cascade of events leading to wound healing, perhaps through its promoting activity on keratinocytes proliferation and vascular neoangiogenesis.⁴ Topical application of NGF may represent a powerful pharmacological tool that may reduce and/or overcome the development of vasculitic ulcers.

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FRI0074 ADENOVIRAL-BASED OVEREXPRESSION OF TIMP-1 REDUCES TISSUE DAMAGE IN THE JOINTS OF TNF- α -TRANSGENIC MICE

G Schett, S Hayer, M Tohidast-Akrad, Q Xu, G Kollias, G Steiner, J Smolen. *Department of Rheumatology, University of Vienna, Vienna, Austria*

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Background Rheumatoid arthritis is a prototype of a destructive inflammatory disease. Inflammation triggered by the overexpression of TNF- α is a driving force of this disorder and mediates tissue destruction. The particular impact of TNF- α -induced molecules, such as matrix metalloproteinases, in tissue destruction is however unknown.

Objectives Herein, the effect of an overexpression of tissue inhibitor of metalloproteinases (TIMP)-1, a physiological antagonist of metalloproteinases, was studied in the arthritis model of TNF- α -transgenic mice.

Methods Systemic treatment was carried out by replication-defective adenoviral vectors for TIMP-1 (AdvTIMP1, n = 7) or b-galactosidase (AdvLacZ, n = 6) or phosphate buffered saline (PBS, n = 7), which were applied once at the onset of arthritis. Clinical, serological, radiological and histological outcomes were assessed 18 days after the treatment.

Results The AdvTIMP1 group showed a significantly reduced paw swelling and increased grip strength compared to the two control groups, whereas total body weight, TNF- α and IL-6 levels were similar in all three groups. Radiological assessment revealed a significant reduction of joint destruction in the AdvTIMP1 group; this was confirmed by histological analyses, showing reduced formation of pannus as well as erosions in the AdvTIMP1 group as compared to the AdvLacZ- and PBS- control groups. The formation of arthritis-specific autoantibodies to hnRNP-A2 was not observed in the AdvTIMP1 group but was present in the two control groups.

Conclusion These results indicate a central role of matrix metalloproteinases in TNF- α -mediated tissue damage *in vivo* and a promising therapeutic role of TIMP-1.

FRI0075 COMP LEVELS IN SERUM LOWERED AFTER SIX MONTHS TREATMENT WITH ETANERCEPT IN PATIENTS WITH RHEUMATOID ARTHRITIS

¹Å Thörner, ²C Freiburghaus, ¹S Ernestam, ¹J Bratt. *¹Department of Rheumatology, Huddinge University Hospital, Stockholm; ²AnaMar, Med., Lund, Sweden*

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Background

Objectives The aim of this study was to evaluate Cartilage Oligomeric Matrix Protein (COMP) levels during TNF- α -blocking therapy with Etanercept (Enbrel) in patients with rheumatoid arthritis (RA). Previous studies have suggested that serum COMP levels is a marker for joint destruction in RA.

Methods 38 patients (34 female, 4 male) with active, longstanding RA were treated with Etanercept 25 mg x2/week. The efficacy measures included ACR response rates after treatment for 3 and 6 months. COMP was measured in serum using sandwich ELISA from AnaMar Med. Lund. Wilcoxon Matched Paired Test was used for statistical analysis.

Results ACR 20, 50 and 70 responses were demonstrated for 79%, 29% and 5% of the patients, respectively, at 3 months and 68%, 35% and 11% at 6 months. 21% of the patients were still non-responders to Etanercept at 3 months and 32% after 6 months. The ACR response rates at 12 months will be presented at the meeting. A significant decrease ($p < 0,05$) in serum COMP levels was seen after 6 and 12 months treatment with Etanercept but not after 3 months. At 3 months COMP levels showed a high degree of variability.

Conclusion Significant reduction in serum COMP levels were seen after six months TNF- α -blocking therapy and was maintained after 12 months. The COMP levels at 3 months gave no indication regarding outcome of treatment.

FRI0076 REDUCED TOXICITY OF METHOTREXATE IN RHEUMATOID

MN Kotevska, M Glickov, A Pusevski, J Calovski, S Percinkova, N Marina, D Antova, M Trajanoska, E Glickova. *Clinic of Rheumatology, Clinical Centre Skopje, Medical Faculty, Skopje, Macedonia*

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Background

Objectives The aim of the study was to investigate whether folic acid (FA) supplementation in patients with rheumatoid arthritis reduces methotrexate (MTX) toxicity.

Methods It was a prospective randomised study. Total of 53 patients with RA who had never used methotrexate before, were randomly assigned to receive either MTX alone (group 1) or MTX and 5 mg. folic acid (group 2). Patients were evaluated for treatment toxicity at three monthly intervals for two years.

Results 1. Significant increases in the hepatic transaminases, ALT and AST, occurred in group 1, over the trial period. 2. After 6 months an increased incidence of nausea in group 1, occurred (43% vs. 7%). 3. More patients withdrew from the study early because of side-effects in group 1 (39% vs. 18% $p = 0,025$).

Conclusion Our results indicate that it is important to continue FA supplementation long term to avoid patients discontinuing MTX treatment due to side-effects. They also suggest that FA supplementation can prevent the changes in AST and ALT.