These results are supplied for informational purposes only. Prescribing decisions should be made based on the approved package insert in the country of prescription.

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<th>Candidate:</th>
<th>ClinicalTrials.gov Identifier:</th>
<th>Study Code:</th>
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<td>NCT00637819</td>
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**Title of the study:** Double blind, randomized, placebo controlled pilot study of leflunomide in systemic lupus erythematosus (SLE)

**Investigator(s):**
- L-S Tam, E. K. Li, C-K Wong, C. W. K. Lam, C-C Szeto
- Department of Medicine & Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong

**Study center(s):** Single Center, Hong Kong
Publications (reference):

Study period:
Date first patient/subject enrolled: 01-Feb-2003
Date last patient/subject completed: 31-Jul-2004

Phase of development:
II

Objectives:
To evaluate the efficacy and safety of LEF to control mild to moderate disease activity in SLE

Primary objective: the mean change of SLEDAI at 24 weeks.
Secondary objective: changes in proteinuria complement levels, anti ds-DNA binding and prednisolone dosage.

Methodology:
Randomized, placebo controlled

Number of patients/subjects:
Planned: 40
Randomized: 12
6 on placebo, 6 on leflunomide
Treated: 12

Evaluated:
Safety: 12
**Diagnosis and criteria for inclusion:**

All patients must 1) fulfill the revised ACR criteria for SLE, 2) with evidence of active disease according to SLE Disease Activity Index (SLEDAI) of ≥6, with the presence of at least one of the following features: arthralgia in more than 3 joints with tenderness or /and swelling for more than 1 week; active discoid or malar rash; pleuritis or pericarditis; cutaneous vasculitis; proteinuria <2 g/day with or without active urinary sediments, 3.) use of prednisolone < 0.5mg/kg/day, 4) use of safe contraceptive method.

Hydroxychloroquine and non-steroidal anti-inflammatory drugs are allowed to continue in patients who have been taking these medications before entering the study. Excluded are patients who are currently on immunosuppressants such as cyclophosphamide, azathioprine or cyclosporin A, pregnant or nursing women, or those with life threatening disease requiring other immunosuppressants such as cyclophosphamide or azathioprine.

**Investigational product:**

| Dose: | 100mg daily for 3 days followed by 20mg daily for the remainder of the study |
| Administration: | Oral |

**Duration of treatment:** 6 months

**Reference therapy:**

| Dose: | unknown |
| Administration: | Oral |

**Duration of observation:** 6 months

**Criteria for evaluation:**

**Efficacy:**

Primary outcome of this study include the number of patients who are able to achieve complete remission, defined as a SLEDAI of 0. Secondary outcomes included number of patients who are able to achieve partial remission, as defined by a SLEDAI of 1-3. Other secondary outcomes included reduction in proteinuria; change in complement levels and anti ds-DNA binding. Treatment failure is defined as premature termination of treatment due to exacerbation of SLE or adverse events as a result of treatment.

**Safety:**

Adverse events reported by the patient/subject or noted by the investigator.

**Statistical methods:**

ANCOVA will be used to evaluate variation in prednisolone dose, SLEDAI score and scores for SF-36. Mann-Whitney U test and chi-squared tests will be used for comparison between baseline demographic and clinical variables between the 2 groups where appropriate. All tests were two-tailed and a p-value of < 0.05 would be considered significant.
**Summary:**

Leflunomide was more effective than placebo in treating SLE patients with mild to moderate disease activity, and was safe and well tolerated. The clinical benefit and safety profile warrants confirmation by larger scale, multi-centered, randomized controlled trial.

**Efficacy results:**

The disease activity of both groups of patients decreased significantly after 6 months of treatment (14.7± 6.0 to 3.7± 2.3 in leflunomide group, p = 0.007 and 9.7± 3.4 to 5.2 ± 4.1 in placebo group, p = 0.005). However, the reduction in the SLEDAI from baseline to 24 weeks was significantly greater in the leflunomide group compared with the placebo group (11.0± 6.1 in the leflunomide group and 4.5± 2.4 in the placebo group respectively, p=0.036). The changes in proteinuria, complement 3 (C3) levels, anti ds-DNA binding and prednisolone dosage were similar between the 2 groups.

**Safety results:**

Minor adverse events were reported in the majority of patients. One patient received leflunomide had elevated ALT > 5 x baseline requiring premature termination of study. She was also taking traditional Chinese herbal medications of unknown nature. The ALT level returned to normal 2 months after stopping both leflunomide and TCM. One patient in each group had transient elevation in ALT > 2x baseline which resolved on repeat testing. Two patients in the leflunomide treated group developed hypertension requiring antihypertensive compared to 1 patient in the placebo group. Leucopenia (WCC < 3x 10^9/l) observed was transient and did not require adjustment of study drug dosage (1 in leflunomide group and 2 in placebo group). No patients reported diarrhea. There was no significant change in the body weight, blood pressure, serum creatinine, albumin, complete blood count and CRP in both groups.

**Date of report:**

19 Mar-2008