"This study specifically highlights the potential of naturally–induced hormones in protecting individuals from developing rheumatoid arthritis in the future. Furthermore, it adds to the growing body of evidence in favor of breast feeding and its positive health implications," said Dr. Keshavarz.

Rheumatoid Arthritis Disease Activity is Significantly Reduced During Pregnancy

Results of a prospective nationwide study (the PARA-study) presented by Yaël de Man, MD, Erasmus MC University Medical Center, Rotterdam, the Netherlands, demonstrated that rheumatoid arthritis (RA) disease activity is significantly reduced during pregnancy.

In the first prospective study conducted among women with RA, patients were monitored for disease activity scores (DAS) throughout their pregnancy and for 6, 12, and 26 weeks postpartum. DAS were calculated using the DAS28 and the level of C-reactive protein (CRP) with 3 variables (DAS28-CRP-3). Remission was defined as DAS28 <2.6.

The change in DAS28 between the 1st and 3rd trimester was used to categorize response using the EULAR response criteria. The change between the DAS28 at 6 weeks and 12 or 26 weeks postpartum was used to determine if a severe or moderate flare was present using inverted EULAR response criteria. The changes in DAS28 were tested for significance by a linear mixed model.

The study population was comprised of 124 women (mean age 31.6 years; median disease duration 5.2 years). Seventy-one percent (71%) of patients were RF positive, 61% were anti-CCP positive, and 72% were erosive. The mean pregnancy duration was 38 weeks and 6 days.

During pregnancy 11% of patients were considered good responders, 40% were at least moderate responders, and 60% were non-responders as indicated by the change in DAS28 between the 1st and 3rd trimesters.

The mean DAS28 decreased significantly by the 3rd trimester (vs prior to conception or to the 1st trimester (p=0.003), indicating an improvement of RA during pregnancy. Remission was seen in 17% of patients as early as the 1st trimester; 26% of patients were in remission by the 3rd trimester.

The DAS28 increased significantly by 12 weeks postpartum (vs 6 weeks postpartum) indicating a relapse of disease activity. Postpartum, 64% of patients remained relatively stable or improved. Only 36% of patients experienced at least moderate flare and only 5% a severe flare. Postpartum, the number of patients in remission decreased to 17% at 12 weeks. With medication, however, the number of patients in remission at 26 weeks postpartum increased to 20%.

DMARD use was lowered before pregnancy, remained stable during pregnancy (52% of patients), but increased postpartum (82% of patients), mainly due to methotrexate and biologics use.

Dr. de Man noted, "…the existence of a complex interaction between female hormones during pregnancy and the epidemiology of RA may contribute to the development of new prevention and treatment approaches in the future".

Strontium Ranelate Reduces the Risk of Vertebral Fracture in Postmenopausal Women with Severe Osteoporosis

Vertebral fractures in postmenopausal women (<65 years of age) with osteoporosis can lead to acute and chronic back pain, loss of weight, reduced pulmonary function, back related disability, depression, and a sustained decrease in quality of life. Early fractures occurring within the first 10 years after menopause are especially troublesome since they are a major risk factor for further additional fractures.

Strontium ranelate is an anti-osteoporotic treatment with a unique mode of action which reduces bone resorption while promoting continued bone formation [Marie PJ et al. *Calcif Tissue Int* 2001]. It has been shown to be effective in reducing the risk of vertebral fractures in two phase 3 studies. In the Spinal Osteoporosis Therapeutic Intervention (SPOTI) study of 1,649 postmenopausal women (mean age 69.4±7.2) with osteoporosis, strontium ranelate 2g/day produced a risk reduction for vertebral fracture of 49% in the first year and 41% over 3 years [Meunier PJ et al. *N Engl J Med* 2004]. The Treatment of Peripheral Osteoporosis (TROPOS) study was designed to examine the effect of strontium ranelate on non-vertebral fractures in postmenopausal women with osteoporosis (mean age 76.7±8). Three thousand six hundred and forty (3,640)

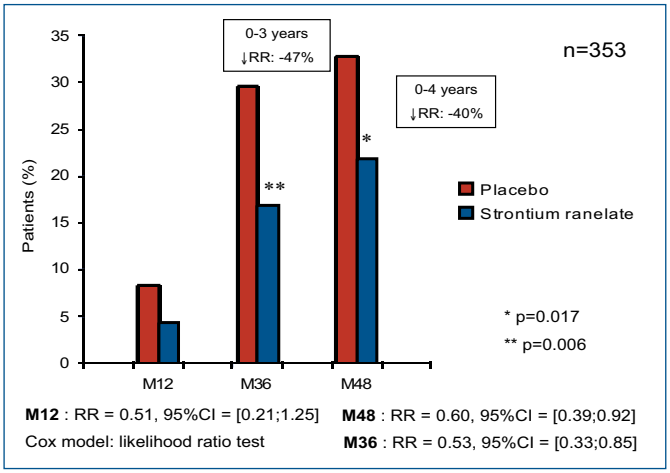
of the 5,091 patients had spine X-rays, which showed a risk reduction of 45% at 1 year and 39% over 3 years [Reginster JY et al. *J Clin Endocrinol Metab* 2005].

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