References:

- [1] Berglund, L.J., Avery, D.T., Ma, C.S., Moens, L., Deenick, E.K., Bustamante, J., Boisson-Dupuis, S., Wong, M., Adelstein, S., Arkwright, P.D., et al. (2013). IL-21 signalling via STAT3 primes human naive B cells to respond to IL-2 to enhance their differentiation into plasmablasts. *Blood* 122, 3940–3950.
- [2] Menon, M., Blair, P.A., Isenberg, D.A., and Mauri, C. (2016). A Regulatory Feedback between Plasmacytoid Dendritic Cells and Regulatory B Cells Is Aberrant in Systemic Lupus Erythematosus. *Immunity* 44, 683–697.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.5752

THU0042

DIFFERENTIAL EFFECT OF ABATACEPT VS TNF BLOCKERS, ON THE FREQUENCY OF CIRCULATING FOLLICULAR HELPER (TFH) AND PERIPHERAL HELPER (TPH) T CELLS IN RHEUMATOID ARTHRITIS

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Background: CXCR5+PD-1^{hi} follicular helper (Tfh) and CXCR5+PD-1^{hi} peripheral helper (Tph) T cells play an important role in the pathogenesis of Rheumatoid Arthritis (RA) by providing help to autoantibody secreting B cells. Whereas Tfh cells typically dwell in the germinal centers of lymphoid organs, Tph cells accumulate at inflamed tissues. An increased frequency of Tph cells and of circulating counterparts of Tfh cells have been described in the peripheral blood of patients with seropositive RA.

Objectives: To examine the effect of treatment escalation using biological agents (TNF blockers or abatacept), on the frequency of circulating Tfh (cTfh) and Tph (cTph) cells in RA.

Methods: Peripheral blood was drawn from seropositive RA patients with an incomplete response to csDMARDs (n=29) who initiated biological therapy with TNF blockers (TNFb) (n= 17) or abatacept (n= 12), prescribed based on routine clinical practice. cTfh and cTph cell frequencies were determined by flow cytometry of freshly isolated PBMCs at the basal visit and 6 months after starting treatment escalation. For each patient, an age and gender-matched healthy control (HC) was also studied at both time points (n=29).

Results: As compared with HC, active RA patients receiving csDMARDs demonstrated a baseline increased frequency of both cTfh and cTph cells. A significant improvement of disease activity as determined by the DAS28 score (Δ DAS28>2.0) was apparent in all of the patients 6 months after initiating biologicals. At that time point, a significant reduction of the previously elevated cTph cell frequency was observed in both treatment groups. However, cTfh cells remained elevated in patients receiving TNFb notwithstanding a good therapeutic response, whereas subjects receiving abatacept experienced a significant abatement of their cTfh cell frequency. Experimental variation of the cTfh and cTph cell numbers in HC was minimal.

Conclusion: Abatacept but not TNFb, are able to bring down cTfh cell numbers in RA. This indicates that costimulation blockade can help attain an immunological remission, whereas TNF neutralization may allow a persistent pathogenic germinal center overactivity. At the same time, treatment with both abatacept and TNF blockers results in a downmodulation of the previously elevated cTph cell numbers, in parallel with the remitting local joint inflammation.

References:

- [1] Simpson N et al, Arthritis Rheum 2010; Craft J, Nat Rev Rheumatol 2012; Arroyo-Villa I et al., Arthritis Res Ther 2014; Rao DA et al., Nature 2017.

Disclosure of Interests: Paula Fortea-Gordo Grant/research support from: BMS, Diana Peiteado: None declared, Alejandro Villalba: None declared, Maria-Jose Santos-Bornez Grant/research support from: BMS, Laura Nuño: None declared, Irene Monjo: None declared, Alejandro Balsa Grant/research support from: BMS, Roche, Consultant of: AbbVie, Gilead, Lilly, Pfizer, UCB, Sanofi, Sandoz, Speakers bureau: AbbVie, Lilly, Sanofi, Novartis, Pfizer, UCB, Roche, Nordic, Sandoz, Maria-Eugenia Miranda-Carus Grant/research support from: BMS, Roche

DOI: 10.1136/annrheumdis-2020-eular.1823

THU0043

EXPRESSION OF B CELL CHEMOKINE-CHEMOKINE RECEPTOR PATHWAYS IS ALTERED IN GIANT CELL ARTERITIS

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Background: The presence of organised B cells in both cranial-giant cell arteritis (C-GCA) (temporal artery) and large vessel (LV)-GCA (aorta) has previously been documented. The number and the extent of organisation of B cells

in tertiary lymphoid organs (TLO) was more prominent in the aorta than in the temporal artery, suggesting possible differences in B cell phenotype, kinetics and tropism between C-GCA and LV-GCA.

