arthritis patients and allow an earlier decision to start proper medication and defining progression or remission of the disease.

## THU0180 IDENTIFYING RAPID RADIOGRAPHIC PROGRESSORS IN RHEUMATOID ARTHRITIS

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**Background** Mounting evidence suggests that radiographically progressive disease identifies rheumatoid arthritis patients at higher risk for developing future disability. Hand and foot radiographs, however, incur additional expense and have not become a part of routine practice.
**Objectives** To determine if clinical parameters can be used to identify patients with radiographic progression.
**Methods** In 2 Dutch cohorts of early rheumatoid arthritis patients from Leiden and Nijmegen, 279 patients had year 2 or 3 radiographs (mean age 50.5 years, 76.7% women, 71.7% RF +, 60.1% HLA DR4+). Using the OMERACT definition, radiographic progression was defined as exceeding the smallest detectable difference (SDD) or 15 modified Sharp units. Because x-rays were done after 2 or 3 years from RA onset, we used the annual radiographic progression rate to define progressors (>7.5) vs non-progressors (
**Results** In this cohort, 199 of the 279 patients (71%) were radiographic ?progressors? after 2 – 3 years of RA. Univariate analysis showed that older age, RF+, higher Disease Activity Score (DAS) and Ritchie articular index (all $p < 0.03$) were associated with radiographic progression. In the multivariate model, RF positivity (OR 4.78, CI 2.32 – 9.86), older age (OR 1.75 per 10 years, CI 1.36 – 2.27) and higher DAS (OR 1.88, CI 1.32 – 2.69) remained significant. The area under the ROC was 0.81. The resulting sensitivity (SEN) and specificity (SP) values using the following cutpoints were (cutpoint = SEN/SP): 0.50 = 94/48, 0.60 = 89/60, 0.70 = 81/68, 0.80 = 64/79. Thus, treating all patients with predicted probabilities above 0.50 would miss 6% of the radiologic progressors and result in treatment of 52% of the non-progressors. Or treating only patients with predicted probabilities above 0.80 would miss 36% of the progressors and treat 21% of the non-progressors.
**Conclusion** Non-radiographic clinical parameters do not adequately identify rheumatoid arthritis patients with radiographically progressive joint disease. Performing routine x-rays to target new RA treatments that stabilise radiologic joint disease toward radiologic progressors is likely to yield the most favourable cost-effectiveness ratios.

## THU0181 CLINICAL RESULTS OF AN OPEN LABELLED EVALUATION OF THE TREATMENT WITH INFLIXIMAB IN THERAPY RESISTANT RHEUMATOID ARTHRITIS

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**Background** Evaluation of the efficacy and safety of the chimeric anti tumour nekrosis factor alpha (TNFa) antibody Infliximab in therapy resistant rheumatoid arthritis (RA).
**Objectives**
**Methods** 22 patients (mean age 59 years, mean duration of disease 9,5 years) with active RA, according to the ACR criteria, which were therapy resistant to two and more disease modifying antirheumatic drugs (DMARDs), including MTX, received 3 infusions of 3 mg/kg Infliximab at week 0, 2 and 6. Nine patients have been observed over a period of 30 weeks (0, 2, 6, 14, 22, 30). Standard clinical and laboratory assessments, including swollen joint count (SJC), tender joint count (TJC), morning stiffness (MST), visual analogue scale of patient pain assessment (VAS), C- reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were evaluated at baseline and at any time of drug administration.
**Results** After 3 infusions 65% of the patients achieved an 20% response (ACR 20). All clinical and laboratory assessments showed a significant improvement [SJC 10,2 before (B) vs.3,2 after 3 infusions (A), $p = 0{,}001$, TJC 26,6 (B) vs.9,1 (A), $p = 0{,}001$, MST 101,2 min (B) vs. 36,8 min (A), $p = 0{,}002$, CRP 26,9 mg/dl (B) vs. 17 mg/dl (A), $p = 0{,}015$, ESR 56,6 mm (B) vs. 31,2 mm (A), $p = 0{,}001$, VAS 7,4 (B) vs. 4,1 (A)]. Only mild adverse events but no severe infections occurred in the observation period.

