Methods 12 systemic RV patients (diagnosed according to the Scott&Bacon criteria) were taken into study after the induction of clinical remission (irrespective of the remissive therapy). Each patient received a daily dose of 600 mg PTX. The following were evaluated upon enrollment and after 3 months: clinical signs of vasculitis (on a modified BVAS log), morning stiffness, ESR, CRP and C4 (Mancini), TNF α (ELISA- R&D). The data were compared using the Student's t test for paired variables.

Results A relapse presenting with constitutional signs appeared only in one of the 12 patients; however, new ocular signs (?red eye?) appeared in 2 patients. Minor cutaneous vasculitis resolved in 1 patient and appeared newly in 3 patients on PTX. Morning stiffness reduced from 107 ± 79 to 75 ± 44 min ($p = 0.01$). ESR decreased (50.4 ± 21.3 to 42.9 ± 13.8 mm/h, $p = 0.02$), but CRP and C4 did not vary significantly. TNF α decreased from 4.2 ± 2.5 to 3.8 ± 1.8 ng/ml ($p = 0.05$).

Conclusion PTX seems to be useful in maintaining the remission of systemic RV and possibly for the prophylaxis of occlusive vasculopathy in these patients. Moreover, PTX is useful also for managing the arthritis of these patients. Its effects in the long-term prevention of relapse of RV have to be evaluated.

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FRI0065 ANTI-TNF ALPHA MONOCLONAL ANTIBODIES ALTER THE ACTIVATION AND DIFFERENTIATION PATTERN OF MONOCYTES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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10.1136/annrheumdis-2001.1194

Background Anti-TNF α monoclonal antibodies (mAbs) have recently been introduced as a treatment for rheumatoid arthritis (RA). Whereas anti-TNF α mAbs are potent inhibitors of inflammation, their effect on the activation and differentiation of myeloid cells has not been elucidated.

Objectives To investigate the function and the phenotype of monocytes from RA patients during their differentiation to macrophages *in vitro* before and 4 weeks after a single administration of mAbs to TNF α .

Methods Patients with highly active disease who were resistant to treatment with disease modifying antirheumatic drugs and corticosteroids were included into the study. Monocytes were isolated from the peripheral blood by negative selection, and their phenotype was analysed directly after isolation and during differentiation to macrophages.

Results Treatment was effective as 4 weeks after mAb application the inflammatory activity, as assessed by DAS 28, and the sedimentation rate were significantly reduced. Whereas the

expression of HLA-DR, CD40, CD25, CD80, CD86, CD14 and CD68 in freshly isolated monocytes was similar before and after treatment with anti-TNF α , marked differences were found during maturation. After treatment, upregulation of HLA-DR and CD80 was markedly enhanced during macrophage differentiation. In contrast, the expression of CD40 was decreased after treatment.

Conclusion The results demonstrate that a single therapy with anti-TNF α mAbs alters the ability of macrophages to upregulate molecules involved in cellular inflammation even 4 weeks after treatment. However, as those changes were associated with clinical benefit, the data suggest that the clinical effect of anti-TNF α mAbs treatment is not restricted to neutralising TNF α but may be due to long lasting anti-inflammatory alterations that remain active even after the mAb has been cleared from the circulation.

FRI0066 LEFLUNOMIDE INHIBITS PROLIFERATION AND DIFFERENTIATION OF PRO-INFLAMMATORY TH1 CELLS

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10.1136/annrheumdis-2001.1195

Background Leflunomide has been recently introduced as a new treatment for rheumatoid arthritis. It has been shown that this immunomodulatory drug blocks the *de novo* pyrimidine synthesis by inhibiting the enzyme dihydroorotate dehydrogenase. However, the functional consequences of this action for T cells are still unclear.

Objectives To evaluate the effect of leflunomide on the proliferation and differentiation of human naive CD4^{pos} T cells isolated from cord blood and of memory CD4^{pos} T cells isolated from peripheral blood of healthy individuals.

Methods The proliferative response of naive and memory T cells activated with anti-CD3 and anti-CD28 was determined by incorporation of ³H-thymidine into newly synthesised DNA. The impact of leflunomide on T cell differentiation was assessed in an *in vitro* system in which effector cells were generated after short term priming. T cell differentiation was induced by priming with anti-CD3 and anti-CD28 in the presence or absence of leflunomide. The phenotype of freshly isolated and primed T cells was determined by cytometric analysis of intracellular cytokines.

Results Leflunomide inhibited T cell proliferation induced by stimulation with anti-CD3 and anti-CD28 in a dose-dependent manner in naive and memory CD4^{pos} T cells. Moreover, the expression of the activation markers CD25, CD69 and CD40L was markedly suppressed. Leflunomide significantly decreased the frequencies of T cells capable of producing IFN- γ . Most interestingly, the generation of Th2 effectors was enhanced by leflunomide in some donors.

Conclusion Leflunomide may exert its anti-inflammatory effect by preventing the proliferation of pro-inflammatory Th1 effectors and by switching the T cell differentiation from the Th1 to the Th2 direction.