Conclusion: B cell subsets might provide a useful diagnostic tool for distinction SLE and pSS. More research needed to investigate clinical value of B-cell subsets in autoimmune rheumatic diseases.

Table 1. Peripheral B-cell subset composition in SLE and SS patients vs. HV group assessed by discriminant analysis.

Parameter	F-test	p-level
Plasmoblasts (CD27hiCD38hi), %	7,93	<0.001
Resting memory B-cells (CD27dimCD38low), %	13,72	<0.001
Transitional B-cells (CD27lowCD38hi)	29,74	<0.001
Mature active B-cells (CD27dimCD38dim), %	5,20	<0.001
Naive mature B-cells (CD27dimCD38low), %	3,10	0,049
Double negative (CD27lowCD38low), %	1,98	0,14
Resting memory B-cells (CD27dimCD38low)	1,02	0,36
Double negative (CD27lowCD38low)	2,32	0,10
Plasmoblasts (CD27hiCD38hi)	1,02	0,36
Naive mature B-cells (CD27dimCD38low)	1,03	0,36
Mature active B-cells (CD27dimCD38dim)	1,02	0,36
Transitional B-cells (CD27lowCD38hi), %	1,03	0,36

Disclosure of Interests: None declared

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AB0026

SELECTIVE INHIBITION OF TYROSINE KINASE 2 WITH AN ORAL AGENT, BMS-986165, COMPARED WITH JANUS KINASE INHIBITORS

A. Chimalakonda¹, J. Burke¹, L. Cheng¹, J. Strnad¹, I. Catlett¹, A. Patel¹, J. Shen¹, I. Girgis¹, S. Banerjee¹, J. Throup¹. ¹Bristol-Myers Squibb, Princeton, United States of America

Background: BMS-986165 is an oral, selective inhibitor of tyrosine kinase 2 (TYK2) with a unique mode of binding to the pseudokinase domain of the enzyme rather than the active site within the kinase domain. This unique mode of binding provides high functional selectivity for TYK2 versus other tyrosine kinases (TYKs) in cellular and other in vitro assays.¹ This approach may provide robust efficacy with a differentiated safety profile due to decreased off-target activity on other kinases. In a 12-week, placebo-controlled Phase 2 trial in patients with moderate to severe plaque psoriasis,² BMS-986165 had a favorable safety profile, and 67%–75% of patients achieved Psoriasis Area and Severity Index 75 (PASI 75) after 12 weeks at doses ≥ 3 mg twice daily versus 7% with placebo. BMS-986165 is currently under investigation in multiple autoimmune disorders such as psoriatic arthritis, psoriasis, and systemic lupus erythematosus.

Objectives: To understand the selectivity of BMS-986165 compared with JAK inhibitors, such as tofacitinib (Tofa), upadacitinib (Upa), and baricitinib (Bari), at clinically relevant doses and plasma concentrations.

Methods: In vitro whole blood assays were developed to measure the activity of common pairings of JAKs (JAK 1/3, JAK2/2, and TYK2/JAK2) and concentrations providing half-maximal inhibition (IC_{50}) for BMS-986165, Tofa, Upa, and Bari were determined. The whole blood IC_{50} values were plotted against pharmacokinetic profiles of these agents at approved doses and/or doses evaluated in their respective Phase 2/3 trials. The time that concentrations were $>IC_{50}$ and projected average daily inhibition were evaluated.

Results: At clinically relevant doses and exposures, BMS-986165 plasma concentrations were higher than the TYK2 whole blood IC_{50} value for a considerable part of the dosing interval. Additionally, the maximal plasma concentration (C_{max}) of BMS-986165 was approximately >9 - to 18-fold lower than the JAK 1/3 whole blood IC_{50} value and >52 - to >109 -fold lower than JAK2/2 whole blood IC_{50} , indicating lack of meaningful inhibition of the JAK 1-3 pathways by BMS-986165 at therapeutic doses. At clinically relevant doses, projected C_{max} values of Tofa, Upa, and Bari were many-fold lower than TYK2 IC_{50} , indicating minimal or no meaningful inhibition of the TYK2 pathway. As expected, Tofa, Upa, and Bari had varying degrees of inhibition against JAK1/3 (daily average inhibition range: 70%–94%) and JAK2/2 pathways (daily average inhibition range: 24%–67%) at clinically relevant doses and exposures.

Conclusion: These results demonstrate the high TYK2 functional selectivity of BMS-986165 at clinically relevant doses and plasma concentrations compared with Tofa, Upa, and Bari and indicate that BMS-986165 is in a different class compared with JAK 1–3 inhibitors. Ongoing studies in psoriasis and other conditions may confirm the expected safety of BMS-986165 based on the above results. The daily average inhibition of JAK1 and JAK2 likely explains some

common laboratory observations and adverse events reported for the JAK1–3 inhibitors.

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AB0027

B CELL SYNOVITIS IN RELATION TO DIAGNOSIS AND CLINICAL PHENOTYPE: COMPARISON BETWEEN RHEUMATOID AND PSORIATIC ARTHRITIS

L. De Stefano¹, S. Bugatti¹, S. Rossi¹, C. Montecucco¹, A. Manzo¹. ¹University of Pavia, Rheumatology and Translational Immunology Research Laboratories (LaRIT), Division of Rheumatology, Pavia, Italy

Background: Rheumatoid arthritis (RA) and psoriatic arthritis (PsA) are both characterized by significant heterogeneity in terms of clinical presentation and outcomes. Furthermore, RA and PsA may share some overlapping features such as autoantibody-negativity, polyarticular involvement, response to certain therapies and pattern of joint damage. The pathobiological bases underlying the intra-disease heterogeneity and the inter-disease similarities between RA and PsA are however unknown.

