 (2.4–4.7)</td>
<td>3.8 × 10⁻⁴</td>
<td>0.16</td>
<td>0.0009</td>
<td>0.18</td>
<td>0.0002</td>
<td></td>
</tr>
<tr>
<td>MCP-1 (pg/mL)</td>
<td>146 (137–160)</td>
<td>74 (61–87)</td>
<td>3.0 × 10⁻⁶</td>
<td>0.23</td>
<td>1.0 × 10⁻⁶</td>
<td>0.23</td>
<td>1.5 × 10⁻⁶</td>
<td></td>
</tr>
<tr>
<td>IL-10 (pg/mL)</td>
<td>1.7 (1.4–1.9)</td>
<td>0.46 (0.10–0.82)</td>
<td>8.1 × 10⁻⁸</td>
<td>0.26</td>
<td>8.6 × 10⁻⁸</td>
<td>0.20</td>
<td>2.8 × 10⁻⁵</td>
<td></td>
</tr>
<tr>
<td>IP-10 (ng/mL)</td>
<td>1.6 (1.4–1.8)</td>
<td>0.5 (0.2–0.6)</td>
<td>1.2 × 10⁻⁶</td>
<td>0.23</td>
<td>1.4 × 10⁻⁶</td>
<td>0.19</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>C4 (g/L)</td>
<td>0.15 (0.15–0.16)</td>
<td>0.21 (0.20–0.22)</td>
<td>3.2 × 10⁻⁷</td>
<td>0.35</td>
<td>8.0 × 10⁻¹⁴</td>
<td>-0.12</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Orosomucoid (g/L)</td>
<td>0.98 (0.95–1.0)</td>
<td>0.72 (0.69–0.75)</td>
<td>7.1 × 10⁻¹⁰</td>
<td>0.21</td>
<td>1.0 × 10⁻⁵</td>
<td>0.28</td>
<td>3.1 × 10⁻⁹</td>
<td></td>
</tr>
<tr>
<td>Sedimentation rate (mm/h)</td>
<td>25.8 (24.2–27.3)</td>
<td>10.2 (8.5–12.1)</td>
<td>5.6 × 10⁻⁴</td>
<td>0.27</td>
<td>7.7 × 10⁻⁹</td>
<td>0.48</td>
<td>4.0 × 10⁻⁵</td>
<td></td>
</tr>
<tr>
<td>P-albumin (g/L)</td>
<td>38.2 (37.7–38.6)</td>
<td>42.7 (42.2–43.2)</td>
<td>1.6 × 10⁻⁶</td>
<td>-0.33</td>
<td>9.0 × 10⁻¹³</td>
<td>-0.31</td>
<td>5.0 × 10⁻¹¹</td>
<td></td>
</tr>
<tr>
<td>Ratio TNF-α/P-albumin</td>
<td>0.16 (0.15–0.17)</td>
<td>0.06 (0.05–0.07)</td>
<td>2.8 × 10⁻⁹</td>
<td>0.37</td>
<td>1.0 × 10⁻¹⁵</td>
<td>0.38</td>
<td>2.0 × 10⁻¹⁶</td>
<td></td>
</tr>
</tbody>
</table>

SLEDAI, SLE Disease Activity Index; SLAM, SLE Activity Measure; TNF, tumour necrosis factor; IL, interleukin; MIP, macrophage inflammatory protein; MCP, monocyte chemotactic protein; IP, interferon gamma-induced protein; C4, complement factor 4; P, plasma.

Discriminatory power was calculated with the student’s T-test or the Mann–Whitney U test as appropriate, depending on biomarker distribution. Correlations between biomarkers and disease activity scores were calculated using Spearman’s correlation coefficients.

responses in clinical trials. We investigated a large set of cytokines and basic laboratory tests as potential biomarkers of disease activity in SLE patients.

Method: In a cross-sectional setting we examined 433 patients with SLE and 322 age- and gender-matched population controls. Disease activity was assessed according to the SLEDAI and the SLAM. Basic laboratory tests and analyses using the Meso Scale Discovery (MSD) 30-plex cytokine assay (K15054D) were performed on fasting blood samples (total > 50 biomarkers).