After 30 weeks 44% maintained an ACR 20 response. A sustained improvement of clinical and laboratory assessments was observed.
**Conclusion** Infliximab seems to be an effective and safe treatment of therapy resistant active RA with a sustained improvement in clinical and laboratory assessments over a period of 30 weeks.

## THU0182 SIGNIFICANT REDUCTION IN SERIOUS UPPER GASTROINTESTINAL (UGI) EVENTS WITH CELECOXIB, A COX-2 SPECIFIC INHIBITOR, COMPARED WITH CONVENTIONAL NSAIDS. THE SUCCESS I TRIAL

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**Background** The Celecoxib Long-term Arthritis Safety Study (CLASS), a North American prospective outcomes study, demonstrated a significant reduction in UGI ulcer complications and improved tolerability.
**Objectives** To extend our understanding of the UGI safety advantages of celecoxib over conventional NSAIDs, a naturalistic study was conducted worldwide.
**Methods** SUCCESS I, a large, 12-week, multinational, prospective, double-blind, randomised trial in 13,274 osteoarthritis patients, was conducted in 39 countries. There were 6547 patients from Europe/Africa, 2756 from North America, 2889 from Latin America, and 1082 from Asia/Pacific. Celecoxib 200 mg/d (n = 4421) and 400 mg/d (n = 4429) was compared with naproxen 1000 mg/d (n = 914) and diclofenac 100 mg/d (n = 3510) with regard to UGI safety. Investigators were required to report all potential clinically significant UGI events and were allowed/requested to follow local standards of care with regard to work-up and treatment of events. Events data were collected

prospectively. An independent Gastrointestinal Events Committee (GEC) reviewed all data in a blinded fashion. Events were categorised as UGI ulcer complications (perforations, gastric outlet obstruction, bleeding) or symptomatic UGI ulcerations (predefined as in CLASS). A total of 144 cases were reviewed and adjudicated by the GEC.

**Results** See Table 1.

**Abstract THU0182 Table 1**

| | Celecoxib N = 8800 | NSAIDs N = 4934 | Odds Ratio | 95% CI |
|---|---|---|---|---|
| Exposure (pt-yr) | 1721.2 | 857.9 | | |
| Ulcer Complications (annualised rate) | 2/1721.2 (0.1%) | 7/857.9 (0.8%)* | 7.02 | 1.46–33.80 |
| Ulcer Complications + Symptomatic Ulcers (annualised rate) | 18/1721.2 (1.0%) | 21/857.9 (2.1%)* | 2.01 | 1.04–3.86 |

*p < 0.05 vs celecoxib.

**Conclusion** These data confirm CLASS results that celecoxib is associated with significantly fewer ulcer complications and symptomatic UGI ulcerations than conventional NSAIDs. The differences in event rates between SUCCESS and CLASS may relate to regional differences in surveillance or clinical practice.

Sponsored by Pharmacia Corporation and Pfizer, Inc.

## THU0183 SIGNIFICANTLY IMPROVED UPPER GASTROINTESTINAL (UGI) TOLERABILITY WITH CELECOXIB, A COX-2 SPECIFIC INHIBITOR, COMPARED WITH CONVENTIONAL NSAIDS. THE SUCCESS I TRIAL

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10.1136/annrheumdis-2001.1085

**Background** The Celecoxib Long-term Arthritis Safety Study (CLASS), a prospective outcomes study conducted in North America, demonstrated a significant reduction in UGI ulcer complications and improved tolerability.

**Objectives** To extend our understanding of the UGI safety advantages of celecoxib over conventional nonsteroidal anti-inflammatory drugs (NSAIDs), in day-to-day practice, a naturalistic study was conducted worldwide.