Objectives: Aim of the current study was to investigate the relationship between the synovial immune phenotype and different clinical subsets in patients with RA and PsA.

Methods: The study population included 96 patients undergoing ultrasound-guided synovial biopsy of the knee and serum sampling on the same day. Patients were recruited according to defined clinical subtypes: anti-citrullinated positive (ACPA) RA (n=26), ACPA-negative RA (n=32), polyarticular (≥ 5 involved joints) PsA (n=15), and oligoarticular PsA (n=23). Patients were compared for: (i) demographic and clinical features; (ii) synovial histopathological characteristics including CD68-positive infiltrating macrophages, CD3-positive T lymphocytes, CD20-positive B lymphocytes (semi-quantitative scores 0-3); (iii) serum levels of the lymphoid chemokine CXCL13 as a marker of germinal centre activity.

Results: Collectively, ACPA-positive RA patients, ACPA-negative RA patients and patients with polyarticular PsA presented comparable demographic and clinical features including gender distribution, age, number of involved joints and levels of acute phase reactants. Patients with oligoarticular PsA were instead younger, more frequently males, and with lower levels of acute phase reactants. The degree of macrophage and T cell infiltration correlated with the erythrocyte sedimentation rate (ρ 0.38, $p=0.001$ and ρ 0.24, $p=0.04$ respectively) and C-reactive protein levels (ρ 0.38, $p=0.001$ and ρ 0.28, $p=0.01$ respectively) irrespective of diagnosis, and was significantly lower in oligoarticular PsA (Figure 1 A, B). In contrast, the degree of B cell infiltration showed significant differences in relation to the disease subtype: the lowest levels were found in oligoarticular PsA, the highest levels in ACPA-positive RA, whilst ACPA-negative RA and polyarticular PsA presented with intermediate and comparable levels between the two extremes (Figure 1 C). Serum levels of CXCL13 correlated with the synovial B cell score (ρ 0.30, $p=0.03$) and, similarly to synovial B cell infiltration, were differentially increased according to the clinical phenotype, with again similarities between ACPA-negative RA and polyarticular PsA (Figure 1 D).

Figure 1.

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.

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

T. Ding¹, R. Wu¹, H. Xue¹, X. F. Li¹, C. Wang¹. ¹The 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 arthrosis. 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 the status of T cell subsets. 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 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 (D-dimer), PLT (platelet count)], and absolute counts of lymphocyte and CD4+ T cell subset. The absolute numbers of lymphocytes and CD4+ T cells in peripheral blood were measured by Flow Cytometer.

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 (P=0.426) and the ratio of Th17/Treg (P=0.202) have no statistically significant differences; 2. DD was significantly increased in AS patients with CVD; 3. The use of NSAIDs between the two groups is significantly different (P=0.013). 86.7% of the AS group have received NSAIDs, while only 58.1% of the AS patients with CVD have received the NSAIDs.

Conclusion: The findings suggested that the cardiovascular events of AS patients correlated with imbalanced T cell subsets and the decreased Th17 cells may be a laboratory feature of AS patients with CVD. Patients with high DD level might have a higher risk of CVD. Monitoring of Th17 cells and DD could be beneficial in cardiovascular burden of patients with AS. However, current studies indicate that Th17 cells mediate the inflammatory response and play a crucial role in the development of CVD [2]. One explanation is that the AS patients with CVD in our study had a long disease duration and immunomodulatory therapy might have an impact on the status of T cell subsets. Meanwhile, the different disease activities of AS patients can be additional factors.

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

Cell count (cells/ μ L)	AS with CVD	AS	P-value
Total T	1447.97 $\pm$ 11.49	1442.49 $\pm$ 11.49	0.970
Total B	217.06 (144.55- 324.97)	291.27 (171.13-321.16)	0.262
NK	268.09 (171.51-396.99)	277.71 (167.08- 462.45)	0.858
Th1	137.23 (69.8-185.45)	127.04 (76.9-197.26)	0.693
Th2	8.42 (5.56-10.47)	8.03 (5.50-9.95)	0.848
Th17	5.77 (4.00-8.61)	8.89 (5.91-13.88)	0.012*
Treg	29.64 (17.07-47.19)	34.51 (23.26-47.19)	0.426
Th1/Th2	14.99 (10.50-24.21)	17.36 (12.71-25.98)	0.430
Th17/Treg	0.23 (0.12-0.39)	0.31 (0.18-0.52)	0.202

*P<0.05 **p <0.01. Data with a normal distribution and homogeneity of variance are presented as mean $\pm$ 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.

Disclosure of Interests: None declared

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AB0029 INHIBITION OF EFFECTOR B CELLS BY IBRUTINIB IN SYSTEMIC SCLEROSIS

J. Einhaus¹, A. C. Pecher¹, E. Asteriti¹, H. Schmid¹, K. A. Secker¹, S. Duerr-Stoerzer¹, H. Keppeler¹, R. Klein¹, C. Schneidawind¹, J. Henes¹, D. Schneidawind¹. ¹University Hospital Tuebingen, Tuebingen, Germany

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^{1,2}