Biomarker discriminatory power was tested between patients and controls. Spearman correlations with SLAM/SLEDAI scores were calculated among patients.

Results: The best discriminatory power between patients and controls was observed for TNF-α (p = 7 × 10⁻⁶), IL-6 (p = 2.5 × 10⁻⁴⁰), orosomucoid (p = 7.1 × 10⁻³⁸), plasma (p)-alumin (p = 1.6 × 10⁻³⁸), and erythrocyte sedimentation rate (p = 5.6 × 10⁻³⁸). The strongest correlations with SLEDAI/SLAM were observed for TNF-α (Spearman’s ρ = 0.32, p = 6.0 × 10⁻¹² for SLEDAI and Spearman’s ρ = 0.34, p = 5.0 × 10⁻¹³ for SLAM) and p-alumin (Spearman’s ρ = -0.33, p = 9.0 × 10⁻¹³ for SLEDAI and Spearman’s ρ = -0.31, p = 5.0 × 10⁻¹¹ for SLAM). The ratio between TNF-α and p-alumin further improved these correlations (see Table 1).

Conclusions: Of more than 50 investigated biomarkers, TNF-α was the best discriminator between SLE patients and controls. Furthermore, TNF-α correlated best with disease activity. These correlations were improved by the ratio TNF-α/p-alumin. We thus propose that the TNF-α/p-alumin ratio merits further investigation as a clinically useful biomarker for diagnostic and surveillance purposes in SLE.

PPS1
Serum ferritin as a marker of clinical and histopathological response to treatment in lupus nephritis

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Objective: Studies have reported elevated serum ferritin in active compared with inactive SLE, and associations with LN. We investigated the role of serum ferritin in LN.

Method: Serum ferritin levels were measured in 64 patients with biopsy-proven LN [52 proliferative LN (PLN) and 12 membranous LN (MLN)], before and after treatment. Post-treatment renal biopsies were performed after a median time of 7.7 months. Clinical responders (CR) were defined by ≥ 50% reduced proteinuria, normal or ≥ 25% improved eGFR, and inactive urinary sediment. Histopathological responders (HR) were defined by ≥ 50% improvement in the Activity Index in post-treatment biopsies.

Results: Serum ferritin decreased following treatment in the entire cohort (p < 0.001) and in PLN (p < 0.001) but not in MLN (p = 0.35). In the entire cohort, ferritin levels decreased in CR (p < 0.001), clinical non-responders (CNR; p = 0.030), and HR (p < 0.001) but not in histopathological non-responders (HNR; p = 0.06). In
PLN, ferritin decreased in CR (p < 0.001) and CNR (p = 0.003), as well as in HR (p < 0.001) and HNR (p = 0.011). In MLN, ferritin decreased in CR (p = 0.03) and HR (p = 0.046) but not in CNR (p = 0.69) or HNR (p = 0.89). In MLN, both baseline and post-treatment ferritin levels were higher in CNR than in CR (p = 0.03 and p = 0.005, respectively).

Conclusions: Our data suggest ferritin as a marker of histopathological treatment outcome in LN. In patients with MLN, high baseline ferritin predicted unfavourable clinical treatment responses and, despite being initially lower, baseline ferritin decreased in CR, implying a role for ferritin in MLN and warranting further investigation.

PP52

Antiphospholipid antibodies in lupus nephritis

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Objectives: The role of antiphospholipid antibodies (aPL) in lupus nephritis (LN) is unclear. We investigated the impact of aPL on short-term and long-term outcomes in LN patients.

Method: We assessed aPL levels cross-sectionally in SLE patients diagnosed with (n = 204) or without (n = 294) LN, and prospectively in 64 patients with active biopsy-proven LN, before and after induction treatment (short-term outcomes). Long-term renal outcome in the prospective LN cohort was determined by eGFR and chronic kidney disease (CKD) stage, after a median follow-up of 11.3 (range 3.3–18.8) years.

