Methods 14 patients with active rheumatoid arthritis and unresponsive to at least 3 DMARDs were treated with methotrexate and infliximab. Before infliximab infusion, weeks 0, 2, 6, 14 and 22, a physical examination, DAS 28 and blood test, which included RF, ANA, immunoglobulin quantification C3 and C4 were done.

Results At the baseline visit 5/14 (35,71%) patients had positive ANA test, 2 (1/40), 1 (1/80), 1 (1/160), 1 (1/640). After the fifth infusion 8/14 (57,14%) had a positive ANA test. Three patients who initially were ANA negative showed a titre of 1/160, 1/320 and 1/640. Three out of 5 patients which previously had a positive test, showed an increase in the ANA titre, 1/40 to 1/80, 1/40 to 1/320 and 1/640 to 1/1280. After the fourth infusion of infliximab, all patients with ANA positive had a Crithidia test performed. In all cases anti DNA were negative.

Conclusion In our experience, treatment with infliximab has shown an increase of the ANA titre in 21,42% of the patients. On the other hand, 21,4% of the patients with a previous negative test for ANA had a positive test after the fourth infusion. All cases were negative for anti-DNA antibodies.

FRI0053 STEROIDS RESTORE THE IMPAIRED CERULOPLASMIN FERROXIDASE ACTIVITY IN SYNOVIAL FLUID OF RHEUMATOID ARTHRITIS

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Background Ceruloplasmin (CP) is an acute phase reactant with significant antioxidative activity. In rheumatoid arthritis (RA), joint destruction continues in spite of high levels of CP in the synovial fluid (SF). The antioxidative activity of CP correlates with its ferroxidase I activity (FerrI). The biology role of the recently discovered ferroxidase II (FerrII) is unknown.

Objectives The present study was aimed to find the effect of drug therapy on CP levels and CP ferroxidase activity in RA SF and to compare it to SF nitrite levels, which indicate the degree of the inflammatory process.

Methods SF was collected from 75 RA patients who were:

- w/o drug therapy (UT).
- with NSAIDs and disease modifying drugs (DMD), mainly MTX who had no steroid in the last 3 months (NST).
- with low dose steroids ($\leq$ 10 mg Prednisone) + DMD (ST).
- SF of osteoarthritic (OA) patients served as control. For CP levels Ravin's method was used.¹ For CP ferroxidase activity Johnson's method was used.² For FerrII activity Johnson's method in the presence of sodium azide. FerrI activity was calculated: Total-FerrII. For nitrite levels Ding's method was used.³

Results In spite of drug therapy and nitrite level similar to OA, CP and total ferroxidase activity remained high in all RA groups. FerrI/FerrII ratio was significantly abnormal in RA without steroids. Low dose steroids restored FerrI/FerrII ratio to levels seen in OA.

Conclusion Low dose steroid therapy in RA did not reduce SF ceruloplasmin concentration, but restored FerrI/FerrII ratio to normal levels.

REFERENCES

- 1 Ravin HA. *J Lab Clin Med.* 1961;**58**:161–8
- 2 Johnson DA, et al. *Clin Chem.* 1967;**13**:142–9
- 3 Ding AH, et al. *J Immunol.* 1998;**141**:2407–13

FRI0054 A LONG-TERM, OPEN-LABEL TRIAL OF THE SAFETY AND EFFICACY OF ETANERCEPT (25 MG TWICE WEEKLY) IN PATIENTS WITH RHEUMATOID ARTHRITIS (INTERIM ANALYSIS)

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Background Several double-blind, placebo-controlled studies previously demonstrated that etanercept was safe and efficacious in treating rheumatoid arthritis (RA) patients who had an inadequate response to disease-modifying antirheumatic drugs (DMARDs).

Objectives To evaluate the long-term safety and efficacy of etanercept in patients who completed prior double-blind clinical studies comparing etanercept to placebo.

