

## **NRI-05 Leflunomide (LEF) versus low dose methotrexate (MTX) in adult Asian patients with active rheumatoid arthritis (RA)**

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**Objective:** To assess the efficacy and safety of LEF 20 mg/day vs MTX 7.5-10 mg/week in adult Asian patients with active RA.

**Methods:** Randomised, double-blind, placebo-controlled, multicentre study design. Patients with active RA (modified Disease Activity Score 28 [DAS28] of >3.2) were assigned to receive LEF or MTX for 16 weeks.

**Results:** 301 patients (LEF: 151; MTX: 150) were included in an intention to treat analysis. There were no differences in the baseline characteristics between patients in the 2 groups. Using the DAS28 score criteria, the responder rates on LEF and MTX were 65.3% and 68.5% respectively (mean [95% CI] difference: -3.2 [-14.5% - 8.2%];  $p=NS$ ). Additionally, no differences were found between the 2 groups with respect to mean changes in tender and swollen joint counts, ESR, physician's global assessment and duration of morning stiffness. However, compared with MTX treatment, patients on LEF had significantly better adjusted mean reduction in general health assessment (LEF vs MTX: 27.6 vs 22.5,  $p=0.012$ ), patient's global assessment (LEF vs MTX: 29.7 vs 24.0,  $p=0.007$ ), and pain intensity scores (LEF vs MTX: 28.7 vs 22.3,  $p=0.003$ ). The overall incidence of clinical and laboratory adverse reactions between the 2 groups was similar. Alopecia was more commonly reported in the LEF group (LEF vs MTX: 26/151 vs 8/150,  $p=0.002$ ) but there was no withdrawal due to this side-effect.

**Conclusion:** LEF 20 mg/day is as efficacious as MTX 7.5-10 mg/week in adult Asian patients with active RA. However, LEF is more effective than MTX with respect to patient's general health status. Additionally, LEF is as safe as MTX in Asian patients.

## **NRI-06 Lymphocyte apoptosis, macrophage function and disease activity in systemic lupus erythematosus (SLE)**

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**Introduction:** Increased lymphocyte apoptosis and defects in macrophage removal of apoptotic cells have been suggested to contribute to the development of SLE. The aim of this study was to investigate the relationship between peripheral lymphocyte apoptosis, macrophage function as determined by the serum levels of neopterin and  $\gamma$ -interferon ( $\gamma$ -IFN), and SLE disease activity.

**Methods:** Peripheral apoptotic lymphocytes (AL) were detected by annexin V-FITC staining and flowcytometry. Serum levels of neopterin and  $\gamma$ -IFN were measured by ELISA. SLE disease activity was determined using the systemic lupus activity measure (SLAM) and the serum titer of anti-dsDNA antibodies.

**Results:** (1) The % of AL in the peripheral blood of active SLE patients was significantly higher ( $13.07 \pm 7.39\%$ ,  $n=30$ ) than that of the inactive SLE patients ( $4.47 \pm 3.39\%$ ,  $n=8$ ,  $p<0.001$ ) and normal controls ( $5.13 \pm 3.37\%$ ,  $n=11$ ,  $p<0.001$ ). (2) Serum levels of neopterin in SLE patients were significantly higher ( $1.39 \pm 1.10 \mu\text{g/dl}$ ,  $n=22$ ) than in controls ( $0.26 \pm 0.19 \mu\text{g/dl}$ ,  $n=20$ ,  $p<0.01$ ). (3) Serum levels of  $\gamma$ -IFN in active SLE patients were elevated ( $58.97 \pm 34.52 \text{ ng/l}$ ,  $n=15$ ) when compared with controls ( $28.06 \pm 2.35 \text{ ng/l}$ ,  $n=16$ ,  $p<0.05$ ). (4) The % of AL correlated significantly with serum levels of neopterin ( $r=0.446$ ,  $p<0.05$ ,  $n=22$ ) and SLAM score ( $r=0.533$ ,  $p<0.001$ ,  $n=38$ ), but not with the serum levels of  $\gamma$ -IFN. The SLAM score was also correlated with the serum levels of neopterin ( $r=0.485$ ,  $p<0.05$ ,  $n=22$ ) but not with those of  $\gamma$ -IFN.

**Conclusions:** Our study supported the hypothesis that increased lymphocyte apoptosis has a pathogenic role in SLE. The increased levels of serum neopterin may suggest an attempt of the patients' macrophage system to remove the apoptotic cell excess. Since serum levels of neopterin correlated with the overall lupus disease activity, they may be regarded as an index of SLE disease activity.