Conclusion: In patients with chronic inflammatory arthritis, synovial B cell infiltration and systemic markers of germinal centre activity are heterogeneously increased irrespective of disease diagnosis. ACPA-positive RA and oligoarticular PsA appear located at the extremes of a pathobiological continuum, whilst ACPA-negative RA and polyarticular PsA present with intermediate and comparable degrees of B cell involvement. Collectively, our findings open the interesting perspective of a tailored management of patients with inflammatory arthritis based on the disease pathotype rather than on clinical diagnosis.

Disclosure of Interests: Ludovico De Stefano: None declared, Serena Bugatti: None declared, Carlomaurizio Montecucco: None declared, Antonio Ludovico De Stefano: None declared, Serena Bugatti

Background: Ankylosing spondylitis (AS) is a common inflammatory joint disease affecting articulations of axial skeleton and asymmetrical peripheral arthritis. It has been highlighted that patients with AS exhibit an increased risk of cardiovascular diseases (CVD) compared to the general population [1]. However, little is known about the relationship between cardiovascular burden in AS patients and Th17/Treg imbalance.

Objectives: We aimed to investigate the relationship between cardiovascular events in AS patients and Th17/Treg imbalance. It has been highlighted that patients with AS exhibit an increased risk of cardiovascular diseases (CVD) compared to the general population [1]. However, little is known about the relationship between cardiovascular burden in AS patients and Th17/Treg imbalance. Therefore, we aimed to investigate the relationship between cardiovascular events in AS patients and Th17/Treg imbalance. Furthermore, we want to identify other clinical and/or laboratory features which are associated with the cardiovascular risk in AS patients.

Methods: The study included 32 AS patients with cardiovascular diseases and 32 age-matched AS patients as controls. All the AS patients were hospitalised at the Second Hospital of Shanxi Medical University, Taiyuan, Shanxi, China. The study included 32 AS patients with cardiovascular diseases and 32 age-matched AS patients as controls. All the AS patients were hospitalised at the Second Hospital of Shanxi Medical University, Taiyuan, Shanxi, China.

Results: 1. There was statistically significant decrease in Th17 levels (P=0.012) in the AS with CVD group compared to the AS group, while the Treg cells number in the AS with CVD group was higher than in the AS group. * P < 0.05 **P < 0.01. Data were compared using the Wilcoxon's rank sum test.

Discussion of Interests: None declared

Disclosure of Interests: None declared

AB0028 IMBALANCES OF TH17/TREG IN CARDIOVASCULAR EVENTS OF PATIENTS WITH ANKYLOSING SPONDYLITIS

T. Ding1, R. Wu1, H. Xue1, X. F. Li1, C. Wang1. \(^{1}\) The Second Hospital of Shanxi Medical University, Taiyuan, Shanxi, China

Background: Ankylosing spondylitis (AS) is a common inflammatory joint disease affecting articulations of axial skeleton and asymmetrical peripheral arthritis. It has been highlighted that patients with AS exhibit an increased risk of cardiovascular diseases (CVD) compared to the general population [1]. However, little is known about the relationship between cardiovascular burden in AS patients and Th17/Treg imbalance.

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Methods: The study included 32 AS patients with cardiovascular diseases and 32 age-matched AS patients as controls. All the AS patients were hospitalised at the Second Hospital of Shanxi Medical University and met the diagnostic criteria for AS revised in New York in 1984. We collected demographics, laboratory features [erythrocyte sedimentation rate (ESR), c-reactive protein (CRP), DD (dimer), PLT (platelet count)], and absolute counts of lymphocyte and CD4+ T cell subset counts (cells/μL) in the AS with CVD group and AS group. There was statistically significant decrease in Th17 levels (P=0.012) in the AS with CVD group compared to the AS group. * P < 0.05 **P < 0.01. Data were compared using the Wilcoxon's rank sum test.

Discussion of Interests: None declared

Disclosure of Interests: None declared

AB0029 INHIBITION OF EFFECTOR B CELLS BY IBRUTINIB IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a connective tissue disease with significant morbidity and mortality. Effective treatment is still missing, and clinical control of the disease remains challenging. In particular, the development of pulmonary and cardiac fibrosis and pulmonary hypertension are severe complications responsible for excessive mortality. Currently available treatment strategies—besides aggressive autologous stem cell transplantation which is an option only for selected patients—only alleviate symptoms and slow disease progression. Previous attempts of immunomodulating therapies addressing B cell pathology like rituximab and tocilizumab in SSc showed mixed efficacy.

