THU0177 PROGNOSTIC FACTORS OF REMISSION IN EARLY RHEUMATOID ARTHRITIS (RA). A MULTIPARAMETER PROSPECTIVE STUDY

¹B Combe, ²P Goupille, ³A Cantagrel, ⁴MC Bozonnat, ⁵J Sibilia, ⁶JF Eliaou, ⁷O Meyer, ¹J Sany, ⁴JP Daures, ⁸M Dougados. ¹Rhumatologie; ²Rhumatologie, Trousseau, Tours; ³Rhumatologie, Ranguel, Toulouse; ⁴IURC; ⁵Rhumatologie, Hautepierre, Strasbourg, France; ⁶Immunologie, Lapeyronie, Montpellier; ⁷Rhumatologie, Bichat, Paris; ⁸Rhumatologie, Cochin, Paris

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Background

Objectives To determine prognostic factors of remission in early RA.

Methods A cohort of 191 patients with RA and disease duration shorter than 1 year were prospectively followed-up for 3 years. Numerous baseline clinical, laboratory, genetic and radiographic data (Sharp's method modified by van der Heijde) were obtained. Remission, defined by a Disease Activity Score (DAS) < 1.6, was used as outcome measure.¹

Results Forty eight patients (25.1%) fulfilled the remission criteria at the 3-year follow-up visit. According to Fisher's exact test, remission was closely related with baseline values of DAS, HAQ score, morning stiffness, tender joint count, C-reactive protein and radiologic scores. No statistically significant correlation was demonstrated for sex, age, extraarticular manifestations, IgM and IgA rheumatoid factors, anti-perinuclear Ab, anti-keratin Ab, anti-HSP 90, anti-calpastatin Ab, antinuclear Ab, YKL-40 and HLA-DRB1* genotypes.

The logistic regression analysis revealed that the independent variables able to predict the 3-year remission were: DAS, HAQ score, morning stiffness and total radiographic score.

Conclusion Pronostic factors of remission in early RA were mainly clinical markers of disease activity and radiological scores.

REFERENCE

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THU0178 CLINICAL SIGNIFICANCE OF RAPID RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS

¹JB Wong, ²CJ Wong, ³JM Hazes, ⁴PL Van Riel, ⁵FC Breedveld, ⁶DM Van der Heijde, ²BG Feagan. ¹Medicine-Clinical Decision Making, Tufts-New England Medical Center, Boston, USA; ²London Clinical Trials Research Group, Robarts Research Institute, London, Canada; ³Rheumatology, University Hospital, Rotterdam; ⁴Rheumatology, University Hospital, Nijmegen; ⁵Rheumatology, Leiden University Medical Center, Leiden; ⁶Rheumatology, University Hospital, Maastricht, Netherlands

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Background New treatments for rheumatoid arthritis have established radiographic stabilisation of joint disease as an achievable therapeutic goal, but the amount of radiologic progression that is clinically significant remains uncertain. OMERACT has defined significant radiographic progression by the smallest detectable difference (SDD) based on random measurement error calculated from between observer variation in pairwise radiographic scoring and interpretation.

Objectives To examine the clinical significance of SDD-defined radiographic progression.

Methods We combined 2 Dutch cohorts of early rheumatoid arthritis patients from Nijmegen and Leiden. Using an SDD of 15 for the modified Sharp score, 279 patients had year 2 or 3 radiographs (mean age 50.5 year, 76.7% women, 71.7% RF+,

60.1% HLA DR4+) and were divided into 2 groups based on their annual radiographic progression rate: rapid (>7.5) vs non-rapid (<7.5) radiographic progressors. Exploratory statistical analyses were performed using the Chi-square and Wilcoxon rank sum tests.

Results In this cohort, 199 of the 279 patients (71%) were ? rapid progressors? after 2 – 3 years of RA. At that time, fast progressors tended to be HLA DR4+ (p = 0.11) but had higher ESR, Ritchie articular index, HAQ and Disease Activity Scores (DAS) (all p < 0.02), and were more likely to be older and RF+ (all p < 0.0001). After 5 – 6 years of RA, fast progressors had higher median modified Sharp scores (102 vs 8, p < 0.0001), HAQ scores (0.50 vs 0.23, p < 0.003), and DAS (2.80 vs 2.02, p = 0.003). After 12 years of RA, fast progressors had higher median HAQ (0.88 vs 0.26, p = 0.013) and DAS (2.88 vs 2.35, p = 0.11).

