Conclusion ENBREL plus MTX remains safe and well tolerated. Improvement of disease activity is sustained even with reduced or discontinued doses of MTX and/or steroids.

REFERENCES

- 1 Kremer JM, et al. *Arthritis Rheum.* 2000;43:S270
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FRI0080 LONG-TERM USE OF ENBREL® (ETANERCEPT) IN PATIENTS WITH DMARD-REFRACTORY RHEUMATOID ARTHRITIS

¹LW Moreland, ²SB Cohen, ³SW Baumgartner, ⁴MH Schiff, ⁵EA Tindall, ⁶DJ Burge. ¹Division of Rheumatology, University of Alabama, Birmingham; ²Clinical Rheumatology, Metroplex Clinical Research Center, Dallas, TX; ³Clinical Rheumatology, Physician's Clinic of Spokane, Spokane, WA; ⁴Clinical Rheumatology, Denver Arthritis Clinic, Denver, CO; ⁵Clinical Rheumatology, Portland Medical Associates, Portland, OR; ⁶Clinical Development, Immunex Corp., Seattle, WA, USA

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Background Results have been previously presented from a long-term safety trial of ENBREL as monotherapy in adult patients with RA who had failed at least one DMARD. In this ongoing study, 628 patients have been followed for up to 4.3 years (median = 2.4 years) for a total of 1336 patient-years.

Objectives Continue to observe the long-term safety and clinical benefit of ENBREL.

Methods Patients were evaluated for disease activity using ACR criteria. Adverse event rates were compared with data from controlled studies.

Results 479 adult patients have received ENBREL as monotherapy for over 1 year, 420 for over 2 years, 164 for over 3 years, and 12 for over 4 years. Response has been sustained for the duration of therapy. At baseline, the median tender joint count was 31 and the median swollen joint count was 25. At 3.5 years, the median tender and swollen joint counts were 3 each, and 69% of patients had achieved the ACR 20, 50% the ACR 50, and 25% the ACR 70. Also at 3.5 years, 24% of patients had zero tender joints, 26% had zero swollen joints, and 15% had disability scores of zero. In addition, 59% of patients who were receiving corticosteroids at study start have decreased their steroid doses by a mean of 71%, 29% of patients have completely discontinued steroids, and only 5% have increased their steroid dose. Compared to events seen in controlled trials or in the normal adult population, no significant differences in rate or type of adverse events were seen in patients treated with ENBREL over time. Serious adverse events occurred at a rate of 0.13 per patient-year in the long-term database compared to 0.13 in ENBREL-treated patients and 0.20 in placebo patients in the controlled studies. Likewise, serious infections (associated with hospitalisation or IV antibiotics) occurred at a rate of 0.05 per patient-year in the long-term database compared to 0.04 in ENBREL patients and 0.05 in placebo patients in the controlled studies. The number of malignancies reported in ENBREL patients was similar to the expected number calculated from the National Cancer Institute SEER database (9 reported vs. 12.7 expected). No opportunistic infections have been observed.

Conclusion ENBREL as monotherapy continues to be safe and effective in patients with DMARD-refractory RA for over 4 years.

REFERENCE

- 1 Moreland LW, et al. *Arthritis Rheum.* 2000;43:S270

FRI0081 IMPROVEMENT OF DISABILITY IN RA PATIENTS WITH EARLY VS ESTABLISHED DISEASE AFTER TREATMENT WITH ENBREL® (ETANERCEPT)

¹R Fleischmann, ²S Baumgartner, ³L Moreland, ⁴M Schiff, ⁵J Markenson, ⁶G Spencer-Green. ¹Rheumatology Associates, Metroplex Clinical Research Center, Dallas, TX; ²Clinical Rheumatology, Physician's Clinic of Spokane, Spokane, WA; ³Division Clinical Immunology and Rheumatology, University of Alabama, Birmingham, AL; ⁴Clinical Rheumatology, Denver Arthritis Clinic, Denver, CO; ⁵Department of Medicine-Rheumatology, Hospital for Special Surgery, New York, NY; ⁶Clinical Development, Immunex Corp., Seattle, WA, USA

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Background Functional health status declines and disability increases early in patients with RA, with half of affected patients developing moderate loss of functional ability within 2 years of diagnosis.¹ Early initiation of aggressive treatment has been suggested as a means to improve long-term outcomes.

Objectives To evaluate the impact of early therapy with ENBREL on disability.

