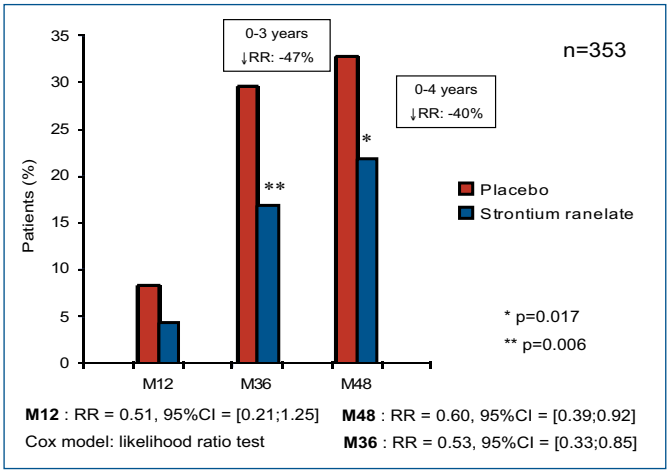
of the 5,091 patients had spine X-rays, which showed a risk reduction of 45% at 1 year and 39% over 3 years [Reginster JY et al. *J Clin Endocrinol Metab* 2005].

The objective of this study, presented at EULAR by Prof. Roux, René Descartes University, Paris, was to assess the efficacy of strontium ranelate in the reduction of vertebral fracture risk in women between the ages of 50 and 65 using data from the SPOTI study.

Women in this database (168 treated with strontium ranelate; 185 in the placebo group) had a mean age of 60.0±3.5 years, lumbar bone mineral density (BMD) T-score of –3.6±1.1, and a femoral neck BMD T-score of –2.5±0.8; 80.5% of the patients had a prevalent vertebral fracture and 23.0% had a prevalent non-vertebral fracture.

Treatment with strontium ranelate, reduced the relative risk of vertebral fractures by 47% over 3 years, and by 40% over 4 years (p=0.006). The incidence of vertebral fractures over 3 years was 16.9% in the strontium ranelate treated group vs 29.6% in the placebo treated group (Figure 1).

Figure 1: Reduction of Vertebral Fracture Risk in Younger Patients.



The reduction in the risk of vertebral fracture was paralleled by a significant increase (14.6%; p<0.001) in the relative change from baseline of lumbar BMD after 3 years, and by 7.5% in the relative change from baseline of femoral neck BMD vs placebo. Nausea, diarrhea, headache, and dermatitis were the most reported adverse events, none of which were significantly different from placebo.

Strontium ranelate significantly reduces vertebral fractures in postmenopausal women <65 years of age with severe osteoporosis.

Alcohol Consumption is Associated with Decreased Risks for Developing Rheumatoid Arthritis: Results from the Swedish EIRA Study

In a recent study in mice [Jonsson IM et al. Proc *Natl Acad Sci* 2007], alcohol consumption prevented development of destructive arthritis. This anti-inflammatory and anti-destructive property of alcohol was mediated by down-regulation of leukocyte migration and up-regulation of testosterone secretion, with the latter leading to decreased NF-kappaB activation. The authors concluded that low but persistent alcohol consumption delays the onset and halts the progression of collagen-induced arthritis by interfering with innate immune responsiveness.

The EIRA (Epidemiological Investigation of Rheumatoid Arthritis) study is a population based case-control study of incident cases of RA among 1,419 subjects aged 18-70 years in a defined area of Sweden. The primary inclusion criterion was first time diagnosis of RA according the 1987 ACR definition. Controls were matched for sex, age, and residential area.

The objective of this subanalysis of data from the EIRA study, presented by PhD student Henrik Källberg of the Karolinska Institute, was to assess the relationship between alcohol consumption and the risk of developing rheumatoid arthritis (RA), as well as the risk of developing subtypes of RA defined by the presence or absence of antibodies toward citrullinated peptides (anti-CCP2). The potential for smoking or HLA-DRB1 SE alleles to modify these associations was also investigated.

DNA from 1,204 cases and 871 controls was examined for the presence of HLA-DRB1 shared epitope (SE) alleles. The cases were also classified with regard to presence or absence of anti-CCP2 antibodies. Gender-specific odds ratios for RA were calculated with 95% confidence intervals for subjects with different consumptions of alcohol (none, 3-5 units per week, >5 units per week), smoking, and HLA-DRB1 SE alleles, compared with subjects with less exposure to alcohol (0-3 units per week), using logistic regression models with adjustments made for possible confounders.

