alpha (OH) vitamin D3 (alphacalcidol) analogue was shown to induce less hypercalcemic side effects.

Objectives We organised open-label therapeutic trial in 20 RA and 15 JRA patients who have had three months active disease on basic therapy. Therapy regime remained unchanged but alphacalcidol in high oral dose was added during next three months (2µgr/day in RA or 0,05µgr/kg/day in JRA pts.).

Methods Spontaneous and PMA stimulated IL1 and TNF production was measured in all patients before and after the trial by ELISA method in PB mononuclear cells after 24 h cultures. GSH-Px (glutathione-peroxidase) and SOD (superoxide-dismutase) activity was measured by RANDOX kits.

Results Three months high oral dose therapy significantly improved clinical signs of disease activity in correlation with parameters we evaluated. Increased IL1 and TNF production was significantly lowered after the trial and riched values in healthy controls. GSH-Px and SOD activity were lowered in all patients before entering into the study. Alphacalcidol therapy induced significant increase of GSH-Px and, on contrary, decrease of SOD activity. Positive correlation trends among this enzymes during disease activity were turned into negative according to disease improvement after the trial finished.

Conclusion High dose alphacalcidol is powerful immunomodulatory agent as it is shown for other vitamin D3 analogues. Its main function seem to be stabilisation of impaired immunoregulation in RA and JRA which could be of benefit as possible therapeutic agent.

FRI0005 SAFETY OF NEW COX-2 INHIBITORS IN NSAID-INTOLERANT PATIENTS

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Background Non-steroidal anti-inflammatory drug (NSAID)-triggered urticaria and angioedema occurs in up to 3% of the population. The tolerance to new COX-2 selective inhibitors in intolerant patients has not been determined.

Objectives To study the clinical tolerance to Rofecoxib and Celecoxib in patients sensitive to conventional NSAIDs who develop urticaria and/or angioedema when exposed to these drugs.

Methods Sixty three subjects (female 44, male 19, mean age 33.0 ± 16.7 years, range 11 – 74 years) with challenge-proved urticaria/angioedema were studied. These patients were challenged by means of the single-blinded oral method, controlled with placebo.

Results Positive challenges were observed in 4 out of 53 subjects challenged with Rofecoxib (7.5%) and in 13 out of 47 individuals submitted to oral provocation with Celecoxib (27.6%) ($p = 0.01$).

Conclusion We conclude that: 1) The clinical tolerance to selective COX-2 inhibitors in NSAID-sensitive patients with skin manifestations differs between new drugs, which may be due to different degrees of enzyme selectivity or to other, not yet determined reasons. 2) COX-1 inhibition would be involved in the production of cutaneous adverse reactions to NSAIDs. 3) Controlled oral challenges are indicated especially for the management of sensitive individuals with chronic inflammatory and/or painful diseases.

FRI0006 DOUBLE-BLIND CLINICAL, LABORATORY AND ULTRASOUND ASSESSMENT OF THE EFFICACY OF ANTIBODIES TO INTERFERON-G (ANTI-IFN-G) IN RHEUMATOID ARTHRITIS (RA)

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Background

Objectives To objectively assess the efficacy and tolerability of anti-IFN-g in treating patients with active RA.

Methods Thirty patients with active RA were randomly assigned to receive intramuscularly injections of anti-IFN-g, antibodies to tumour necrosis factor a (anti-TNF) or placebo for 5 consecutive days (10 patients on each treatment regimen). The patients were clinically assessed daily for 7 days, then weekly up to the 28-th day. Clinical, laboratory and ultrasound indices were used for the evaluation of the treatment efficacy.

Results Both anti-cytokines were equally effective and significantly superior to placebo. Twelve patients stopped treatment due to the lack of efficacy: 1 on anti-TNF, 2 on anti-IFN-g and 9 on placebo. According to the physician's assessment improvement was achieved by the 7-th day on anti-TNF in 9 patients, on anti-IFN-g in 7, and on placebo in 2. At the 28-th day the corresponding figures were 8, 8, and 0, respectively. By the 28-th day each of the anti-cytokine groups showed significant improvement in 5 clinical measures including numbers of swollen and painful joints, pain and fatigue. The single patient in the placebo group who completed the trial had no positive changes in the disease activity. The thickness of the inflamed synovial membrane assessed by the ultrasound method decreased significantly only on anti-IFN-g (both by the 7-th and by the 28-th days).

Conclusion The results obtained suggest that IFN-g plays an important role in the pathogenesis of RA. The use of antibodies to this cytokine can be considered as a promising approach to the therapy of RA, especially its treatment-resistant forms.

FRI0007 PREFERENCES OF RHEUMATOLOGISTS FOR THE TREATMENT OF RHEUMATOID ARTHRITIS FLARE: IS THERE A STANDARD OF CARE?

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Background Differences in physician evaluations, heterogeneity of disease and within patient variability contribute to the lack of a uniform definition of RA flare. As a result, a standardised approach to treatment of RA flare is not likely to exist. However, when presented with the same case scenario, rheumatologists' choice of treatment should establish a standard of care.

Objectives To identify physician medication preferences and the role of steroids in the treatment of rheumatoid arthritis (RA) flare.

Methods A questionnaire describing two versions of the same case of a previously stable RA patient maintained on 17.5 mg/week of methotrexate (MTX), hydroxychloroquine and NSAIDs, and presenting with signs and symptoms suggesting an increase in disease activity was developed; the second version included the addition of a standing dose of 5 mg of prednisone. Rheumatologists were asked to identify their choice (s) of first-line therapy for each version of the case. The questionnaire was

mailed to rheumatologists (adult practice) (n = 995) who were identified through the ACR membership directory. Only physicians currently in practice were included.

