Abstract OP0085 Table 1 Mean ACR-N and change in TSS at weeks 30, 54, and 102 in ACR20 non-responders at week 30

	Placebo	3 mg/kg q 8 wks	3 mg/kg q 4 wks	10 mg/kg q 8 wks	10 mg/kg q 4 wks	Total infliximab
Number of ACR 20	63	39	42	41	32	154
ACR-N at Week 30	1.2	2.3	2.9	3.5*	3.3*	3.0*
ACR-N at Week 54	2.4	9.4*	9.0*	17.1*	17.8*	13.1*
ACR-N at Week 102	3.3	12.2*	6.7	18.7*	10.1*	11.9*
Change in TSS at Week 30	5.1	2.3	0.8*	<0.1*	0.5*	0.9*
Change in TSS at Week 54	7.2	3.0*	1.9*	0.2*	0.3*	1.3*
Change in TSS at Week 102	13.5	3.7	1.8*	0.9*	-0.8*	1.4*

*p < 0.05.

OP0086 THE FULLY HUMAN ANTI-TNF MONOCLONAL ANTIBODY, ADALIMUMAB (D2E7), DOSE RANGING STUDY: THE 24-WEEK CLINICAL RESULTS IN PATIENTS WITH ACTIVE RA ON METHOTREXATE THERAPY (THE ARMADA TRIAL)

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Background

Objectives To investigate the clinical efficacy and safety of adalimumab (D2E7), given subcutaneously in combination with methotrexate (MTX) to rheumatoid arthritis (RA) patients who are partial responders to MTX treatment.

Methods The ARMADA Trial was a double-blind placebo controlled study of 271 patients who had active RA despite concurrent stable doses of MTX. The patients were randomised to receive placebo or the fully human anti TNF monoclonal antibody, adalimumab (D2E7), at one of 3 doses (20, 40 and 80 mg every other week). Baseline demographic characteristics included: 76.8% females, 81% rheumatoid factor positivity, mean age 55.5 years, mean duration of RA 12.3 years, mean dose of MTX 16.8 mg/week, mean number of previous DMARDs 3.0. These characteristics were well matched between treatment groups.

Results Clinical efficacy results for the placebo controlled 24-week period are displayed in the Table 1 below. Adverse events in the adalimumab (D2E7) groups are similar to placebo. Only injection site reactions occurred more frequently with adalimumab (D2E7) in 14.8% of the patients versus 3.2% in the placebo group.

Abstract OP0086 Table 1

	Placebo	20 mg every other week	40 mg every other week	80 mg every other week
ACR20	14.5%	49.3% ^a	65.7% ^a	65.7% ^a
ACR50	8.1%	31.9% ^b	53.7% ^a	52.7% ^a

ACR70	4.8%	10.1%	26.9% ^b	19.2% ^b
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a = p < 0.0001, b = p < 0.02.

Conclusion The efficacy of the fully human anti-TNF α monoclonal antibody, adalimumab (D2E7), in addition to MTX in patients with longstanding RA is significantly better than placebo when given every other week subcutaneously. The ACR50 and ACR70 responses were impressive in this group of patients with refractory RA.

OP0087 INFILIXIMAB PLUS METHOTREXATE INHIBITS STRUCTURAL DAMAGE, REDUCES SIGN AND SYMPTOMS AND IMPROVES DISABILITY IN PATIENTS WITH ACTIVE EARLY RHEUMATOID ARTHRITIS

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Background In the ATTRACT trial, 428 pts with active RA despite methotrexate (MTX) therapy received MTX alone or infliximab at 3 mg/kg or 10 mg/kg every 4 or 8 weeks along with MTX for 102 weeks. Since joint damage may progress rapidly early in the disease course, pts with early RA (disease duration < = 3 yrs) were analysed. In this study, 82 of 428 pts (17 placebo, 19 in each of the 3 mg/kg infliximab group, 20 in the 10 mg/kg q8 group and 7 in the 10 mg/kg q4 group) had early RA.

Objectives To determine prevention of structural damage, reduction in signs and symptoms and improvement in disability in pts with early RA after two years of treatment.

Methods Structural damage was assessed using the Van der Heijde modification of the Sharp score (TSS). Radiographs of hands and feet were obtained at baseline, and after 30, 54 and 102 weeks. Two trained readers scored the films independently. The mean score of the two readers for each set of radiographs was used for further analysis. A clinical response was defined as an ACR 20 response at week 102. Disability was assessed by analysing patients' weighted mean change from baseline HAQ scores through week 102. The changes in TSS and HAQ score from baseline to week 102 were compared between the infliximab treatment groups and the placebo group by using analyses of variance of van der Waerden normal scores. The proportions of pts with a clinical response at week 102 were compared by using chi-square test.

Results The change in TSS from baseline through week 102 was significantly lower in each infliximab dose regimens compared to placebo, as shown in the Table 1. The clinical response rate was 29% for the placebo group, 37% for the 3 mg/kg q8 group, 53% for the 3 mg/kg q4 group, 45% for the 10 mg/kg q8 group and 43% for the 10 mg/kg q4. The median improvement in HAQ was 0.2 for the placebo group, 0.2 for the 3 mg/kg q8 group, 0.5 for the 3 mg/kg q4 group, 0.4 for the 10 mg/kg q8 group and 0.5 for the 10 mg/kg q4. The results for clinical response and HAQ did not reach statistical significance. However, they are consistent with the results of overall study population.

Conclusion Treatment through 102 weeks with any of the 4 infliximab regimens plus MTX, inhibits structural joint damage. Early intervention with infliximab in pts with active disease despite MTX may protect joints during the early, rapidly-progressive, destructive phase of the disease.