Increased alcohol consumption (>3 units per week) was associated with a decreased risk of developing RA (OR 0.5; 95% CI 0.4-0.7). There was evidence of a dose dependency in that the higher alcohol consumption

lowered the risk of RA. The estimated odds ratio associated with alcohol consumption was about the same regardless of the presence of anti-CCP positive RA or anti-CCP negative RA. Furthermore, the association between alcohol consumption and RA was modified by both smoking and HLA-DRB1 SE alleles.

The results from the present study thus indicate that alcohol consumption is associated with a protective effect in relation to risk of developing RA, and that this effect is independent of anti-CCP status. The study points to the need to investigate mechanisms behind the protective effect of alcohol in both man and mice in order to understand the effect of life style on RA, and to identify new targets for therapy.

Induction of Remission in Early Rheumatoid Arthritis with Infliximab and Methotrexate Therapy

Early treatment with a combination of methotrexate (MTX) and infliximab (IFX) may be effective in inducing remission and altering the course of early rheumatoid arthritis (RA), according to the results of a study presented by Cornelia F. Allaart, MD, Leiden University Medical Center, Leiden, The Netherlands.

The BeSt study was a randomized trial comparing 4-year clinical and radiological outcomes using 4 different treatment strategies (groups) in patients with early and active RA [Goekoop-Ruiterman YP et al. *Ann Intern Med* 2007]. Patients in Group 4 (n=120) started treatment with IFX 3 mg/kg + MTX 25 mg/week. IFX treatment was adjusted every 8 weeks (ie, prior to each IFX infusion; if IFX was stopped the DAS was calculated every 3 months) throughout the study period based on Disease Activity Scores (DAS). In case of a continued DAS ≤2.4, IFX was discontinued and MTX was tapered to 10 mg/week. Beginning in year 3, MTX 10 mg/week was tapered to zero if the DAS remained <1.6.

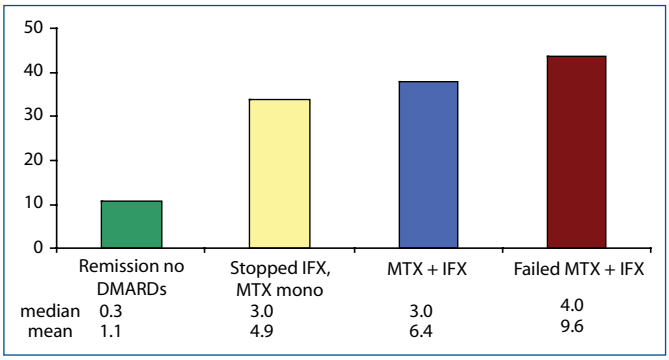
Disease progression over the course of the trial was determined by the Health Assessment Questionnaire (HAQ) and the van der Heijde modification of the Sharp score (SHS) to assess damage on hand and foot x-rays at initiation of the trial and at 4 years.

After 4 years, 113 patients remained in the study; 61 had successfully discontinued IFX after a mean of 13 months. At year 4 all of these patients had maintained a DAS ≤2.4, indicating a mean IFX-free period of 35 months. Twenty (20) of these patients had stopped all anti-rheumatic therapy and maintained a DAS <1.6 (mean 12 months without DMARDs).

During the 4th year, 4 patients who had previously discontinued all anti-rheumatic drugs were restarted on MTX (due to a DAS ≥1.6); 6 others who were on MTX monotherapy stopped using this medication. Four (4) patients who had previously discontinued IFX were required to restart, resulting in 22 patients on MTX+IFX combination therapy after 4 years. Thirty (30) patients failed on MTX+IFX and proceeded as per the protocol to the next pre-specified treatment steps.

SHS progression (>SDC, smallest detectable change) after 4 years was highest in patients who had failed MTX+IFX and minimal in the 20 patients who discontinued all anti-rheumatic therapy (Figure 1).

Figure 1. Percent of Patients with Progression SHS.



Four (4) years after receiving IFX and MTX as initial treatment for RA, 17% of patients have discontinued all anti-rheumatic medications and remain in clinical remission with minimal joint damage progression. Study leader Dr. Allaart commented, "Our findings indicate that clinical remission from RA is achievable, provided effective treatment is administered early in the course of the disease."

The RANKL Inhibitor Denosumab Reduces Progression of the Total Sharp Score and Bone Erosions in Patients with Rheumatoid Arthritis

Denosumab is a fully human monoclonal antibody that binds to and inhibits RANK Ligand (RANKL), a key mediator of osteoclast formation, function, and survival. There is no detectable binding to TNFα, TNFβ, TRAIL, or CD40L. RANKL-driven osteoclast activity has been