Results: Cross-sectional analysis revealed no association between LN and IgG/IgM anticardiolipin (aCL) or anti-β2-glycoprotein I (anti-β2-GPI) antibodies, or lupus anticoagulant. aPL positivity and levels were similar in patients with active LN vs. non-renal SLE. Following treatment for LN, serum IgG/IgM aPL levels decreased

Figure legend. Box plots of creatinine concentrations in LN patients with and without IgG aPL at active LN and after induction treatment.
in responders (p < 0.005 for all) but not in non-responders. Both at active LN and post-treatment, patients with IgG aPL had higher creatinine levels compared with patients without. Neither aPL positivity nor aPL levels were associated with changes in eGFR from either baseline or post-treatment up to long-term follow-up. aPL positivity and aPL levels both at baseline and post-treatment were similar in patients with long-term follow-up CKD stage ≥ 3 vs. 1–2.

Conclusions: Neither aPL positivity nor aPL levels were found to be associated with the occurrence of LN. However, IgG aPL positivity in LN patients was associated with a short-term renal function impairment while no effect on long-term outcome was observed. aPL levels decreased following treatment in responders, indicating that aPL levels are affected by immunosuppressive drugs.

PP53
Soluble tumour necrosis factor receptor 2 (sTNFR2) as a biomarker of kidney tissue damage and long-term renal outcome in lupus nephritis
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Objectives: Accumulating evidence indicates the involvement of tumour necrosis factor receptors (TNFRs) in lupus nephritis (LN). We investigated the performance of soluble (s)TNFR2 as a biomarker of renal activity, damage, treatment response, and long-term outcome in LN.

Method: sTNFR2 levels were assessed in 64 patients with active LN (52 proliferative, 12 membranous) and post-treatment. Renal biopsies were performed on both occasions. Clinical responders (CR) were defined by ≥ 50% reduction in proteinuria, normal or improved eGFR, and inactive urinary sediment. Histopathological responders (HR) were defined by ≥ 50% improvement in the renal Activity Index. Long-term renal outcome was determined by the chronic kidney disease (CKD) stage after a median follow-up of 11.3 (range 3.3–18.8) years.

Results: Levels of sTNFR2 decreased following treatment for LN (p < 0.001). In membranous LN, baseline TNFR2 levels were higher in CR (p = 0.048) and HR (p = 0.03) vs. non-responders, and decreased only in CR (p = 0.03). Baseline sTNFR2 levels correlated with the Chronicity Index in both baseline (r = 0.34, p = 0.006) and post-treatment (r = 0.43, p < 0.001) biopsies. Long-term follow-up eGFR correlated inversely with both baseline (p = 0.02, r = −0.29) and post-treatment (p = 0.04, r = −0.26) sTNFR2. Both baseline (p = 0.02) and post-treatment (p = 0.03) sTNFR2 levels were associated with decreases in eGFR. Post-treatment sTNFR2 levels were higher in patients with a CKD stage ≥ 3 vs. 1–2 at the last follow-up (p = 0.008).

Conclusions: Our data suggest sTNFR2 as a non-invasive marker of kidney tissue damage and a predictor of clinical and histopathological outcome following induction treatment in membranous LN.

Figure. Serum TNFR2 as a predictor of (A) clinical and (B) histopathological response to induction treatment in membranous LN.
**PP54**

Serum insulin-like growth factor-binding protein 2 (IGFBP2) as a biomarker of clinical and histopathological treatment response in lupus nephritis

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**Objectives**: Expression of insulin-like growth factor-binding protein 2 (IGFBP2) has been found to increase in anti-glomerular basement membrane glomerulonephritis and MRL/lpr lupus mice. We investigated the role of IGFBP2 in lupus nephritis (LN).

**Method**: Serum IGFBP2 levels were assessed in 64 patients with a biopsy-proven LN and after induction treatment. Post-treatment biopsies were performed after a median time of 7.7 months. Clinical responders (CR) were defined by ≥ 50% reduced proteinuria, normal or ≥ 25% improved eGFR, and inactive urinary sediment. Histopathological responders (HR) were defined by ≥ 50% improvement in the Activity Index (AI).

