Conclusions: We observed with ibrutinib treatment (0.1 µM) that the potential of ibrutinib to inhibit B cells in a subset-specific manner, reducing the production of the profibrotic 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 IFN-γ 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 endorsed 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.

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

References:

Disclosure of Interests: None declared.

Background: The background of regulatory B cells seems to vary along the course of the disease in murine models of inflammatory conditions. Decreased numbers of circulating regulatory CD19+CD24hiCD38hi transitional B cells (cTrB) have been described in patients with longstanding RA.

Objectives: To examine the frequency and evolution of cTrB cells in the peripheral blood of early RA (ERA) patients.

Methods: Freshly isolated PBMCs from 48 steroid and DMARD-naïve ERA patients with a disease duration below 24 weeks and 48 healthy controls (HC) were examined by flow cytometry. Cocultures of isolated memory B cells were established with autologous T cells, in the absence or presence of TrB cells.

Results: As compared with HC, ERA patients demonstrated an increased frequency of cTrB cells. cTrB of ERA and HC displayed an anti-inflammatory cytokine profile and were able to downregulate T cell IFNy and IL-21 production, together with ACPA secretion in autologous B/T cell cocultures. Basal frequencies of cTrBs above the median value observed in HC were associated with a good EULAR response to MTX at 12 months (RR=2.91; 95% CI, 1.37-6.47). A significant reduction of cTrB was observed 12 months after initiating MTX, when the cTrB cell frequency was no longer elevated but decreased, and this was independent of the degree of clinical response or the intake of prednisone.

Conclusion: An increased frequency of regulatory cTrB cells is apparent in untreated ERA, and the baseline cTrB cell frequency is associated with the clinical response to MTX at 12 months.

References: