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

MW Cravets, E Ng, MB Bear. *Department of Biostatistics, Amgen Inc., Thousand Oaks, USA*

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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?

D Erkan, Y Yazici, MJ Harrison, SA Paget. *Division of Rheumatology, Hospital for Special Surgery – Weill Medical College of Cornell University, New York, USA*

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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.

therapy except in the RA scenario with severe disease activity/severity. For mild disease activity/severity: 1) a surprisingly high percent employed NSAID and/or CS alone; 2) half of the rheumatologists did not prefer MTX, gold, azathioprine, cyclosporine or any of the newer DMARDs (leflunomide, etanercept, infliximab) in this broad RA patient population. For the first-line treatment of early RA, aggressive DMARD therapy is not universally employed by all rheumatologists in the regions studied.

OP0119 RADIOLOGICAL PROGRESSION IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS IS SIGNIFICANTLY RETARDED BY COMBINATION THERAPY WITH METHOTREXATE AND CYCLOSPORIN-A COMPARED TO CYCLOSPRIN-A ALONE

¹AH Gerards, RB Landewé ², ¹AP Prins, ³GA Bruijn, ²HS Goei The, ¹BA Dijkmans. ¹Rheumatology, Vrije Universiteit Medical Centre, Amsterdam; ²Rheumatology, University Hospital, Maastricht; ³Rheumatology, Medisch Centrum, Leeuwarden, The Netherlands

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Background Cyclosporin-A (CsA) added to low dose methotrexate (MTX) in patients with advanced rheumatoid arthritis (RA) is clinically superior to MTX alone.¹ The potential of CsA and MTX to inhibit radiological progression has not been established yet.

Objectives To assess in patients with early, active and potentially aggressive RA whether the combination of CsA and MTX results in less radiological progression as compared to CsA alone.

Design A randomised double blind placebo controlled trial of 48 weeks duration.

Methods 120 patients with active RA: mean age 52 yrs, mean disease duration 3 months, 95% rheumatoid factor positive, 49% erosions and/or joint space narrowing. Patients received CsA and MTX or CsA and placebo. MTX was started at 7.5 mg/week, and was increased to 15 mg/week after 16 weeks. CsA was started at 2.5 mg/kg/day, and was increased to a maximum of 5 mg/kg/day. Plain X-rays of hands and feet were obtained at week 0 and week 48 and were read in chronological order by two independent observers, blind for the study medication, using the Larsen-modified Larsen score.²

Results The Table 1 summarises the Larsen Score of patients in which 2 sets of films were available.

Abstract OP0119 Table 1

	Baseline	Change from baseline
CsA and MTX (n = 58)	2.0 (0.0–5.5)*	4.0 (1.0–10.5)
CsA and placebo (n = 57)	2.5 (0.5–5.5)	10.0 (3.5–13.3)
p-value for the difference**		0.004

*Median (interquartile range).

**Mann-Whitney two-sample test.

Conclusion CsA and MTX significantly retards radiological progression in comparison with CsA alone in patients with early, active and potentially aggressive RA.

REFERENCES

- 1 Tugwell. *NEJM* 1995;**333**:137–41
- 2 Larsen. *J Rheum.* 1995;**22**(10):1974–5

OP0120 CAUSE OF DEATH IN A PROSPECTIVE STUDY OF RA PATIENTS: DO RHEUMATOLOGY DRUGS PLAY A PART?

¹S Stafford, ¹CA Mayes, ¹A Young, ²P Williams. ¹Rheumatology, St Albans City Hospital, St Albans; ²Rheumatology, Medway District Hospital, Gillingham, UK

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Background Few prospective studies in RA have reported on the occurrence of comorbid conditions and mortality, and what proportion could be either disease or treatment related. The Early Rheumatoid Arthritis Study (ERAS) has prospective outcome data on patients followed for as long as 13 years.

Objectives To classify the cause of death and investigate any possible relationship with second line (disease modifying), steroidal or non steroidal anti-inflammatory drugs (NSAIDs).

Methods Consecutive patients with RA of less than two years duration have been recruited into an inception cohort from 9 rheumatology units. 1500 patients have been recruited into the study, prior to the use of second line drugs within 2 years of onset of symptoms of RA. Standard clinical and laboratory data were recorded yearly. Details of medication have been collected prospectively. Nearly all patients received non steroidal anti-inflammatory drugs (NSAIDs) at some stage, 84% received second line (disease modifying) drugs and 4% steroids alone. 166 deaths have been recorded from clinical notes, death certificates and the NHS Central Register (NHSCR). Cause of death has been categorised according to both aetiology and main organ involvement.

Results Major causes of death in 166 patients (males n = 71 and females n = 95) were as follows: cardiovascular disease (n = 56,33.7%), cerebrovascular (n = 14,8.4%), malignancy (n = 45,27.1%) and respiratory (n = 32,19.3%). Pulmonary infections were recorded in 22 of the latter, Pulmonary Fibrosis in 6 (2 on methotrexate, but present prior to start of therapy), and others (n = 4). 19 miscellaneous conditions included gastrointestinal haemorrhage (n = 4, NSAID related in 3) and septicaemia (n = 5, 2 on steroids and 1 with neutropenia probably methotrexate induced).

Conclusion No direct link could be established between cause of death and rheumatoid disease or drug therapy in most patients, except those with Pulmonary Fibrosis (4%), and in 6 patients where drug therapy could have been a contributory factor to cause of death.

OP0121 ENBREL® (ETANERCEPT) VS. METHOTREXATE (MTX) IN EARLY RHEUMATOID ARTHRITIS (ERA TRIAL): TWO-YEAR FOLLOW-UP

¹M Genovese, ²RW Martin, ³R Fleischmann, ⁴E Keystone, ⁵J Bathon, ⁶G Spencer-Green, ⁶B Finck. ¹Department of Medicine/Immunology and Rheumatology, Stanford University School of Medicine, Palo Alto; ²Clinical Rheumatology, Michigan State University, Grand Rapids; ³Rheumatology Associates, Metroplex Clinical Research Center, Dallas; ⁴Center for Advanced Therapeutics, Mount Sinai Hospital, Toronto, Canada; ⁵Asthma and Allergy Center, Johns Hopkins University, Baltimore; ⁶Clinical Development, Immunex Corporation, Seattle, USA

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Background The first year of this 2-year study of patients with early erosive RA (mean disease duration 1 year) demonstrated that ENBREL 25 mg twice weekly gave a more rapid clinical response and was more effective in preventing erosions than high dose (median 20 mg/wk) oral MTX.¹