Conclusion Although SDD-based radiographic progression is defined as a statistically significant worsening beyond random measurement error, such radiologic progression of joint disease appears to identify rheumatoid arthritis patients who are significantly more likely to experience clinically progressive disease. Identifying and targeting the use of new biologic therapies toward this group of radiologically rapidly progressive rheumatoid arthritis patients is likely to yield the most favourable cost-effectiveness ratios because in the absence of these new treatments, these patients are at higher risk of developing progressive disability.

THU0179 MAGNETIC RESONANCE IMAGING OF THE HAND IN EARLY RHEUMATOID ARTHRITIS

¹I Ertenli, ²D Altınok, ¹S Kiraz, ²Y Karadeniz, ¹MA Öztürk, ¹S Apras, ¹M Çalgüneri. ¹Rheumatology, Hacettepe University School of Medicine, Ankara; ²Radiology, Kırıkkale University Medical School, Kırıkkale, Turkey

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Background

Objectives This study is planned as a prospective investigation of the accuracy of magnetic resonance imaging for the demonstration of early-stage rheumatoid arthritis findings of both hands, with the goal of differentiating magnetic resonance imaging and plain film findings of the patients having early -stage rheumatoid arthritis.

Methods Ten patients who met American Rheumatism Association criteria for rheumatoid arthritis and symptoms of less than one year duration were accepted for the study. After full clinical assessment, laboratory tests and radiographs of the hands were undertaken, magnetic resonance imaging was performed on a 1.5 tesla imager using an extremity coil using SE T1, TSE T2, fat suppressed T2, flash 2d 3D GRE and postcontrast fat suppressed T1 weighted sequences.

Results 6 of 10 patients had periarticular osteoporosis on plain radiography. All of the 10 patients had subcondral erosions, 8 patients had effusion in proximal interphalangeal joints, 8 had synovial hypertrophy, 7 had tendonitis, 5 had tendon erosions and tears and 2 had ulnar collateral ligament ruptures.

Conclusion Magnetic resonance imaging not only allows direct visualisation of the inflammatory soft tissue, but also its effect on the bone, cartilage, tendons and ligaments. Magnetic resonance imaging, due to its superior soft-tissue contrast and tomographic changes is more sensitive to than plain radiography in demonstrating the changes due to rheumatoid arthritis. This may contribute to more accurate diagnosis in early-stage rheumatoid

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

¹JB Wong, ²CJ Wong, ³PL Van Riel, ⁴JM Hazes, ⁵FC Breedveld, ⁶DM Van der Heijde, ²BG Feagan. ¹Medicine – Clinical Decision Making, Tufts – New England Medical Center, Boston, USA; ²London Clinical Trials Research Group, Robarts Research Institute, London, Canada; ³Rheumatology, University Hospital, Nijmegen; ⁴Rheumatology, University Hospital, Rotterdam; ⁵Rheumatology, Leiden University Medical Center, Leiden; ⁶Rheumatology, University Hospital, Maastricht, Netherlands

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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

M Spak, E Cauza, U Hanusch, G Haberhauer, A Dunky. Department of Rheumatology, 5. Med., Wilhelminen Spital, Vienna, Austria

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Background Evaluation of the efficacy and safety of the chimeric anti tumour nekrosis factor alpha (TNF α) 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

¹JL Goldstein, ²G Eisen, ³W Stenson, ⁴N Agrawal, ⁵AE Bello, ⁵JG Fort, ⁵SP Boots. ¹Department of Medicine, University of Illinois at Chicago, Chicago; ²Department of Medicine, Vanderbilt University Medical Center, Nashville; ³Department of Medicine, Washington University Medical School, St Louis; ⁴Department of Medicine, Duke University Medical Center, Durham; ⁵Research and Development, Pharmacia Corporation, Skokie, USA

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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