Results: In patients with chronic inflammatory arthritis, synovial B cell infiltration and systemic markers of germinal centre activity are heterogeneously increased irrespective of disease diagnosis. ACPA-positive RA and oligoarticular PsA appear located at the extremes of a pathobiological continuum, whilst ACPA-negative RA and polyarticular PsA present with intermediate and comparable degrees of B cell involvement. Collectively, our findings open the interesting perspective of a tailored management of patients with inflammatory arthritis based on the disease pathotype rather than on clinical diagnosis.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.5604

References:

Table 1. Absolute lymphocyte and CD4+ T cell subset counts (cells/μL) in the AS with CVD group and AS group

<table>
<thead>
<tr>
<th>Cell count (cells/μL)</th>
<th>AS with CVD</th>
<th>AS</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total T</td>
<td>1447.97±11.49</td>
<td>1442.49±11.49</td>
<td>0.970</td>
</tr>
<tr>
<td>Total B</td>
<td>217±06 (144.55—324.97)</td>
<td>291.27</td>
<td>0.262</td>
</tr>
<tr>
<td>NK</td>
<td>268.09 (171.51—396.99)</td>
<td>277.71</td>
<td>0.858</td>
</tr>
<tr>
<td>Th1</td>
<td>137.23 (69.8-185.45)</td>
<td>127.04</td>
<td>0.693</td>
</tr>
<tr>
<td>Th2</td>
<td>8.42</td>
<td>8.03</td>
<td>0.848</td>
</tr>
<tr>
<td>Th17</td>
<td>5.56-10.47</td>
<td>8.89</td>
<td>0.012*</td>
</tr>
<tr>
<td>Treg</td>
<td>29.64</td>
<td>34.51</td>
<td>0.426</td>
</tr>
<tr>
<td>Th17/Th2</td>
<td>14.99</td>
<td>17.36</td>
<td>0.430</td>
</tr>
<tr>
<td>Th17/Treg</td>
<td>0.23</td>
<td>0.31</td>
<td>0.202</td>
</tr>
</tbody>
</table>

*P<0.05 **p <0.01. Data with a normal distribution and homogeneity of variance are presented as mean±standard deviation. Data without a normal distribution are presented as the median (interquartile range)

**Figure 1.** Differences in Treg, Th17 cell counts and Th17/Treg between AS with CVD group and AS group. There was statistically significant decrease in Th17 levels (P=0.012) in the AS with CVD group. * P < 0.05 **P < 0.01. Data were compared using the Wilcoxon's rank sum test.
Objectives: Here, we investigated the therapeutic potential of ibrutinib, a Bruton’s tyrosine kinase (BTK) inhibitor used in B cell malignancies, to alter B cell pathology in SSC in an in vitro model of autoreactivity.

Methods: PBMCs were isolated from 24 patients with SSC, with SSc were used for functional testing after stimulation with hypomethylated DNA fragments (CpG) to induce an innate immune response. The effects of ibrutinib on cytokine production, autoantibody release and activation of the transcription factor NFκB were evaluated via multiplex cytokine assay, ELISA and flow cytometry.

Results: Ibrutinib was able to reduce the production of the proinflammatory hallmark cytokines IL-6 and TNF-α, which are mainly released by the effector B cell population, in response to TLR9-stimulation. Importantly, small doses of ibrutinib (0.1 µM) preserved the production of immunoregulatory IL-10 and IFNγ while effectively inhibiting the cardinal cytokines of hyperactivated proinflammatory effector B cells in SSc. Intracellular cytokine staining of IL-6 in B cell subsets further endowed the potential of ibrutinib to inhibit B cells in a subset-specific manner, reducing IL-6+ naïve B cells significantly but not IL-6+ memory B cells. The subset specificity was abolished when high doses of ibrutinib (10 µM) were applied. In a flow cytometry analysis of phosphorylated NFκB, an important transcription factor in the induction of innate immune responses in B cells, significantly less activation was observed with ibrutinib treatment (0.1 µM). Higher doses of ibrutinib were unable to further reduce the abundance of pNFκB.

Conclusion: Our data could pave the avenue for a clinical application of ibrutinib for patients with SSc as a novel treatment option for the underlying pathogenetic immune imbalance contributing to disease onset and progression.

References:

Disclosure of Interests: None declared.

Scientific Abstracts

AB0031 T HELPER 17 CELLS WERE SIGNIFICANTLY DECREASED BY MITOCHONDRIAL ELECTRON TRANSPORT CHAIN COMPLEX INHIBITOR IN PATIENTS WITH RHEUMATOID ARTHRITIS

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2Chungnam National University Hospital, Daejeon, Korea, Rep. of (South Korea)

Background: Reactive oxygen species (ROS) and T helper 17 (TH17) cells have been known to play an important role in the pathogenesis of rheumatoid arthritis (RA). However, the interrelationship between ROS and TH17 remains unclear in RA.