Methods As reported in previous updates, 549 patients entered this 4-year, open-label study and began treatment with etanercept 25 mg twice weekly at 58 centres in Europe following completion of double-blind clinical studies. All patients previously had inadequate responses to DMARDs. Safety assessments were performed at regular intervals to determine the incidence of treatment emergent adverse events including malignancies and serious infections (those associated with hospitalisation and/or the administration of intravenous antibiotics). The numbers of painful and swollen joints were predefined as primary efficacy endpoints; other efficacy measures included ACR response rates and acute phase reactants. Efficacy was analysed with the last observation carried forward (LOCF).

Results Of the 549 patients initially enrolled, 437 (80%) are currently active, 479 (87%) completed 1 year, and 94 (17%) completed 2 years. A total exposure of 927 patient-years has been accrued. The rate of withdrawal from the study was similar for efficacy- and tolerance-related reasons (7% and 8%, respectively). Adjusted for patient exposure, the most frequent adverse events were injection site reactions and upper respiratory infections. Rates of serious infections and malignancies have remained unchanged over the course of the study. Maintained efficacy was observed as demonstrated by a mean 71% and 72% reduction in painful and swollen joint counts, respectively. Similar to results measured at the early time points of this open-label trial, ACR 20, 50, and 70 response rates were determined to be 79%, 47%, and 25%, respectively, as patients approached two years of treatment.

Conclusion Following the accumulation of substantial exposure in patients with RA, etanercept demonstrates an acceptable safety profile and continues to provide significant and maintained clinical benefit.

FRI0055 EXPERIENCE WITH COMMERCIAL REMICADE (INFLIXIMAB) AT A LARGE COMMUNITY-BASED RHEUMATOLOGY PRACTICE

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Background Infliximab, a monoclonal antibody that binds with high affinity and specificity to TNF-alpha and neutralises its biologic activity, is approved for the reduction of the signs and symptoms of rheumatoid arthritis (RA). The Rheumatology

Associates of North Alabama (RANA) is a large, community-based rheumatology practice that treats approximately 6,000 patients with RA.

Objectives To document the experience with commercial infliximab in patients with RA treated in a community rheumatology practice.

Methods In an ongoing chart review of all patients receiving infliximab at RANA, the following information was documented: age, concomitant medication use, tender and swollen joint counts, and adverse side effects.

Results Baseline information was collected for 137 patients with RA. These patients ranged in age from 33 to 84 yrs (mean of 62.7 yrs). Among the 114 patients receiving concomitant methotrexate (MTX), doses ranged from 2.5 to 30 mg/day (mean of 17.2 mg/day). At baseline (prior to the first infliximab dose), the mean dose of prednisone was 6.2 mg/day, and the mean tender and swollen joint counts were 22.4 and 13.7, respectively. Patients were treated with the currently recommended dosing regimen of 3 mg/kg at Weeks 0, 2, and 6 followed by q 8 wk dosing. Forty (29%) patients received concomitant disease-modifying antirheumatic drugs (DMARDs); 15 of these patients received concomitant leflunomide (12 with and 3 without MTX). Nine patients received infliximab without a concomitant DMARD. Data were available for 74 of these patients at Week 14 (fourth infliximab infusion). At this time point, the mean prednisone dose was 5.1 mg/day, and mean tender and swollen joint counts had improved by 65% and 69% (to 7.8 and 4.3), respectively. Improvements in steroid use and tender and swollen joint counts also were observed at Week 30 (n = 42; mean prednisone dose of 2.9 mg/day and tender/swollen joint counts of 4.4/1.7) and Week 54 (n = 14; mean prednisone dose of 2.1 mg/day and tender/swollen joint counts of 1.6/0.8) among the patients who had received treatment this long. Ten patients discontinued the use of infliximab due to lack of response (3 patients), rash (3 patients), cost (2 patients), abdominal pain (1 patient), and an unrelated side effect (neck pain in 1 patient). Five patients experienced infections (shingles, soft tissue abscess, pneumonia, and bronchitis in 2 patients); all patients responded to antibiotic therapy and continued treatment with infliximab.

Conclusion In a community rheumatology practice, infliximab 3 mg/kg, both with and without MTX, produced compelling improvement in the signs and symptoms of RA. Infliximab was safe and well tolerated when administered in the outpatient infusion setting.

FRI0056 TNF α THERAPY INITIATION AUDIT: RATIONING ON AN EQUITABLE BASIS – THE NORFOLK AND NORWICH (N/N) EXPERIENCE

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Background BSR¹ and EULAR² consensus guidelines have been published regarding the evolving use of TNF α therapy in rheumatoid arthritis (RA). It is anticipated that demand will exceed supply. Norfolk Health Authority has allocated £210,000 (for approximately 30 patients) for initiation of this treatment during 2000–01. An initial review highlighted discrepancies between the DAS28 (ie consensus guidelines), and our individual clinical assessment of patients.

Objectives To evaluate prospectively a cohort of consecutive eligible patients, prioritise them according to a weighted scoring system, which we developed and observe changes in the profile of those fulfilling these revised criteria for treatment.

Methods In a 3 month period, potential patients were recruited to an assessment clinic. Those fulfilling the criteria were further stratified using a 5- point cumulative scoring system based on 4 variables: 1) DAS28, 2) Age, 3) Disease duration and 4) Steroid dose. This weighted towards younger patients with shorter disease duration, requiring steroids and having a high DAS28, on the assumption that treating such patients would be more cost-effective. This resulted on a final list of 30 patients selected for treatment (N/N Priority).

Results 135 out of 139 patients assessed, fulfilled the BSR eligibility criteria. Nearly two thirds of the 30 patients with the highest DAS28 (BSR priority) were subsequently replaced on our stratified list (N/N Priority). However, funding is still not available for 78% of our patients, who are otherwise eligible for treatment.

Abstract FRI0056 Table 1

Variables	N	DAS28 (Range)	Age (Years)	Duration
TOTAL	135	7.06 (5.1–8.9)	57 (17–82)	14 (0.6–55)
BSR PRIORITY	30	8.16 (7.69–8.9)	59 (30–82)	14 (1–35)
N/N PRIORITY	30	7.57 (5.1–8.9)	46 (17–78)	8.1 (0.6–20)

Conclusion Rationing creates difficult choices. We have attempted to select patients according to need and cost effectiveness. These decisions should be debated openly as they have important implications for health policy and clinical management.

REFERENCES

- 1 British Society for Rheumatology – Report of a Working Party, April 2000
- 2 Updated consensus statement on TNF blocking drugs for the treatment of RA. *Ann Rheum Dis.* 2000;**59**(Suppl 1):i1–i2

FRI0057 EFFECTS OF CYCLOSPORINE/METHOTREXATE COMBINATION THERAPY FOLLOWED BY SINGLE AGENT TREATMENT ON RADIOGRAPHIC PROGRESSION IN EARLY RHEUMATOID ARTHRITIS

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Background Early treatment of severe rheumatoid arthritis (RA) with cyclosporine (CsA) and methotrexate (MTX) in combination is now considered one of the best strategies to control the arthritic symptoms and prevent structural joint deterioration.

Objectives This trial was aimed at evaluating the clinical and radiographic outcome of a cohort of patients with early rheumatoid arthritis (RA) first treated with an association of CsA and MTX, and then randomly stepped down to one of two agents.

Methods Fifty-seven patients (54 F and 3 M) (mean age 49.5 yr., range 20–64) with early, active RA (mean disease duration 0.8 yr., range 0.5–2), were treated with CsA (3 mg/kg/day) and MTX (10–15 mg/week) in combination for 6 months and then 49 of them were randomised to receive single therapy with either CsA (22 patients) or MTX (27 patients) for another 18