**Results**: IGFBP2 levels decreased following treatment in CR (p < 0.001) and HR (p < 0.001) but not in clinical (p = 0.44) or histopathological (p = 0.16) non-responders. Post-treatment, but not baseline, IGFBP2 levels were higher in clinical non-responders vs. CR (p = 0.004), and correlated with AI (r = 0.31, p = 0.015) and Chronicity Index scores (r = 0.35, p = 0.006) in post-treatment biopsies, and with post-treatment SLE Disease Activity Index (SLEDAI) 2000 scores (r = 0.32, p = 0.009). IGFBP2 levels correlated with proteinuria, both at baseline (r = 0.34, p = 0.006) and post-treatment (r = 0.48, p < 0.001). Despite an overall improvement in eGFR (p < 0.001), baseline IGFBP2 levels were associated with decreases in eGFR following treatment (p = 0.028).

**Conclusions**: Our data suggest serum IGFBP2 as a marker of renal activity and treatment response in LN. Post-treatment, but not baseline, levels mirrored both global SLE activity and histopathological findings, which together with the observed correlation with proteinuria levels suggests IGFBP2 as a marker of activity in patients with a history of LN and no or low-grade proteinuria.

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**PP55**

Serum anexelektro (Axl) as a novel biomarker of renal activity, treatment response, and long-term outcome in patients with lupus nephritis

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**Objectives**: Anexelektro (Axl) is a receptor tyrosine kinase involved in apoptotic cell clearance. We investigated serum Axl in lupus nephritis (LN) to clarify its role in renal disease activity, damage, and treatment response.

**Method**: Axl levels were assessed in 64 LN patients, before and after induction treatment. Renal biopsies were performed at baseline and post-treatment. Patients were classified as clinical responders (CR) or non-responders (CNR) based on the American College of Rheumatology (ACR) response criteria, and histopathological responders (HR) or non-responders (HNR) based on changes in the renal Activity Index (AI). Long-term renal outcome was determined by the last chronic kidney disease (CKD) stage, after a median follow-up time of 11.3 (range 3.3–18.8) years.

**Results**: According to baseline biopsies, 52 cases were classified as proliferative and 12 as membranous LN. Baseline Axl levels decreased following treatment in CR (p < 0.001) and HR (p < 0.001) but not in non-responders, and were higher in HR vs. HNR (p = 0.003). Baseline Axl correlated with the Chronicity Index in post-treatment biopsies (r = 0.26, p = 0.04), and inversely with baseline (r = −0.29, p = 0.02), post-treatment (r = −0.31, p = 0.01), and long-term (r = −0.29, p = 0.02) eGFR. Baseline Axl levels were higher in patients with CKD stage ≥ 3 vs. 1–2 at the last follow-up (p = 0.03).

**Conclusions**: Our data suggest serum Axl as a candidate biomarker of renal activity, treatment response, and damage accrual in LN. High baseline Axl levels were paradoxically...
associated with both histopathological improvement following treatment and an unfavourable long-term outcome. Our findings merit further investigation of the contribution of the Axl pathway to tissue damage in LN.

**Systemic inflammatory disorders**

**PP56**

A selective JAK1 inhibitor, filgotinib, suppresses lymphocytic infiltration in salivary gland of NOD mice through suppression of BAFF production of salivary gland epithelial cells

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**Background:** Interferon (IFN) signatures are upregulated in patients with primary Sjögren’s syndrome (pSS) and interferons are considered to play a pathogenic role in pSS. Therefore, Janus kinase (JAK), which mediates the IFN signalling pathway, may be a good therapeutic target.

**Objectives:** We set out to investigate whether a selective JAK1 inhibitor, filgotinib, would ameliorate disease-related parameters in non-obese diabetic (NOD) mice, an animal model for SS.

**Method:** Filgotinib (1.5 mg/kg) or vehicle (saline) was injected intraperitoneally three times a week from 8 weeks after birth. Salivary flow rate (SFR) was measured at 8, 12, 16, and 20 weeks. Histological analysis was performed at 20 weeks. The effects of filgotinib on the expressions of BAFF and chemokines [CXCL10 (IP-10), CXCL3 (fractalkine), CCL-2 (MCP-1)] in human salivary gland epithelial cells (SGECs) or primary epithelial cells of patients with pSS were determined in vitro.

