Targeted therapy using intradermal injection of etanercept for remission induction in discoid lupus erythematosus (TARGET-DLE): first results from a proof-of-concept phase 2 trial

Md Yuzaiful Md Yusof, Miriam Wittmann, Catherine Fernandez, Duncan Wilson, Sara Edward, Giuseppina Abignano, Adewonuola Alase, Linda Sharples, Phil Laws, M J Goodfield, Edward M Vital, Paul Emery

Objectives: To assess efficacy and safety of a novel route of TNF-inhibitor administration using an intra-dermal injection of etanercept (ETN) for remission induction in discoid lupus erythematosus (DLE).

Methods: A prospective single arm, Simon's 2-stage minimax design, phase II open label trial was conducted in Leeds [NCT02656082]. Inclusion criteria were i) adults, ii) ≥1 active DLE lesion and iii) refractory to anti-malarials. One most symptomatic lesion was treated with weekly injection up to 10mg ETN. Primary endpoint was ≥ 6/25 meeting the modified limited Score of Activity and Damage (ML-SADDLE) 20 (reduction of score ≥20% from baseline) at Week 12. Other endpoints were change in thermography and laser Doppler imaging (LDI).

Results: All 25 DLE patients were recruited over 18 months (18 female, mean age 47 years, 6 had SLE and median (range) number of previous therapies 5 (1-16). 17 patients completed the primary efficacy assessment. The primary endpoint was met with 13/25 (52%, 95% CI 31-73) meeting ML-SADDLE 20. The rates for ML-SADDLE 50 and 70 were 48% and 20% respectively. Key secondary endpoints were met (Table 1). Fifty-one AEs (treatment-emergent=28, Grade 3/4=4) were recorded. There was no worsening of BILAG or SLEDAI in patients with SLE. Trough serum ETN levels were detected in 6/23 (26%).

Table 1: Results for secondary endpoints (per protocol; n=17)

Endpoint	Pre-Treatment	Post-Treatment	p-value
Physician VAS, mean (SD) mm	53.1 (16)	23.2 (20)	<0.001
Patient VAS, mean (SD) mm	56.9 (28)	29.7 (28)	0.001
DLQI, mean (SD)	11.4 (7)	6.5 (6)	<0.001
LDI, mean (SD) perfusion unit	495.1 (224)	376.2 (223)	0.018
Thermography, mean (SD), ºC	1.92 (1.17)	1.08 (1.05)	0.005

Conclusion: A low dose intra-dermal injection of ETN substantially reduced clinical activity, met its primary and key secondary endpoints including patient-reported outcomes and objective measures. This therapy was tolerable in DLE patients who were refractory to anti-malarials and other systemic therapies. The results support further development of therapy in multi-centre trials. Analyses of other imaging and histological biomarkers are in progress and can help stratifying patients for response.