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

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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.

Adverse events were well matched between the adalimumab treatment arm and placebo during the placebo-controlled period. After two years of treatment 14 patients were still receiving study drug. Reasons for drop out were lack of efficacy (4 pts), adverse events (3 pts), death (1 pt on placebo, 1 on adalimumab, both myocardial infarction), and protocol violation (1 pt).

Abstract OP0083 Table 1

	Baseline	6 mo	12 mo	18 mo	24 mo
% pts EULAR response		91	78	78	74
% pts ACR 20		78	65	65	61
% pts ACR 50		26	26	35	35
DAS*	5.23	3.46	2.78	2.49	2.60
Ritchie Index*	18.0	6.0	4.0	3.0	4.0
SJC [0–44 joints]*	20.0	5.0	2.0	4.0	2.0
CRP [mg/L]*	35.0	19.8	13.5	9.6	11.8

*median.

Conclusion Repeated weekly s.c. injections of a dose of 0.5 mg/kg or 1 mg/kg adalimumab (D2E7) given to patients with active rheumatoid arthritis over a period of two years were efficacious and well tolerated.

OP0084 PEG STNF-RI IMPROVES HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH RHEUMATOID ARTHRITIS

¹JR Tesser, ²MH Schiff, ³MW Davis, ³JM Woolley. ¹Arizona Rheumatology Center, Phoenix, USA; ²Denver Arthritis Clinic, Denver, USA; ³Amgen Inc., Thousand Oaks, USA

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Background

Objectives To evaluate the effect of PEG sTNF-RI on the health related quality of life (HRQOL) of subjects with rheumatoid arthritis.

Methods In a 12-week, multicenter, randomised, double-blind clinical trial, 194 subjects received either 400- or 800-mcg/kg of PEG sTNF-RI or placebo SC weekly (1:1:1). The study population included subjects with or without background DMARDs (combination therapy involving methotrexate with sulfasalazine or hydroxychloroquine, or sulfasalazine plus hydroxychloroquine). To measure HRQOL, the SF-36 was administered at baseline and at weeks 4 and 12. The SF-36 consists of 36 items designed to assess physical function (PF), role limitations due to physical problems (RP), body pain (BP), general health (GH), vitality/energy (VT), social function (SF), role limitations due to emotional problems (RE), and mental health (MH). The SF-36 is scored from 0 to 100, with higher scores indicating better HRQOL. Differences of 3 to 5 points are considered clinically and socially relevant. The mean change in each SF-36 scale score was compared between subjects receiving PEG sTNF-RI and those on placebo using a repeated measure mixed effect model analysis. The analysis set was a modified intent-to-treat sample, i.e. all patients who received at least one dose were included (n = 193).

Results Subjects using either dose of PEG sTNF-RI experienced statistically significant, and clinically and socially relevant improvements in each SF-36 scale (see Table 1). These improvements exceeded those for subjects on placebo in every scale and

were statistically significantly improved over placebo for 7 of 8 scales for the 800-mcg/kg dose, and 6 of 8 scales for the 400-mcg/kg dose.

Abstract OP0084 Table 1 Mean change in SF-36 scales from baseline to week 12

Dose of PEG sTNF-RI	PF	RP	BP	GH	VT	SF	RE	MH
800 mcg/kg (n = 66)	12.5*	25.4*	22.0*	7.0	16.9*	13.2*	19.8*	5.2*
400 mcg/kg (n = 67)	8.2	24.3*	14.7*	9.4*	13.9*	12.8*	14.3	6.8*
Placebo (n = 61)	4.8	6.1	6.0	2.2	6.7	1.3	0.8	-1.3

*p < 0.05 for comparison with placebo.

Conclusion Subjects receiving PEG sTNF-RI experienced statistically significant, clinically and socially relevant improvements in their SF-36 scores. These improvements occurred across a full range of health-related quality of life scales, from the physical to the psychosocial, and exceeded those for subjects on placebo. In this population of patients with rheumatoid arthritis, some of whom received DMARD or combination DMARD therapy, PEG sTNF-RI leads to significant and meaningful improvements in health-related quality of life.

OP0085 INFILIXIMAB PLUS METHOTREXATE IMPROVES SIGNS AND SYMPTOMS IN INITIAL NON-RESPONDERS WHO CONTINUE TREATMENT

¹E Keystone, ²K Patel, ³G Keenan, ³T Schaible. ¹Rheumatology, Mount Sinai Hospital, Toronto, Canada; ²Biostatistics; ³Immunology Medical Affairs, Centocor, Inc., Malvern, USA

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Background In an international, placebo-controlled, randomised trial, 428 patients with active RA despite methotrexate (MTX) therapy received placebo (i.e. MTX alone) or infliximab at 3 mg/kg or 10 mg/kg every 4 or 8 weeks along with MTX for 102 weeks. In this trial, infliximab plus MTX improved signs and symptoms, inhibited progression of structural damage, and improved physical function compared to MTX alone.

Objectives To determine if continued treatment with infliximab benefits patients who are not ACR20 responders at week 30.

Methods Patients who were not responders according to ACR20 criteria at week 30 were identified. Their clinical response to continued treatment was assessed based on ACR-N at the week 54 and week 102 visits. Analysis of variance on the van der Waerden normal scores was used to compare the ACR-N values at these time points. Radiologic response is based on the modified total Sharp score (TSS).

Results The ACR-N and change in TSS at weeks 30, 54 and 102 are shown in the Table 1. The ACR-N was higher in the infliximab treated groups, compared to the placebo treated group at weeks 54 and 102. The change in TSS was higher at all time points in the placebo group as compared to the infliximab treated groups.

Conclusion Patients who did not initially benefit from infliximab treatment derived clinical benefit when they continued to be treated long-term. Radiographic benefit was noted over time in all of the infliximab treated groups. The time point at which patients can be categorised as clinical non-responders to infliximab therapy needs further examination.