Objectives: We sought to analyse B cell differentiation subsets in both C-GCA and LV-GCA and to investigate differences in the expression of chemokine pathways involved in B cell migration and TLO organisation.

Methods: Blood was collected from C-GCA (n=11) and LV-GCA (n=22) patients at baseline, before start of glucocorticoid treatment, and after 3 months of treatment. The LV-GCA groups consisted of 11 patients with isolated LV-GCA and 11 patients with overlap LV/C-GCA. Also, age- and sex- matched healthy controls (HC, n=24) were included. The following chemokines were measured with Luminex in the sera of patients and HC: BAFF, CCL19, CCL21, CXCL9, CXCL10, CXCL11, CXCL12, and CXCL13. Thawed PBMC of 7 C-GCA, 10 LV-GCA and 24 HC were stained with antibodies against CD19, CD27, IgD, IgM, CD38, CXCR3, CXCR4, CXCR5, and CCR7 to allow identification of B cell differentiation subsets and their chemokine receptor expression.

Results: We found a lower absolute number of CXCR3+ memory and double negative (late stage) B cells in GCA patients when compared to healthy controls. Also, the absolute number of CXCR5+ memory B cells was lower in patients than in controls. Chemokine receptor expression on circulating B cells did not significantly differ between C-GCA and LV-GCA at baseline. After 3 months of treatment, frequencies and absolute numbers of both CXCR3+ and CXCR5+ memory B cells increased. In sera of all GCA patients, CXCL9 (which is a chemokine involved in migration of B cells to sites of inflammation) and CXCL13 (which is involved in local organization of B cells) were significantly increased. BAFF and CCL21 were increased only in LV-GCA when compared to HC. Serum chemokine levels did not differ between C-GCA and LV-GCA patients. An inverse correlation was observed between B cell counts and CXCL9 as well as CXCL13 in LV-GCA, only. After 3 months of treatment, CXCL9 levels remained elevated whereas CXCL13 increased even further.

Conclusion: At diagnosis, CXCL9 and CXCL13 were significantly increased in all GCA patients as compared to HC. Elevated CXCL9 levels inversely correlated with B cells numbers in LV-GCA, only, which may suggest that B cells preferentially migrate to the inflamed aorta via a mechanism involving CXCL9. In addition, CXCL13 may be linked to local TLO organization in LV-GCA. Currently, we are studying the local expression of chemokines and chemokine receptors at the site of inflammation in both C- and LV-GCA.

Disclosure of Interests: Jacoba Graver: None declared, Annemieke Boots Consultant of: Grünenthal GmbH until 2017, Wayel Abdulahad: None declared, Johan Bijzet: None declared, Daphne Wolbers: None declared, Elisabeth Brouwer Consultant of: Roche (consultancy fee 2017 and 2018 paid to the UMCG), Speakers bureau: Roche (2017 and 2018 paid to the UMCG), Maria Sandovici: None declared

DOI: 10.1136/annrheumdis-2020-eular.4435

THU0044

SINGLE CELL ANALYSIS OF BONE MARROW AND PERIPHERAL ALTERED B CELL DIFFERENTIATION IN PATIENTS WITH ACTIVE SLE AND THE MECHANISM OF ABNORMAL EARLY B CELL DEVELOPMENT

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Background: B cell differentiation and dysfunction play a key role in the pathogenesis of Systemic lupus erythematosus (SLE). Bone marrow (BM) is the development organ of B cells, and also the home and residence place of plasma cells and memory B cells. However, there is a lack of studies on B cells in BM with lupus.

Objectives: To map the development of BM and peripheral B cells and investigate the mechanism of abnormal early B cell development in SLE.

Methods: A total of 11 SLE patients and 5 age- and sex-matched controls were recruited. BM and peripheral B cell subsets were measured by flow cytometry. Sorting-purified B cell subsets were subject to single-cell RNA sequencing (scRNA-seq) and functional studies. Plasma cytokines and secreted immunoglobulins were detected by Luminex or ELISA. Disease activity of SLE patients was measured using the SLE Disease Activity Index (SLEDAI).

Results: In the present study, we find out that the percentage of monocytes in MNC (p=0.070) and plasma cells (p=0.001) in CD19+ were significantly decreased in BM of SLE, compared to healthy controls. While, SLE patients had increased T%MNC (p=0.008) and B%CD19+ (p=0.002) in BM than controls. In detail, the B cell subsets of bone marrow in patients with active lupus (SLEDAI≥8 score) were seriously disordered, showing the increasing T%MNC (p=0.049), prope-B%CD19+ (p=0.006) and immature B cell%CD19+ (p=0.010) than healthy donors. prope-B%CD19+ exhibited good relationship with SLEDAI. By