Objectives: To explore whether ROS affect TH17 cells in peripheral blood mononuclear cells (PBMC) of RA patients, we analyzed ROS expressions among T cell subsets following treatment with mitochondrial electron transport chain complex inhibitors.

Methods: Blood samples were collected from 40 RA patients and 10 healthy adult volunteers. RA activity was divided according to clinical parameter (DAS28). PBMC cells were obtained from the whole blood using lymphocyte separation medium density gradient centrifugation. Following PBMC was stained with Live/Dead stain dye, cells were incubated with antibodies for CD3, CD4, CD8, T cell receptors and CD163. The combination of antibodies for FoxP3 and IL-17A. MitoSox were used for mitochondrial specific staining. Mitochondria were analyzed with CellQuest analysis.

Results: The frequency of TH17 cells was increased by 4.83 folds in moderate disease activity group (DAS28>3.2) of RA patients compared to healthy control. Moderate RA activity patients also showed higher ratio of TH17/Treg than healthy control (3.57 folds). All RA patients had elevated expression of mitochondrial specific ROS than healthy control when the TH17 cell frequency was no longer elevated but decreased, and this ratio was increased by 4.83 folds in moderate disease activity group of RA patients compared to healthy control. Moderate RA activity patients also showed higher ratio of TH17/Treg than healthy control.

Conclusion: The mitochondrial electron transport chain complex III inhibitor markedly downregulated the frequency of TH17 cells in moderate disease activity patients with RA. These findings provide a novel approach to regulate TH17 function in RA through mitochondrial metabolism related ROS production.

References:

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2020-eular.3441

AB0032 ABNORMAL STATUSES OF PERIPHERAL CD4+ T CELL SUBSETS IN PATIENTS WITH GOUT AND THEIR CHANGES AFTER RECEIVING COMBINED IMMUNOMODULATORY THERAPY

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Background: Gout is a chronic systemic inflammatory disease that results from the deposition of monosodium urate crystals in joints and the associated activation of the innate immune system associated with hyperuricemia. As the pathogenesis of gout is still a matter of speculation and debate, accumulating evidence converges on inflammammasome activation and immunological dysregulation. However, the detailed statuses of lymphocyte subsets in patients with gout are unknown and influence of immunomodulatory combination therapies on the lymphocyte subsets remain to be clearly evaluated.

Objectives: Here, we investigated the therapeutic potential of ibrutinib, a Bruton’s tyrosine kinase (BTK) inhibitor used in B cell malignancies, to alter B cell pathology in SSc in an in vitro model of autoreactivity.

Methods: PBMCs were isolated from 24 patients with SSC, with SSc were used for functional testing after stimulation with hypomethylated DNA fragments (CpG) to induce an innate immune response. The effects of ibrutinib on cytokine production, autoantibody release and activation of the transcription factor NFκB were evaluated via multiplex cytokine assay, ELISA and flow cytometry.

Results: Ibrutinib was able to reduce the production of the proinflammatory hallmark cytokines IL-6 and TNF-α, which are mainly released by the effector B cell population, in response to TLR9-stimulation. Importantly, small doses of ibrutinib (0.1 µM) preserved the production of immunoregulatory IL-10 and IFNγ while effectively inhibiting the cardinal cytokines of hyperactivated proinflammatory effector B cells in SSc. Intracellular cytokine staining of IL-6 in B cell subsets further endowed the potential of ibrutinib to inhibit B cells in a subset-specific manner, reducing IL-6+ naïve B cells significantly but not IL-6+ memory B cells. The subset specificity was abolished when high doses of ibrutinib (10 µM) were applied. In a flow cytometry analysis of phosphorylated NFκB, an important transcription factor in the induction of innate immune responses in B cells, significantly less activation was observed with ibrutinib treatment (0.1 µM). Higher doses of ibrutinib were unable to further reduce the abundance of pNFκB.

Conclusion: Our data could pave the avenue for a clinical application of ibrutinib for patients with SSc as a novel treatment option for the underlying pathogenetic immune imbalance contributing to disease onset and progression.

References:

Disclosure of Interests: Paula Fortea-Gordo Grant/research support from: BMS, Alejandro Villalba: None declared, Laura Nuño: None declared, Maria-Jose Santos-Borzone Grant/research support from: BMS, Diana Peleidac: None declared, Irene Monjo: None declared, Amaya Puig-Kröger: None declared, Paloma Sanchez-Mateos: None declared, Emilio Martin-Mola Grant/research support from: BMS, Roche, Alejandro Balsa Grant/research support from: BMS, Roche, Consultant of: AbbVie, Gilead, Lilly, Pfizer, UCB, Sanofi, Sandoz, Speak-