Results 375 (37.7%) questionnaires were returned between March 12, 2000 and April 25, 2000. 280 qualified for analysis. The results (A: No baseline steroid use, B: 5 mg/d prednisone) below illustrates the frequency with which rheumatologists cited each drug or drug combination as their first choice of treatment for each scenario. The most common change in medication for both cases was addition/adjustment of prednisone (A: n = 248; B: n = 229, C2 = 4.58, p = 0.03). Of those given oral steroids for a limited amount of time, mean increase in daily dose of prednisone was A: 16.4 ± 12.5 mg, B: 18.3 ± 12.5 mg. Duration of increased dose was highly variable ranging from 1 day (bolus) to 3 months. Some rheumatologists chose to continue increased prednisone indefinitely, (A: n = 19; B: n = 14). There appeared to be no consistent relationship between steroid dose and duration. For both cases there was no difference in the number of rheumatologists who increased MTX dose (A: n = 84; B: n = 85). The number of rheumatologists who added another DMARD to the patient's regimen were more in group A and differed significantly ($\chi^2 = 3.97$, p = 0.046) from group B. Similarly, rates of initiation of anti-TNF therapy was higher in group A ($\chi^2 = 4.68$, p = 0.03). However, rates of addition of leflunomide showed no statistically significant difference.

Conclusion Though the cases presented were accepted by rheumatologists as RA flare requiring intervention; no consistency of practice other than an increase in steroids could be identified. Further studies determining optimal therapy for increases in RA activity are necessary.

FRI0008 DIFFICULT TO TREAT RHEMATOIDS RESPOND TO LEFLUNOMIDE

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Background Leflunomide (LEF) is a new disease modifying agent for rheumatoid arthritis (RA). It was successful in treating relatively recent onset rheumatoid patients with a good safety record.¹

Objectives Our aim was to assess the safety and efficacy of LEF in difficult to treat and chronic rheumatoid patients in a district general hospital.

Methods Patients with difficult to treat RA (n = 39) were commenced on LEF. Patients were followed every 4 for 6 months for side effect profiles and efficacy recordings. We documented all side effects of LEF, routine blood test results and blood pressure measurements. Pre-treatment and 6th month erythrocyte sedimentation rate (ESR) and haemoglobin (Hb) levels, patients' and doctors' global disease activity Visual Analogue Scores (VAS) were Statistically compared.

Results Mean age of patients was 48+14 and duration of disease was 13+10 years. Combination of methotrexate with LEF was the choice of treatment for 12 patients. Until now 25 patients completed 6 months evaluation and 9 out of 39 patients discontinued LEF due to side effects or infections. 6 further patients discontinued LEF after 6 months. Alopecia, diarrhoea and rash were the most common side effects (28%, 26% and 23% respectively). The most serious adverse effect was sensory neuropathy of the lower limbs in a young male patient. This occurred within

10 months of LEF treatment and showed some improvement 2 months after discontinuation. Another elderly male was admitted to hospital twice with severe abdominal pains and diverticulitis.

Patients felt better on LEF treatment and showed significant improvement in reduction of ESR (p < 0.02), increase of Hb (p < 0.02) and a reduction of VAS of patients' (0.0001) and doctors' (p < 0.0001) global disease activity over a 6 month period (Wilcoxon Rank Sum Test). Due to clinical improvement we were able to stop or reduce dosage of other concomitant treatment.

Conclusion In conclusion LEF was reasonably well tolerated by difficult to treat rheumatoids even though side effects were more frequent than published studies (1). The clinical response was good considering the long disease duration and history of poor response to treatment in our group.

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FRI0009 INFILIXIMAB IN THE TREATMENT OF RHEUMATOID ARTHRITIS (RA): REFERRAL PATTERNS, RESPONSE TO TREATMENT, AND ADVERSE EVENTS IN A REAL WORLD SETTING

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Background Infliximab is a chimeric, monoclonal antibody against tumour necrosis factor (TNF) alpha, recently developed to complement methotrexate therapy in RA patients with a less than optimal response to treatment. To date it has only been studied in clinical trials.

Objectives To describe referral patterns, patient response to treatment, and adverse events in a cohort of RA patients treated with infliximab in a real world setting.

Methods Patients who had received their first dose of infliximab between 1/00 and 6/00 were included to ensure the possibility of at least 6 months of drug exposure. We evaluated patients at baseline, and followed them prospectively every 2 months for a total of 6 months. Patients completed several questionnaires regarding RA history, treatment, and disease activity (HAQ, pain, fatigue, tender and swollen joint counts) at each infusion. All subjects were contacted between infusions for reporting of side effects.

Results 36 patients were treated with infliximab between January 1 - June 30, 2000 (female n = 33, mean age = 63 ± 12.9 y, disease duration = 15.3 ± 10.2 y). They had previously failed an average of 3 DMARDs. 24 patients were on oral steroids at baseline. 16 patients received infliximab without concurrent MTX. 12 of 36 patients discontinued treatment before 6 months. Discontinuation reasons were inadequate response (n = 5), repeated episodes of dyspnea (n = 3), asthma (n = 1), chest tightness (n = 1), phlebitis (n = 1), and patient noncompliance (n = 1). Table 1 shows individual measures of disease activity in 24 patients who completed 6 months of infliximab. We detected a significant improvement in HAQ scores, and trends toward improvement in pain scores and tender joint counts. HAQ scores improved in 19/24, stiffness in 14/24, pain in 13/24, fatigue in 13/24, tender joint counts in 13/24 and swollen joints in 15/24 of patients. Since initiating infliximab therapy, of the 36 patients receiving 198 infusions, 18 patients reported a total of 33