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RELIABILITY OF LA AND DIAGNOSTIC PERFORMANCE OF APS/PT IN DIFFERENT CLINICAL SETTINGS OF APS: A MULTICENTER STUDY

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Background: Correct interpretation of lupus anticoagulant (LA) tests is crucial for diagnosis of antiphospholipid syndrome (APS). However, testing patients during vitamin K antagonist (VKA) or other anticoagulant remains a contentious issue and has been discouraged by official guidelines¹ because of interpretational problems affecting the mixing test. Similarly, the clinical significance of weak LA, especially in the context of VKA, remains uncertain and certainly needs a more thorough evaluation. Autoantibodies that recognise a phosphatidylserine/prothrombin (PS/PT) complex have been reported to be associated with APS and may have diagnostic relevance in these settings.

Objectives: To evaluate the reproducibility of LA testing when performed in different centres and to assess the diagnostic performance of anti-PS/PT in different clinical settings of APS.

Methods: aPL testing was performed in a blind fashion in 4 centres. LA was tested as per the current criteria from the ISTH Subcommittee on LA-Phospholipid-dependent antibodies.¹ Thirty-two patients were enrolled in this study, as follows: 13 patients with thrombotic APS treated with vitamin K antagonist; 5 patients thrombotic APS treated with DOAC; 14 patients with transitory/low aPL titer. Anti-PS/PT IgG/IgM (aPS/PT, Inova Diagnostics) were tested by ELISA. We analysed the categorical agreement and degree of linear association, for LA and aPS/PT, respectively.

Results: Demographic, clinical and laboratory characteristics are summarised in table 1. Categorical agreement for LA among the centres, as expressed by Cohen's kappa coefficients, ranged between 0.61 and 0.80 (as substantial agreement). The correlation among quantitative results in the aPS/PT IgG was strong (when dichotomizing for positive Vs. negative results, Cohen's kappa coefficients=0.81–1. Spearman rho 0.84). We observed 12 (37.5% of the total) cases (7/12, 58% patients on VKA) in which LA results were discordant (as defined by lack of agreement in ≥2 laboratories) or inconclusive. Conversely, in those cases, we observed a good correlation for aPS/PT IgG testing (Cohen's kappa coefficients=0.81–1, Spearman rho 0.86).

	Patients	% (32 Patients)
Anagraphic		
mean age (S.D.) at data collection	49.4 (14,1)	
gender(females)	20	62.5
Clinical manifestations of APS		
Thrombosis	25	81.3
Arterial Thrombosis	10	31.3
Venous Thrombosis	15	46.9
Obstetric APS	0	0.0
aPL profile at diagnosis		
LA (positive, n)	26	81.3
ACA (IgG/M)	26	81.3
anti-β2GPI (IgG/M)	21	65.6
Anticoagulant Therapy		
VKA (warfarin)	13	40.6
LMWH	3	9.4
DOAC	5	15.6
None	11	34.4

Conclusions: Despite the progress in the standardisation of aPL testing, we observed up to 37.5% of discrepant results for LA, especially in patients on VKA. Our findings showed that some discordances in the reliability of LA testing still exist. The introduction of aPS/PT antibodies in the diagnostic process of APS might represent a further diagnostic tool, especially when LA is not available or nor reliable.

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FRI0328

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

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Background: A significant proportion of patients with discoid lupus erythematosus (DLE) are resistant to conventional therapies. Tumour necrosis factor (TNF) is pathogenic in DLE. A concern with systemic TNF- α administration is induction of pathogenic autoantibodies and flare of disease. This could be overcome using a low-dose intra-dermal injection, which may be sufficient to neutralise the TNF in lesions, **without systemic TNF effects.**

Objectives: To assess the efficacy and safety of a novel route of administration of a TNF- α using a low dose intra-dermal injection of etanercept (ETN) for remission induction in DLE.

Methods: A prospective single arm, Simon's 2-stage minimax design with Hybrid adaptation, phase II open label trial was conducted in Leeds [NCT02656082]. Key inclusion criteria were i) adults aged 18–80 y; ii) ≥1 active DLE lesion and iii) refractory to anti-malarials. One index lesion with the highest activity was treated with weekly intra-dermal injection of up to 10 mg ETN. The primary endpoint was ≥6 patients achieving the modified limited Score of Activity and Damage in DLE (ML-SADDLE) 20 response (defined as reduction ≥20% in total activity comprises erythema, induration and scaling from baseline) at Week 12 for a Phase 3 trial to be recommended. Secondary endpoints included change in objective outcome measures; lesional thermography and laser Doppler imaging.

Results: All 25 DLE patients were recruited over 18 months (18 female, mean age 47±12 y, 6 had SLE, 9 had positive ANA and median (range) no. of previous systemic therapies was 5(1–16) 17 patients completed the primary efficacy assessment [Did not attend Week 12 visit=1, early withdrawals=7 (personal choice=2, AE=2, worsening of DLE=1, non-compliance=1, pregnant=1)]. The primary endpoint was met with 13/25 (52%, 95% CI 31–73) meeting the ML-SADDLE 20 in full-set analysis. 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%).

Abstract FRI0328 – Table 1. 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
Laser Doppler Imaging, mean (SD) perfusion unit	495.1 (224)	376.2 (223)	0.018
Infrared thermography, mean (SD), °Celsius	1.92 (1.17)	1.08 (1.05)	0.005

Conclusions: Intradermal injection of ETN substantially reduced clinical activity, met its primary, secondary endpoints and was tolerable in DLE patients who were refractory to anti-malarials and other systemic therapies. This drug warrants further development in multi-centre trials. Analyses of other imaging and histological biomarkers are ongoing and can help stratifying patients for response.

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