**Results:** The SFR of NOD mice in both groups decreased over time. Of note, SFRs of filgotinib-treated mice were greater than those of controls. Histological evaluation of the salivary gland revealed that the lymphocytic infiltration of the salivary gland was markedly reduced in the mice treated with filgotinib. Filgotinib suppressed STAT1 phosphorylation in IFN-treated SGECs. In addition, IFN-induced BAFF and chemokine production of SGECs or primary epithelial cells was abrogated by filgotinib treatment.

**Conclusions:** Filgotinib suppresses the SFR decrease and lymphocytic infiltration of salivary glands in NOD mice by inhibiting the IFN signalling pathway, thus suppressing BAFF and chemokine production of SGECs. JAK inhibition may be a novel therapeutic approach for SS.

**PP57**

Activation of plasmacytoid dendritic cells by apoptotic particles: mechanism for the loss of immunological tolerance in androgen-depleted Sjögren’s syndrome

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**Background:** Sjögren’s syndrome (SS) is a common autoimmune disease targeting salivary and lacrimal glands. It is strongly female dominant, characterized by low oestrogen levels combined with a local intracrine dihydrotestosterone defect. It is assumed that the primary effect in SS is the abnormal apoptosis of salivary gland cells, combined with increased production and abnormal handling of the apoptotic particles.

**Objectives:** The working hypothesis was that these hormonal defects lead to increased apoptosis of the epithelial cells and pro-inflammatory plasmacytoid dendritic cell (pDC)-mediated host responses. Apoptosis-induced particles contain SS autoantigens, which may affect immune cells.

**Method:** Apoptotic particles were collected by different centrifugation steps and were used to stimulate pDCs with and without sex steroids. Flow cytometry was used to analyse the expression and localization of SS autoantigens. The effect of the particles on TLR7/9 expression and the cytokine profile in pDCs were studied.

**Results:** Apoptosis-induced apoptotic particles contained SS autoantigens and hy1-RNA. These particles were internalized by pDCs, which stimulated the TLR expression and the production of pro-inflammatory cytokines. Androgens inhibited the particle-induced increase of TLR9 expression in pDCs.

**Conclusions:** Apoptosis of salivary gland cells leads to the formation of apoptotic particles, which might affect immunotolerance, the production of autoantibodies, and the onset of autoinflammation. This might explain how immunological tolerance is broken down in the early stages of SS.

**PP58**

Characterizing the effects of epigenetic regulation in assays using peripheral blood mononuclear cells from patients with inflammatory diseases

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**Background:** Systemic inflammatory diseases, such as systemic lupus erythematosus (SLE) and idiopathic inflammatory myositis (IIM), have a largely unknown
aetiology and represent a disease area with major unmet medical needs. In collaboration with the Structural Genomics Consortium (SGC), we investigate the cellular effects of chemical probes, which are drug-like molecules that can enter cells and selectively inhibit potential new drug targets at therapeutically relevant doses.

**Method:** We investigated the cellular effects of 47 probes, most of which bind and inhibit epigenetic enzymes and regulators, such as bromodomains and histone methyltransferases and kinases. The viability of peripheral blood mononuclear cells (PBMCs) incubated in the presence of titrated doses (typically 0.01–10 μM) of the probes for 1, 3, and 6 days was investigated using the fluorometric microculture cytotoxicity assay (FMCA), which is based on measurements of fluorescein diacetate (FDA) hydrolysis, or by flow cytometry using the LIVE/DEAD IR marker. In addition, probe effects on B-cell maturation and secretion of IgG upon stimulation with cytokines was studied in PBMCs from patients with SLE and IIM.

**Results:** The viability of PBMCs was affected by some of the epigenetic and kinase inhibitors and, in these cases, cell death was typically seen in T cells as well as in B cells. Using the highest tolerable dose, some probes decreased B-cell maturation and/or IgG secretion induced by IL-4, IL-10, IL-21, sCD40L, and CpG.

**Conclusions:** Following these preliminary findings, we intend to study a selected set of the probes in detail using proteomic and metabolomic methods, with the aim of identifying novel drug pathways for inhibition of B-cell function.