**Methods** SUCCESS I, a large, 12-week, multinational, double-blind, randomised trial in 13,274 osteoarthritis patients, was conducted in 39 countries. There were 6547 patients from Europe/Africa, 2756 from North America, 2889 from Latin America, and 1082 from Asia/Pacific. Celecoxib 200 mg/d (n = 4421) and 400 mg/d (n = 4429) was compared with naproxen 1000 mg/d (n = 914) and diclofenac 100 mg/d (n = 3510) with regard to GI tolerability.

**Results** The frequency of all reported GI adverse events (AEs), the three most frequently reported UGI AEs, and withdrawals due to GI AEs are shown in the Table 1.

**Abstract THU0183 Table 1**

| | NSAIDs (N = 4394) | Celecoxib (N = 8800) | % Reduction | p Value |
|---|---|---|---|---|
| All GI AEs | 21.0% | 16.7% | 20.4% | <0.001 |
| UGI AEs | 15.6% | 11.9% | 23.7% | <0.001 |
| Abdominal pain | 6.2% | 4.8% | 22.5% | <0.001 |
| Dyspepsia | 5.9% | 4.8% | 18.6% | <0.008 |
| Nausea | 3.4% | 2.4% | 29.4% | <0.001 |
| Withdrawals due to GI AE | 6.8% | 5.2% | 23.5% | <0.001 |

**Conclusion** UGI symptoms, more commonly associated with NSAID use, were consistently and significantly lower with celecoxib. The percent reduction ranged from 18.6% to 29.4%. These data confirm the superior GI tolerability of celecoxib vs conventional NSAIDs and establish that this difference is clinically meaningful in terms of discontinuation of therapy for such symptoms. Sponsored by Pharmacia Corporation and Pfizer, Inc.

## THU0184 POLYMORPHONUCLEAR CELL COUNTS (PMN) EFFECTIVELY PREDICT MORTALITY IN RHEUMATOID ARTHRITIS (RA) PATIENTS FOLLOWED FOR UP TO 20 YEARS

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**Background** Mortality is increased in rheumatoid arthritis (RA), and this increase is related to disease severity markers, disease activity and psychosocial factors. It has been previously reported that white cell counts (WBC) predict total joint replacement in RA,[1] and WBC levels are associated with cardiovascular mortality in non-RA populations.[2] The effect of WBC, especially PMN, on mortality has not been studied in RA, but might be clinically important.

**Objectives** To investigate the relation between PMN and mortality in RA.

**Methods** During a 20-year period ending in 2000, 1500 consecutive RA patients had 21,581 clinic visits at which 18,850 WBC tests were performed. 544 patients died. The predictability for mortality of PMN and other variables obtained 1) during the first 2 years of follow-up and 2) over the entire course of RA was examined using Cox regression models (Cox). To assess the impact of covariates on the predictability of PMN, we controlled for RF, ESR, age, disease duration, sex, HAQ, and prednisone use in multivariate Cox models. Generalised estimating equations (GEE) were used to describe the relation of PMN to other variables.

**Results** The mean (SD) of WBC and PMN was 8.0 (2.8) and 6.0 (2.5), respectively. Total PMN but not lymphocyte counts predicted mortality ($p < 0.05$ and $p = 0.522$, respectively). The mean PMN values in its quartiles were 3.5, 4.9, 6.2 and 9.0. Over the entire course of RA the hazard ratios (HR) for mortality compared with Q1 were Q2 1.5 (1.1,1.9), Q3 1.9 (1.4,2.5) and Q4 2.8 (2.2,3.7). By contrast, the HR for rheumatoid factor positivity (RF) was 1.6 (1.3, 2.1). HR for PMN during the 1st 2 years of follow-up were Q2 1.5 (1.1,1.9), Q3 2.0 (1.6, 2.6) and Q4 2.4 (1.8, 3.1). For those in Q1-Q4 during the 1st 2 years, the predicted 25% time to death was 11.7, 8.8, 7.2 and 4.6 years, respectively. To assess the effect of covariates on the predictive ability of PMN, covariates that included RF, ESR, age, disease duration, sex, HAQ, and prednisone use were added to the 2-year and lifetime PH models. PMN remained significant in the multivariate Cox models, and was a stronger predictor of