Methods In this analysis, we compared the improvement in Health Assessment Questionnaire (HAQ) disability scores over 2 years in 207 patients with early disease (mean duration of RA was 1 year) to 563 patients with long-standing disease (mean duration of RA 12 years) who were treated with 25 mg ENBREL SC twice weekly.

Mean baseline patient characteristics in the early vs. late groups were similar, including HAQ (1.5 vs 1.6), number of tender (31 vs 32) and swollen (24 vs 26) joints, CRP (3.3 vs 4.4 mg/dL), presence of RF (87% vs 81%), and age (51 vs 53 years). Patients with early disease had been treated with fewer DMARDS (0.5 vs 3.3).

Results Patients with both early and late RA achieved rapid and sustained clinical responses and improvement in HAQ scores, but the magnitude of improvement in HAQ was greater in patients with early disease. At 2 years, mean HAQ scores declined from 1.5 to 0.6 in the early RA group and from 1.6 to 1.0 in patients with established disease. The proportion of patients who achieved zero HAQ scores was greater for patients with early disease (29%) compared to patients with late disease (14%) ($p < 0.001$).

Conclusion While patients with early or long-standing disease had significant improvement in disability with ENBREL therapy, patients with early disease had greater benefit. Aggressive therapy in patients with early RA has greater potential to improve disability as measured by HAQ than in patients with more established disease who have failed multiple DMARDS.

REFERENCE

- 1 Wolfe F. A Reappraisal of HAQ disability in rheumatoid arthritis. *Arthritis Rheum.* 2000;43:2751-61

FRI0082 EFFECT OF HYDROXYCHLOROQUINE THERAPY ON CARTILAGE INJURY IN RHEUMATOID ARTHRITIS

HB Lindsley, D Eyre, L Atley, DD Smith. *Internal Medicine, University of Kansas Medical Center, Kansas City, USA*

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Background Better methods for assessing articular injury are needed to monitor efficacy of disease-modifying therapy in rheumatoid arthritis (RA).

Objectives The purpose of this study was to measure serum levels of cross-linked peptides from the C-telopeptide of type II collagen (col²CTx) during treatment of patients with RA.

Methods Serial serum samples were taken from a previous clinical trial¹ in which 213 subjects with active RA received a loading dose of hydroxychloroquine 400, 800 or 1200 mg/d for six weeks, then 400 mg/d for up to Week 24. They also received naproxen 1000 mg/d. From 213 subjects in the original trial, 152 paired sera were available for study; col²CTx levels were measured at Weeks 0 and 24, using an ELISA that measures a breakdown product of human cartilage. These levels were compared with tender (TJC) and swollen (SJC) joint counts, and the erythrocyte sedimentation rate (ESR).

Results Median ($\pm$ SEM) col²CTx levels decreased by 10% ($p = 0.006$, Wilcoxon signed ranks) by 24 weeks. Clinical variables decreased much more dramatically by 24 weeks; the TJC declined by 67% ($p = 0.000$), and the SJC, by 56% ($p = 0.000$). The ESR declined by 33% ($p = 0.000$) during this same period. Thus, the magnitude in reduction of circulating col²CTx was less than TJC, SJC and ESR but did show significant improvement.

Abstract FRI0082 Table 1

Outcome	Week 0	Week 24
Col ² CTx (ng/ml)	7.2 $\pm$ 1.2	6.4 $\pm$ 0.8
TJC (No.)	12.0 $\pm$ 0.7	4.0 $\pm$ 0.8
SJC (No.)	9.0 $\pm$ 0.6	4.0 $\pm$ 0.6
ESR (mm/hr)	35.5 $\pm$ 2.1	24.0 $\pm$ 2.8

Conclusion This limited improvement in col²CTx may be due to a lag in suppression of structural damage to cartilage. Since joint radiographs typically require a year or more to show a reduction in joint destruction, the measurement of col²CTx may give an earlier indication of reduction in injury to cartilage. Further clinical studies need to be done in patients treated with more intensive antirheumatic therapy and over longer time periods.