**PP59**

**Risk factors for thromboembolic events (TEs) in patients with idiopathic inflammatory myopathies (IIM)**

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**Objectives:** Patients with idiopathic inflammatory myopathies (IIM) have an increased risk of thromboembolic events (TEs) compared with the general population. Our aim was to investigate the prevalence of, and risk factors for, TEs [pulmonary embolism (PE), deep venous thrombosis (DVT), myocardial infarction (MI), stroke, transitory ischaemic attack (TIA), or peripheral arterial thrombosis (PAT)] in IIM patients.

**Method:** In this study, 286 IIM patients were identified. Information on traditional risk factors for TEs, disease activity, and medical treatment was retrieved. Adhesion molecules (i.e. VCAM, ICAM, and E-selectin) were analysed in the patients at the time of IIM diagnosis and TEs as well as in 40 healthy individuals.

**Results:** Sixty-seven (23.4%) patients had at least one TE: 33 had arterial thrombosis (MI, stroke, TIA, PAT), 31 venous thrombosis (DVT, PE), and three had both arterial and venous thrombosis. Higher age at diagnosis (p < 0.001), male gender (p < 0.05), and hypertension (p < 0.05) occurred more frequently in patients with a TE. Significantly higher levels of VCAM, ICAM, and E-selectin (p < 0.001, p < 0.001, and p < 0.05, respectively) were found in IIM patients compared to controls. However, there was no significant difference in the levels of adhesion molecules between IIM patients with TE and those without, either at the time of IIM diagnosis or at the time of a TE.

**Conclusions:** The main finding of this study is the striking prevalence of TEs in IIM patients, which should alert the clinician to screen for TEs when clinically indicated as well as to consider prophylactic treatment in risky situations. Male gender, higher age at IIM diagnosis, and hypertension should be taken into account when estimating TE risk.

**PP60**

**Antiphospholipid antibodies in systemic sclerosis and their association with ischaemic arterial events and atherosclerosis**

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**Objectives:** The prevalence of antiphospholipid (aPL) antibodies and their impact on macrovascular events in SSc remains unclear. The aims of this study were to evaluate the prevalence of aPL antibodies and lupus anticoagulant (LA) in SSc patients and controls. We also investigated whether they were associated with ischaemic arterial events or with measures of atherosclerosis.

**Method:** This study included 110 SSc patients fulfilling the ACR/EULAR classification criteria for SSc and 104 age- and gender-matched population-based controls. Medical records were reviewed for ischaemic events, defined as ischaemic heart disease (IHD), ischaemic cerebrovascular disease (ICVD), and ischaemic peripheral vascular disease (IPVD). A carotid ultrasound was performed to determine the occurrence of carotid plaque and the intima–media thickness (IMT). The ankle-brachial index (ABI) was calculated. Specific aPL antibodies (cardiolipin and anti-β2-glycoprotein-I, IgG, IgM and IgA) were measured by a multiplex immunoassay (Bioplex 2200 system), in patients and controls. A modified dilute Russell viper venom test (DRVVT) was used to determine LA in the patients.

**Results:** The prevalence of aPL antibodies was higher in SSc patients than in controls (12% vs. 3.9%, p = 0.04). The presence of cardiolipin IgM was associated with IHD (p = 0.027). The presence of at least two different isotypes (IgA, IgG, or IgM) of anticardiolipin antibodies was associated with ischaemic arterial events (p = 0.03).
Conclusions: aPL antibodies are more common in SSc patients than in controls and they are associated with cardiovascular events. Therefore, these antibodies should be taken into consideration in clinical practice, and anticoagulation therapy could be used as a measure to prevent cardiovascular involvement in some cases of SSc.

PP61
Pulmonary fibrosis and levels of total IgA in patients with systemic sclerosis
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Background: Interstitial lung disease (ILD) is a major cause of mortality in patients with systemic sclerosis (SSc). A study in idiopathic ILD suggested that a higher total level of immunoglobulin A (IgA) is a biomarker for worse prognosis, especially in patients with an IgA level > 2.85 g/L. We scored the extent of ILD and investigated whether high levels of IgA were associated with more widespread ILD in SSc patients.

