less severe inflammation in lupus. However, we still need to determine the mechanism behind the changes in the migration of B cells to the gut immune tissue, the production of IgA, and the microbiome composition as well as the role of P. distasonis in lupus inflammation.

S01.3 RNA-SEQ IN PERIPHERAL BLOOD IMMUNE CELLS IDENTIFIES MODULAR NETWORKS PREDICTIVE AND PROTECTIVE FOR PROGRESSION FROM ANA POSITIVITY TO CLASSIFIABLE SYSTEMIC AUTOIMMUNE DISEASE

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10.1136/lupus-2022-elm2022.3

ANA-positivity represents a complex 'At-Risk' state for development of connective tissue disease (CTD). While ANA may become positive years in advance of clinical CTD, they are also positive in up to 25% of the population, of whom only a small fraction ultimately develop symptoms. Complex immune disturbances iare evident even among ANA-positive individuals who do not ultimately progress to overt disease [1]. In a prospective observational cohort of ANA positive individuals 'At-Risk' for CTD we have shown that a validated blood IFN-Score was predictive of progression to classifiable SLE [2]. However, the wider transcriptional fingerprint of the 'At-Risk' state and other factors modifying risk of progression are not known. We hypothesise that diverse immune processes, both independent and interacting with IFN pathway activation, could modulate risk of progression.

Purpose To investigate how peripheral blood immune cell transcriptional signatures derived by RNA Seq associate with progression or non-progression from At-Risk ANA positivity to clinically apparent CTD.

Methods Peripheral blood mononuclear cells (PBMCs) were isolated at baseline from ANA-positive At-Risk individuals demonstrating ≤1 clinical criterion for classifiable CTD, symptom duration <12 months and naive of glucocorticoid or immunosuppressive therapy. Progression was prospectively adjudicated at 12 months and defined as accrual of clinical/immunological criteria sufficient to meet classification for SLE (SLICC 2012) or other relevant CTDs. Bulk RNASeq was performed on PMBCs from 16 Progressors and 19 non-Progressors. Weighted gene co-expression network analysis (WCGNA) was performed using WCGNA package and gene ontology (GO) enrichment was envaluated using ClusterProfiler, in R Bioconductor. The top 20% genes ranked by connectivity were defined as hub genes. Major cell subsets were quantified in parallel by multiparameter flow cytometry.

Results 29 modules were identified by WCGNA. Eigengenes for 3 modules were significantly associated with progression status. A single, 152 gene module showed strong positive correlation with progression (R=0.55, p<0.001). Hub genes were significantly enriched for type I IFN-siganlling pathway and included established interferon stimulated genes such as IFI44 and IRF7.

Two further modules had a negative, ie protective, association with progression; a smaller 37 gene module, correlated negatively with both blood interferon score (R=-0.46, p=0.005) and with progression (R=-0.43, p=0.01). A larger 252 gene module was also negatively related to progression (R=-0.43, p=0.009) and demonstrated significant pathway enrichment for regulation of cell morphogenesis and actin cyctoskeleton organisation.

Conclusions We identify novel modular transcriptomic signatures implicated in SLE disease initiation. We show (i) IFN-pathway activation is the single strongest transcriptomic risk marker of progression from the 'At Risk state' and (ii) we identify 2 novel protective signatures in peripheral blood immune cells for which further functionally characterization is ongoing.

S01.4 BELIMUMAB DISRUPTS MEMORY B-CELL TRAFFICKING IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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10.1136/lupus-2022-elm2022.4

Purpose Belimumab (BEL), a recombinant human monoclonal antibody directed against B-cell activating factor (BAFF), is the first approved biological agent for patients with systemic lupus erythematosus (SLE) and a high level of disease activity or lupus nephritis (LN). BEL inhibits primary humoral immune responses by depleting naive B-cells that are dependent on BAFF for their survival while secondary humoral immune responses by memory B cells (MBCs) remain intact. Indeed, some studies reported an increase of circulating MBCs following neutralization of BAFF1,2. So far these effects of BEL on the MBC compartment in SLE patients have not been investigated. This study aimed to establish the dynamics of circulating MBCs in patients with SLE treated with BEL and to perform an in-depth analysis of the impact of BEL on the MBC compartment.

Methods First, extensive B cell subset phenotyping was performed prospectively by employing high-sensitivity flow cytometry (HSFC) based on EuroFlow protocols3 in severe SLE/LN patients treated with BEL4. Additionally, in-depth characterisation of surging MBCs in circulation was performed by single-cell RNA sequencing (scRNA-seq).

Results HSFC established that the increase in MBCs was non-specific and observed in a broad range of MBC immunoglobulin subclasses peaking as early as 2 weeks after BEL initiation. Subsequent scRNA-seq analysis of the emerging MBCs revealed a non-proliferating phenotype with a prominent decrease in activation status. In these circulating MBCs, a large amount of migration and adhesion genes were downregulated suggesting that the accumulation of MBCs following BEL treatment was related to their impaired cell-cell adhesion, disrupting cell-trafficking and preventing extravasation.

