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.

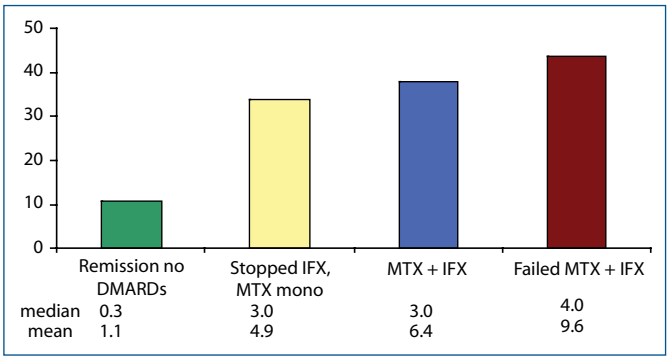
Disease progression over the course of the trial was determined by the Health Assessment Questionnaire (HAQ) and the van der Heijde modification of the Sharp score (SHS) to assess damage on hand and foot x-rays at initiation of the trial and at 4 years.

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