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+ follicular helper (Thf) and CXCR5+PD-1+ peripheral helper (TPh) T cells play an important role in the pathogenesis of Rheumatoid Arthritis (RA) by providing help to autoreactive B cells. Whereas Thf 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 Thf 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 Thf (cThf) 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), described based on routine clinical practice. cThf 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 cThf and cTPh cells. A significant improvement of disease activity as determined by the DAS28 score (ΔDAS28>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 cThf cell frequency was observed in both treatment groups. However, cTPh cells remained elevated in patients receiving TNFβ notwithstanding a good therapeutic response, whereas subjects receiving abatacept experienced a significant abatement of their cTPh cell frequency. Experimental variation of the cThf and cTPh cell numbers in HC was minimal.

Conclusion: Abatacept but not TNFβ, are able to bring down cThf cell numbers in RA. This indicates that costimulation blockade may 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 cThf cell numbers, in parallel with the remitting local joint inflammation.


Disclosure of Interests: None declared.