Conclusions After initiation of BEL treatment, a substantial increase of circulating MBCs was firmly established in patients with SLE/LN. The surge of circulating MBCs appeared to be associated with disrupted lymphocyte trafficking of MBCs, thereby suggesting a new potential therapeutic mechanism of BEL on MBCs in SLE. These findings have important implications to our understanding and consequent improvement of B-cell targeted treatment strategies in patients with active SLE and LN as MBC accumulation in circulation might allow for more efficient targeting of the B-cell compartment.

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Thursday 06 October 2022 from 10:20 to 11:50

S02 Activity and outcome with patients

S02.1 TREAT TO TARGET IN SYSTEMIC LUPUS ERYTHEMATOSUS FROM THE PATIENTS' PERSPECTIVE – RESULTS FROM AN INTERNATIONAL PATIENT SURVEY

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10.1136/lupus-2022-elm2022.5

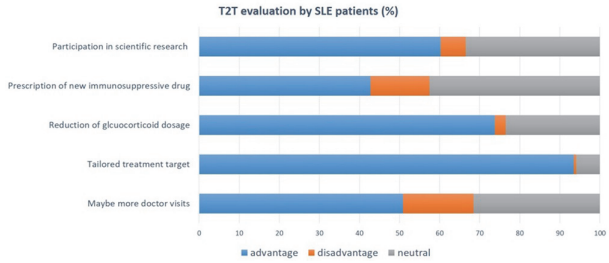
Purpose Treat-to-target (T2T) is considered the emerging concept to significantly improve systemic lupus erythematosus (SLE) care and the patients' outcomes. However and although the success of T2T is largely determined by the involvement of patients, their perspective on T2T has so far not been assessed. It was our aim to investigate patients' attitude towards T2T.

Methods A new-designed questionnaire of 13 questions on T2T, its acceptance, the need and willingness to participate in a T2T trial and possible obstacles for T2T was distributed among members of the patient organizations of the Netherlands (NL), Austria (AU), Germany (GE) and Bulgaria (BG) via newsletter (GE, AU, BG), personal invitation (NL) and a closed Facebook group (BG).

Results A total of 863 patients (n=316 NL, n=271 GE, n=232 BG, n=44 AU), 93.3% female, 52.2% aged 41–60 years with self-declared diagnosis of SLE completed the questionnaire. 48.4% declared being currently in remission, 13% did not know if they were in remission.

Regarding the satisfaction with the current health status, 56.2% were somewhat to all the way satisfied, 29.3% were not at all or hardly satisfied. 65.5% were satisfied with their current therapeutic treatment, while 14.8% where not at all or hardly satisfied with their treatment. Longer disease duration and Dutch origin were associated with higher satisfaction of both health status (disease duration: estimate 0.15, 95%CI 0.09–0.22, p<0.001; Dutch origin: estimate 0.42, 95%CI 0.27–0.61, p<0.001) and therapeutic treatment (disease duration: estimate 0.11, 95%CI 0.05–0.17, p<0.001; Dutch origin: estimate 0.58, 95%CI 0.40–0.75, p<0.001).

As most important treatment goal, normalization of quality of life was chosen most frequently (37.4%) followed by prevention of organ damage (24.6%) and the absence of disease activity (22.6%).



Abstract S02.1 Figure 1 Consequences of T2T rated as advantage or disadvantage by SLE patients. T2T treat-to-target, SLE systemic lupus erythematosus

Regarding shared decision making, the majority reported to be somewhat to all the way involved in treatment decisions (62.1%) while 20,7% where hardly or not at all involved. Dutch patients and patients with longer disease duration reported a stronger involvement in treatment decisions (disease duration: estimate 0.19, 95%CI 0.12–0.26, p<0.001; Dutch origin estimate 0.59, 95%CI 0.39–0.78, p<0.001).

As most difficult decisions in T2T and shared decision making, respondents named the start of new SLE medication (37.9%) and to change medication while feeling good (39.4%). An increase in the dose of glucocorticoids to reach remission was difficult for 22.7%. The perceived advantages and disadvantages of T2T are depicted in figure 1.

Conclusions A substantial number of patients was not satisfied with their health status and therapeutic treatment, whereby Dutch patients and patients with longer disease duration showed higher satisfaction. Reasons and potential biases for this country specific discrepancy remain to be elucidated. Advantages of T2T did overweigh possible disadvantages of T2T with the possibility of more doctors' visits and the prescription of a new drug as biggest disadvantage. Quality of life named as most important treatment goal emphasizes its importance as outcome parameter.

Thursday 06 October 2022 from 15:40 to 17:10

S03 Cardiovascular and thrombotic disease

S03.1 ENDOTHELIAL FUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: IMPACT OF CAFFEINE CONSUMPTION ON ENDOTHELIAL PROGENITOR CELLS SURVIVAL

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10.1136/lupus-2022-elm2022.6

Purpose Circulating endothelial progenitor cells (EPCs) are widely demonstrated biomarkers of endothelial function. Their frequency and function varied in systemic lupus erythematosus (SLE) patients, with a significant association with subclinical atherosclerosis.[1] Caffeine, one of the most widely consumed products in the world, seems to improve endothelial cells number and EPCs migration in coronary artery disease both in mouse models and in patients.[2] The purpose of this study