Method: Data from 74 SSc patients with signs of ILD were collected. A senior chest radiologist evaluated the HRCT scans using the Kazeeroni score modified by Goldin. Each lung was evaluated in three zones and each zone was evaluated for ground-glass opacity, fibrosis, honeycombing, and emphysema. Diffusing capacity of the lungs for carbon monoxide (DLCO) and forced vital capacity (FVC) were obtained with lung function tests performed in clinical practice. The patients stated their symptoms on a visual analogue scale (VAS) for breathing. Blood samples were collected for measurement of IgA.

Results: Higher HRCT scores were associated with decreased lung function (DLCO and FVC; p < 0.0001) and higher rating of symptoms by the patients (VAS breathing; p = 0.001). IgA levels were 2.6 (1.7–3.9) g/L and 47% of the patients had IgA > 2.85 g/L. Higher levels of IgA were associated with a higher HRCT score (p = 0.001)

Conclusions: The extent of HRCT pathology was associated with both lung function tests and patients’ rating of symptoms. Patients with more widespread disease on HRCT have higher IgA levels. Total IgA might be a new marker of more severe ILD in patients with SSc.

PP62
Early phenotypic presentation of Blau syndrome
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Introduction: Blau syndrome is a rare granulomatous autoinflammatory disorder that primarily affects the skin, joints, and eyes. It is a dominantly inherited condition due to mutations in the caspase recruitment domain gene CARD15/NOD2 mapped on the chromosomal region 16q12.1–13. To date, more than 139 sequence variant mutations have been described in the Infevers registry, predominantly from European countries. Several cases have been reported from Japan, China, Mexico, and India.

Objectives: To describe the first case of Blau syndrome of Arab/Middle Eastern ethnicity from the Sultanate of Oman presenting in infancy.

Method: An 8-month-old male child, born to consanguineous parents, presented to Sultan Qaboos University Hospital with a history of undocumented fever and papular skin rash since the age of 2 months. He developed extensive severe symmetrical boggy polyarthrits at 4 months of age and was found to have anterior uveitis on routine screening. His skin rash and anterior uveitis were compatible with granulomatous vasculitis and granulomatous uveitis. Treatment consisted of intravenous methylprednisolone, oral prednisolone, and subcutaneous methotrexate. However, because of the ongoing active arthritis, etanercept was introduced at 18 month of age.

Results: Genomyic DNA analysis identified a heterozygous missense mutation, NM_022162.2:c.2010C>G (p.Asn670Lys) in exon 4 of the NOD2 gene.

Conclusions: The rarity of Blau syndrome has made it a challenge to fully characterize the disease. However, with the NOD mutation being catalogued regularly in the Infevers registry and the creation of the Blau international registry, novel insights have been provided regarding the need to develop effective targeted therapies.

PP63
Immunogenicity of the 13-valent pneumococcal conjugate vaccine (Prevenar 13) in patients with primary systemic vasculitis receiving standard of care therapy and controls
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Objectives: To study the effect of standard of care therapy on antibody response and functionality of antibodies following pneumococcal vaccination using a 13-valent conjugate vaccine in patients with systemic vasculitis and healthy controls.

Method: Forty-nine patients with systemic vasculitis and 49 controls were immunized with single-dose Prevenar 13. Vasculitis patients were treated with azathioprine (n = 11), cyclophosphamide+prednisolone (n = 6), MTX (n = 9), prednisolone (n = 16), rituximab+DMARDs (n = 3), anti-TNF (n = 2), mycophenolate mofetil (n = 1),
and no DMARD (n = 1). Antibody concentrations for serotypes 6B and 23F were measured using ELISA in samples taken before and 4–6 weeks after vaccination. The percentages of individuals with post-vaccination antibody concentrations ≥ 1 µg/mL (protective levels) and those with at least a twofold increase from pre-vaccination concentrations (positive response) were calculated. Functionality of antibodies against 23F was performed using the opsonophagocytic assay (OPA).

**Results:** Controls were younger than patients (mean age 50.6 vs. 61.5 years) and more were women (63% vs. 51%). Antibody concentrations pre- to post-vaccination increased in both patients and controls (p < 0.001). OPA activity after vaccination increased significantly in both patients and controls (p < 0.001) although more in controls. Fewer patients receiving any DMARD reached protective antibody levels (p = 0.04) and were responders for both serotypes. This was most pronounced for azathioprine and rituximab+DMARD. Prednisolone was not associated with impaired antibody responses (Figure 1).

**Conclusions:** The pneumococcal conjugate vaccine was immunogenic in patients with systemic vasculitis. The functionality of serotype specific antibodies was confirmed in both patients and controls although the opsonophagocytic activity was more pronounced in controls. Azathioprine or rituximab combined with DMARD but not systemic prednisolone led to impaired antibody response.

**PP64**

**Mycoplasma infection inducing flare of Behcet’s disease in a young man**

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**Background:** Behçet’s disease (BD) is a rare systemic vasculitis of unknown aetiology (1). Epidemiological findings suggest an autoimmune process triggered by...
an infectious agent. Mycoplasma pneumoniae stimulates production of the interleukins and TNF-α and may be a potential cause of flare of BD, as described in this case report.

Case presentation: A 18-year-old Syrian male was hospitalized with a 10-day history of dysphagia, fever, and impaired general condition. He had previously had two episodes of oral aphthous ulcers healing spontaneously. On admission, his white cell count was $12.3 \times 10^9$/L, CRP 168 g/L, and body temperature 38.9°C. He was treated with broad spectrum antibiotics with insignificant effect. He developed a severe flare of BD in the form of genital/oral ulcers, rash, and conjunctivitis. Mycoplasma pneumoniae was confirmed by a positive serological test, and laboratory tests excluded herpes simplex virus, cytomegalovirus, Epstein–Barr virus, varicella zoster, chlamydia, HIV, hepatitis, and syphilis. Biopsy of the oral ulcer and scrotum showed unspecific inflammation. He was HLA-B52 positive.

He was diagnosed as having BD based on recurrent oral/genital ulceration and eye lesions. Treatment with systemic and local steroids resulted in clinical remission.

Conclusion: Mycoplasma pneumoniae can be a trigger for flare of BD, and should be taken into consideration, particularly in those with prolonged or recurrent episodes of BD.

Reference

PP65
Rituximab-induced hypogammaglobulinaemia and intravenous immunoglobulin replacement therapy do not protect against relapse in granulomatous with polyangiitis

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Background: Rituximab (RTX) is effective in inducing and maintaining remission in patients with granulomatous with polyangiitis (GPA). However, RTX decreases serum levels of immunoglobulin (Ig) leading to hypogammaglobulinaemia and infections in some patients. This study aimed to examine the use of intravenous immunoglobulin (IVIG) in GPA patients treated with RTX.

Method: The study included 35 GPA patients from our vasculitis registry who received long-term pre-emptive RTX maintenance between April 2004 and June 2011. These patients (54% male) had a mean age of 50 (range 14–81) years and had received 16 (0–250) g of cyclophosphamide. They also received an RTX cumulative dose of 9 (2–14) g and were followed up for 77 months. Hypogammaglobulinaemia was defined as total Ig < 6 g/L.

Results: Nineteen patients (54%) developed hypogammaglobulinaemia 33 (4–71) months after RTX initiation and RTX was readministered in 16 patients. Seven patients (20%) received IVIG 31 (0–43) months after the diagnosis of hypogammaglobulinaemia. Two patients discontinued IVIG after 3 and 4 months; however, five patients were still on IVIG at the last visit, receiving 360 (150–390) g yearly in the past 3 years. Total Ig levels increased from 4.7 g/L before IVIG to 7.4 g/L. Eight patients (23%) relapsed after 3 years of RTX maintenance: five had hypogammaglobulinaemia and four required IVIG. All three relapsing patients with subglottic or endobronchial stenosis were on IVIG (p = 0.036).

Conclusions: The risk of hypogammaglobulinaemia and the need for IVIG increase during long-term RTX maintenance in GPA. If treatment of hypogammaglobulinaemia is required, IVIG use is usually prolonged. RTX-induced hypogammaglobulinaemia and IVIG do not protect against relapse.

PP66
Enhanced compliance to osteoporosis prophylaxis in glucocorticoid (GC)-treated polymyalgia rheumatica (PMR) patients: the role of ongoing follow-up support at nurse consultations

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