Results The mean CsA dosage at 48 weeks was 2.8 mg/kg/day in the CsA and placebo group and 3.0 mg/kg/day in the CsA and MTX group. After 48 weeks of treatment mean creatinine rose significantly 19 μ mol/L (+25%) in the CsA and placebo group, and 21 μ mol/L (+28%) in the CsA and MTX group ($p = 0.28$ between groups). Changes in blood pressure and liver enzymes were not significant and clinically different between the two groups.

Table 1: premature discontinuations due to:

Abstract FRI0031 Table 1

	Renal toxicity and/or hypertension	Other kinds of toxicity
CsA + placebo (n = 60)	2	4
CsA + MTX (n = 60)	9	3
P-value (Fischer exact tests)	0.05	1.0

Conclusion Therapy with CsA and MTX in early RA does on average not result in more clinically relevant renal or hepatic toxicity than CsA alone, but a trend towards more discontinuations due to renal toxicity and hypertension was observed

FRI0032 INCIDENCE OF CLINICALLY RELEVANT INFECTIONS ASSOCIATED WITH RHEUMATOID ARTHRITIS (RA) THERAPIES

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Background

Objectives To evaluate incidence of clinically significant infections in RA patients treated with various RA therapies.

Methods Retrospective analysis of linked medical and outpatient pharmacy claims from 10/98–9/99 was conducted using a large managed care database (Protocare Sciences). Patients age 35 and older, having at least 2 claims more than 20 days apart with an ICD-9CM diagnosis for RA were selected for analysis. RA therapies, including anti-inflammatory agents, steroids, DMARDs, and other systemic anti-arthritis agents were classified and clinically significant infections were identified. Comparisons of infection rates between various therapies were assessed using Incidence Density Ratios.

Results Most of the 2,443 RA patients (86%) received drug therapy specific for RA during the study period. Overall, 1,207 patients (49%) had at least one infection, 783 patients (32%) had at least one upper Respiratory Infection (RI), and 716 patients (29%) had at least one non-RI. A greater proportion of patients who received direct RA therapy experienced an upper RI compared to those patients who did not (32.8% vs. 27.8%). Patients had a statistically higher occurrence of infections for pneumonia and bronchitis during use of potentially immunomodulating therapy (IMT). Subgroup analysis of patients receiving IMT by steroid exposure is presented Table 1. Incidence Density Ratios (95% CI):

Abstract FRI0032 Table 1

	Bronchitis	Pneumonia	All upper RI
IMT vs.	1.98	2.73	1.14
Non-IMT	(1.36, 2.88)	(1.29, 5.77)	(0.93, 1.39)
IMT w Steroids vs.	2.48	12.00	1.61
IMT w/o Steroids	(1.38, 4.47)	(1.63, 88.09)	(1.16, 2.23)

Conclusion Infections were common in patients on RA therapies with nearly half of all patients experiencing at least one infection during the 12 months studied. Selection of therapy associated with infections should be considered in the overall management of patients with rheumatoid arthritis.

FRI0033 ERYTHROPOIETIN-RECEPTOR-EXPRESSION IN FIBROBLAST-LIKE SYNOVIOCYTES

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Background The anaemia of chronic disease in patients with rheumatoid arthritis (RA) can be corrected by treatment with recombinant human erythropoietin (rHu-Epo). In addition to an increase of haemoglobin concentration during therapy with rHu-Epo, a significant reduction of disease activity was observed in different RA-studies. Especially the decrease of the number of swollen and tender joints during rHu-Epo treatment suggests a direct anti-inflammatory effect of rHu-Epo.

Objectives As the expression of the erythropoietin-receptor (Epo-R) was recently shown for different non-erythroid cells – as for example endothelial and neuronal cells, we investigated the expression of Epo-R in fibroblast-like synoviocytes to gain a first experimental approach for the observed anti-inflammatory effect of rHu-Epo in RA.

Methods We cultivated fibroblast-like synoviocytes derived from synovial membranes (n = 17) or synovial fluid (n = 13) that were gained from patients with RA (n = 22), osteoarthritis (n = 3) or spondylarthropathy (n = 5). Biopsy material has been minced and digested with collagenase, fluid derived cells have been directly cultured. Cells were passaged two to five times and characterised by FACS analysis. Expression of Epo-R was determined by nested RT-PCR. The chosen primers annealed at Exon III (forward primer 1 and 2), Exon VIII (backward primer 1) and Exon VII (backward primer 2). The obtained PCR-product was sequenced by automated fluorescent DNA sequencing.

Results The cultured cells morphologically represented fibroblast-like cells. It was shown by FACS analysis that they were CD14 and CD86 negative and CD54 and CD90-Thy-1 positive. RT-PCR products representing the human Epo-R could be demonstrated in fibroblast-like synoviocytes from biopsy and arthrocentesis from patients with RA, OA and SpA. The specificity of the PCR products could be proven by sequencing of the product of three different cell-lines. The obtained sequence was completely identical with that of the DNA data base for more than 350 bases (Exon IV to Exon VI).

Conclusion We could demonstrate for the first time the expression of Epo-R in fibroblast-like synoviocytes. This observation gives evidence that rHu-Epo directly afflicts fibroblast-like synoviocytes (via Epo-R) and therefore provides a possible