Abstract OP0087 Table 1

	Placebo	3 q8	3 q4	10 q8	10 q4	All
		wks	wks	wks	wks	Infliximab
Total pts	88	86	86	87	81	340
Early RA pts	17	19	19	20	7	65
Pts evaluated	12	10	16	17	6	49
Change in TSS	25.0	-0.6	-2.5	1.7	-1.4	-0.5
Mean						
SD	26.8	8.3	9.8	5.0	3.5	7.5
Median	14.5	-1.4	0.4	0.5	-0.8	0.5
p-value		< 0.001	< 0.001	0.004	0.001	< 0.001

OP0117 THE EFFECT OF ANAKINRA IN SLOWING RADIOLOGIC PROGRESSION IN RHEUMATOID ARTHRITIS PATIENTS? EVIDENCE FROM A BOOTSTRAP ANALYSIS

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Background Anakinra was studied in a randomised placebo-controlled study of 473 patients with rheumatoid arthritis (RA). Patients were randomised to one of 4 treatment groups (placebo, 30 mg, 75 mg or 150 mg anakinra) and treated for 24 weeks. Radiographic assessments of the hands and wrists based on Larsen score (Larsen 1977) were collected at baseline and 24 weeks. At the end of the study, about 27% of the patients withdrew. To assess the anakinra effect on reducing joint damage, the potential influence of dropouts on the study conclusions must be taken into account.

Objectives To demonstrate that the effect of anakinra in reducing the rate of radiologic disease progression is robust and insensitive to potential biases due to losses of followup.

Methods The 3 anakinra dose groups were combined into a single treatment group which was then compared to placebo. For each treatment group, x% of the missing Larsen score changes from baseline to week 24 were imputed by randomly selecting the observed change scores from the same treatment group, and the rest of the missing data were imputed similarly from the opposite treatment group. The resampled (bootstrapped) data were then analysed by an ANOVA model. This resampling procedure was repeated 1000 times, resulting in the estimation of 1000 p-values for testing the treatment effect. These 1000 p-values were then summarised to give an estimated picture of the IL-1ra treatment effect. By changing the proportion of sampling (x) systematically, the effect of anakinra on radiologic progression can be studied under different scenarios of missing data.

Results The results from all the analyses indicated that there was improvement in radiologic progression with anakinra treatment for 24 weeks. Statistical significance was maintained when up to 40% of the missing data were sampled from the opposite treatment group (mean and median p-values range from 0.021 to 0.078, and 0.011 to 0.05 respectively).

Conclusion Anakinra has a statistically significant effect on slowing the progression of disease for 24 weeks of treatment as

measured by the Larsen Score, even when as much as 40% of the missing anakinra scores are imputed with placebo values.

OP0118 TREATMENT PREFERENCES FOR EARLY RHEUMATOID ARTHRITIS PATIENTS: HOW AGGRESSIVE ARE RHEUMATOLOGISTS?

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Background Epidemiologic and clinical data point to the need for early and aggressive DMARD treatment of rheumatoid arthritis (RA) in order to improve functional outcome and prevent joint damage.

Objectives To identify the pharmacoeconomic, physician, and geographic variables that might modify physician choice (s) of first-line therapy for early RA.

Methods A questionnaire describing 3 RA cases with differing levels of disease severity/activity was developed. Each scenario portrayed a patient of the same age/gender, but presenting with a 6-month's history of the signs/symptoms of mild, moderate, and severe disease activity/severity. The questionnaire was mailed to rheumatologists (adult practice) (n = 995) within four geographical regions of the United States (Northeast-NY; South-TX; Midwest-MO/NE/KS; West-CA) who were identified through the membership directory of the American College of Rheumatology. Rheumatologists were asked to identify their choice (s) of first-line therapy for each of the case profiles, first incorporating and second not incorporating cost as a factor in their treatment decision (s).

Results 375 (37.7%) questionnaires were returned between March 12 and April 25, 2000. Response rates were similar among the different geographical regions. The Table 1 demonstrates the use of NSAID/COX2 inhibitors and/or corticosteroids (CS) alone as well as the use of DMARD therapy (including anti-TNF medications) with or without NSAID/COX-2, and/or CS. Various combinations of only NSAID/COX2/CS/Hydroxy-chloroquine/Sulfasalazine as the initial treatment were cited by 53–56% for mild, 3–5% for moderate, and 1–2% for severe disease activity/severity. DMARD monotherapy was chosen by nearly 3/4 of all rheumatologists for the treatment of mild RA, and by 40–60% for the treatment of moderate-severe RA regardless of cost issues. For severe disease activity/severity, when cost was a consideration the use of triple DMARD therapy significantly increased. Neither geographic location nor age (as a proxy for years of training) of the rheumatologist appeared to play a role in the treatment choices.

Conclusion For the first-line therapy of early RA, medication cost played no role in the choice of mono, double, or triple

Abstract OP0118 Table 1

	MILD RA \$not vs \$	MODERATE RA \$not vs \$	SEVERE RA \$not vs \$
NSAID/COX2/CS	9% vs 10% (NS)	2% vs 3% (NS)	1% vs 1% (NS)
1 DMARD	73% vs 75% (NS)	55% vs 60% (NS)	41% vs 47% (NS)
2 DMARDs	14% vs 12% (NS)	35% vs 26% (NS)	45% vs 29% (p = 0.00001)
3 DMARDs	4% vs 3% (NS)	8% vs 11% (NS)	12% vs 23% (p = 0.00002)

\$not: Cost is not a consideration, \$: Cost is a consideration, NS: Not significant.