REFERENCE

- 1 Furst DE, et al. *Arthritis Rheum.* 1999;**42**(2):357–65

OP0062 THE FULLY HUMAN ANTI-TNF ANTIBODY ADALIMUMAB (D2E7) IN COMBINATION WITH METHOTREXATE (MTX) IN THE TREATMENT OF ACTIVE RHEUMATOID ARTHRITIS: RESULTS OF A 2-YEAR STUDY

¹FC Breedveld, ¹CF Allaart, ²R Rau, ²G Herborn, ²S Wassenberg, ³EJ Kroot, ³PL Van Riel, ³LB Van de Putte, ⁴C Böger, M Schattenkirchner ⁴, ⁵J Kempeni, ⁵K Beck, ⁵H Kupper. ¹Department Rheumatology, University Hospital, Leiden; ²Rheumaklinik, Ratingen; ³University Medical Center, Nijmegen, The Netherlands; ⁴Rheumaeinheit, Universität München; ⁵Knoll AG, Ludwigshafen, Germany

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Background

Objectives To evaluate the long-term efficacy and safety of a combination of methotrexate (MTX) with the fully human anti-TNF antibody adalimumab (D2E7) in patients with active rheumatoid arthritis (RA).

Methods 54 patients, who were partial responders to standard doses of MTX (mean 16 mg/week), were included in this randomised double blind, placebo-controlled study (DE010). Initially, patients were randomised into three treatment arms of 18 patients each and then injected double blind (first and second injection) with either 1 mg/kg adalimumab i.v., 1 mg/kg

adalimumab s.c., or placebo (double dummy). Thereafter, all patients received open-label s.c. injections of 1 mg/kg adalimumab. The frequency of administration (every other week up to every other month) depended on the individual response to treatment.

Results The overall efficacy results for the open label period of 24 months are summarised in the Table 1 below.

Adverse events were well matched between both adalimumab treatment arms and placebo during the initial double blind study period. A total of 44 patients (81%) were able to complete the 2-year study period. Reasons for drop out were adverse events (6 pts), lack of efficacy (2 pts), death (1 pt, myocardial infarction), and protocol violation (1 pt).

Abstract OP0062 Table 1

	Baseline	6 mo	12 mo	18 mo	24 mo
% pts EULAR response		87	85	80	78
% pts ACR 20		72	63	63	50
% pts ACR 50		30	28	43	30
DAS*	4.72	2.86	3.03	2.48	2.58
Ritchie Index*	16.0	6.0	7.0	4.5	4.5
SJC [0–44 joints]*	19.0	7.0	8.0	6.0	4.5

*median.

Conclusion Repeated subcutaneous injections of 1 mg/kg adalimumab (D2E7) over a period of two years showed sustained efficacy and were well tolerated when given in combination with stable standard doses of MTX to patients with active RA.

OP0083 LONG-TERM USE OF THE FULLY HUMAN ANTI-TNF ANTIBODY ADALIMUMAB (D2E7) IN DMARD-REFRACTORY RHEUMATOID ARTHRITIS

¹M Schattenkirchner, ²R Rau, ³LB Van de Putte, ¹I Vallbracht, ²G Herborn, ³EJ Kroot, ³PL Van Riel, ⁴R Dressler, ⁴D Compagnone, ⁴H Kupper. ¹Rheumaeinheit, Universität München, Germany; ²Rheumaklinik, Evangelisches Fachkrankenhaus, Ratingen, Germany; ³Department Rheumatology, University Medical Center, Nijmegen, The Netherlands; ⁴Knoll AG, Ludwigshafen, Germany

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Background

Objectives To evaluate the long-term efficacy and safety of the fully human anti-TNF antibody adalimumab (D2E7) given by the s.c. route to patients with active rheumatoid arthritis.

Methods 24 patients with active rheumatoid arthritis who had previously failed a mean of 3.5 DMARDs were included in this 12-week randomised double blind, placebo-controlled study (DE004), and continued thereafter in an open label part of the study for up to two years on adalimumab. Initially, patients were assigned to either 0.5 mg/kg adalimumab s.c. weekly (18 patients) or placebo (6 patients). 22 patients entered the open-label part of the study: 15 patients who achieved EULAR response continued their previous adalimumab treatment schedule (0.5 mg/kg weekly), 2 patients who did not achieve a EULAR response at week 8 increased their adalimumab dose to 1 mg/kg weekly, and 5 patients previously on placebo received 1 mg/kg adalimumab s.c. weekly.

Patient characteristics at baseline: 60 years mean age, 10 years mean RA duration, 5.35 mean Disease Activity Score (DAS).

Results The overall efficacy results for the open label period of 24 months are summarised in the Table 1 below.