FRI0069 EFFICACY AND SAFETY OF REMICADE (INFLIXIMAB) PLUS ARAVA (LEFLUNOMIDE) IN RHEUMATOID ARTHRITIS (RA)

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Background Leflunomide is a new disease-modifying antirheumatic drug (DMARD) approved for the treatment of active RA as an alternative to methotrexate (MTX) therapy. Infliximab is approved for the treatment of RA when used in combination with MTX. However, in patients either intolerant of or refractory to MTX therapy, combination therapy with leflunomide is sometimes utilised.

Objectives To assess the efficacy and safety of infliximab plus leflunomide in patients with RA.

Methods Select community practices were surveyed about the use of infliximab in combination with leflunomide for the treatment of RA. Demographic data and information on prior and concomitant medications were documented. Further data regarding efficacy (numbers of swollen and tender joints, functional class, ESR/CRP) and safety (occurrence of nausea, vomiting, alopecia, or any other symptoms) are being collected at baseline (prior to start of the combination) and after 4 to 5 doses of the combination.

Results Twenty-one community practices were included in the survey; 31 patients were identified who recently started on the combination of infliximab plus leflunomide. The patient population consisted of 20 (65%) women and 11 (35%) men. Patients ranged in age from 29 to 80 yrs (mean of 56.3 yrs). The duration of RA ranged from 2 to 50 yrs (mean of 10.6 yrs). Twenty-six (84%) patients had received MTX at a mean dose of 18.2 mg/wk. 42% of the population developed intolerance to MTX. MTX was ineffective in 45% of patients and contraindicated in 16% of patients. Patients were generally started on leflunomide at 20 mg QD. Rheumatologists added infliximab (3 mg/kg q 8 wks after loading doses at Weeks 0, 2, and 6 in the majority of patients) due to an incomplete response achieved with leflunomide. 71% of these patients also continued to receive concomitant prednisone at 2.5 to 20 mg/day. While patients had only received a few doses each, no serious adverse experiences were reported. This population will continue to be followed over time for both safety and efficacy of the infliximab/leflunomide combination.

Conclusion Infliximab has been used in combination with leflunomide in select RA patients in whom MTX has not been tolerated, is ineffective, or is contraindicated. The ongoing clinical experience of these and similar patients will be monitored.

FRI0070 SAFETY AND TOLERABILITY OF A RAPID INFUSION OF REMICADE (INFLIXIMAB) IN THE TREATMENT OF RHEUMATOID ARTHRITIS

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Background The safety of infliximab has been established in both open-label and randomised controlled clinical trials in which patients received infliximab over 2 hrs. In clinical trials,

no difference was observed in the incidence of infusion reactions at any infliximab dose between 3 and 10 mg/kg given over 2 h. This clinical experience supported the safety of administering infliximab 3 mg/kg over 1 hr (Maini, 1999). Current guidelines advise infusing infliximab over at least 2 h.

Objectives To determine if infliximab given at 3 mg/kg over 1 hr is safe and well tolerated in the clinic setting.

Methods Patients with active RA enrolled at selected sites in an ongoing open-label clinical trial of infliximab were eligible to receive two open-label 1-hr infusions of infliximab 3 mg/kg if they had previously tolerated four 2-hr infusions (at Weeks 0, 2, 6, and 14) without any moderate to severe infusion related reactions or hypersensitivity reactions and had no significant history of cardiac or renal impairment. Safety evaluations included measurements of vital signs during and immediately after the infusions of infliximab and assessment for adverse events.

Results One hundred ninety patients (76% women and 24% men) received infliximab 3 mg/kg given over 1 hr. Patients ranged in age from 26 to 82 yrs (mean of 59.4 yrs). Twelve (6%) patients reported adverse events associated with the first or second 1-hr infusion of infliximab. Headache, hypersensitivity, and hypertension were each reported by two (1%) patients. The following adverse reactions were reported by one (0.5%) patient each: anaphylactic reaction, blood pressure decreased, chest tightness, dizziness, itching, maculopapular rash, and somnolence. Only 3 patients discontinued infliximab therapy as a result of an infusion-related reaction (1 with anaphylactic reaction and 2 with allergic reaction). All reactions, which were generally mild or moderate in nature, resolved within 1 day of onset.

Conclusion Infliximab 3 mg/kg administered over 1 hr was well tolerated by these patients with active RA.

REFERENCE

- 1 Maini RN, St. Clair EW, Maini RN, *et al.* Infliximab (chimeric anti-tumour necrosis factor alpha monoclonal antibody) versus placebo in rheumatoid arthritis patients receiving concomitant methotrexate: a randomised phase III trial. *Lancet* 1999;**354**:1032-1039

FRI0071 RESPONSES TO INFLIXIMAB THERAPY IN THE ATTRACT TRIAL ASSESSED WITH THE DISEASE ACTIVITY SCORE (DAS): CLINICAL RESPONSE MEASURED BY DAS AT 102 WEEKS CORRELATES WITH ARREST OF RADIOLOGIC PROGRESSION AND SHOWS HIGHER RESPONSE RATE THAN ACR20 CRITERIA

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Background In the ATTRACT trial, the anti-TNF-monoclonal antibody infliximab showed significant improvement in disease activity score (DAS), reduction in signs and symptoms, inhibition of progression of structural damage and improved quality of life in rheumatoid arthritis (RA) patients, at 54 weeks. Inhibition of radiologic progression by infliximab occurred in both ACR20 responders and non-responders. This suggests that the ACR20 criteria might underestimate clinical responses to therapeutic agents.

Objectives To examine effect of infliximab on DAS RA patients after two years of treatment.

Methods DAS was calculated as follows: