SUPPLEMENTARY MATERIALS

A RANDOMIZED PROSPECTIVE TRIAL TO ASSESS THE CLINICAL UTILITY OF MULTIANALYTE ASSAY PANEL WITH COMPLEMENT ACTIVATION PRODUCTS IN THE DIAGNOSING OF SYSTEMIC LUPUS ERYTHEMATOSUS

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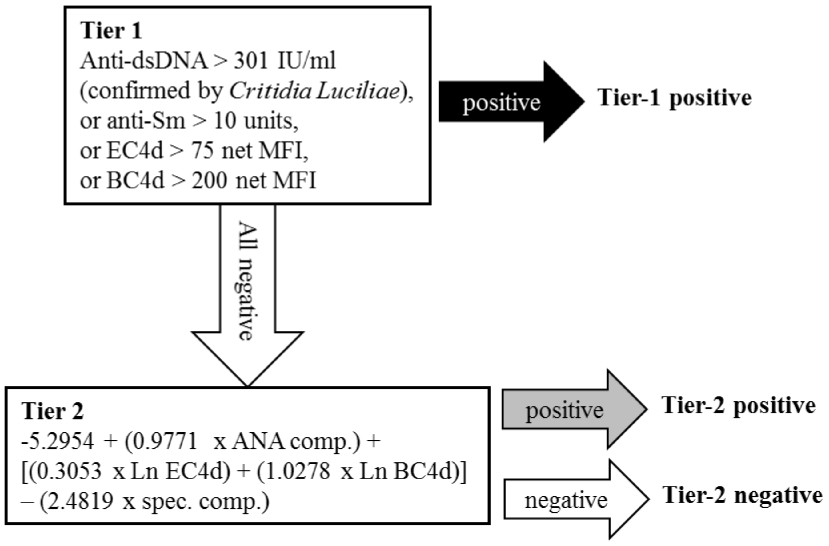
Figure S1: 2-tiered method

Two-tier diagnostic methodology. Samples are tier-1 positive if they are positive for anti-dsDNA (confirmed using *Crithidia Luciliae*) or anti-Sm antibodies or have highly elevated EC4d or BC4d. The index score (tier 2) is calculated for tier-1 negative specimens. The ANA component (ANA comp) utilizes two thresholds and can have a value of 0 (ANA<20 units), a value of 1 (20≤ANA<60 units) or a value of 2 (ANA≥60 units). The CB-CAPs component corresponds to the sum of the log normalized EC4d and BC4d values. The antibody specificity component (Spec comp.) can have a value of 0 (ACPA, SSB, CENP, Jo-1, Scl-70 all negative) or 1 (either ACPA, SSB, CENP, Jo-1, or Scl-70 positive).

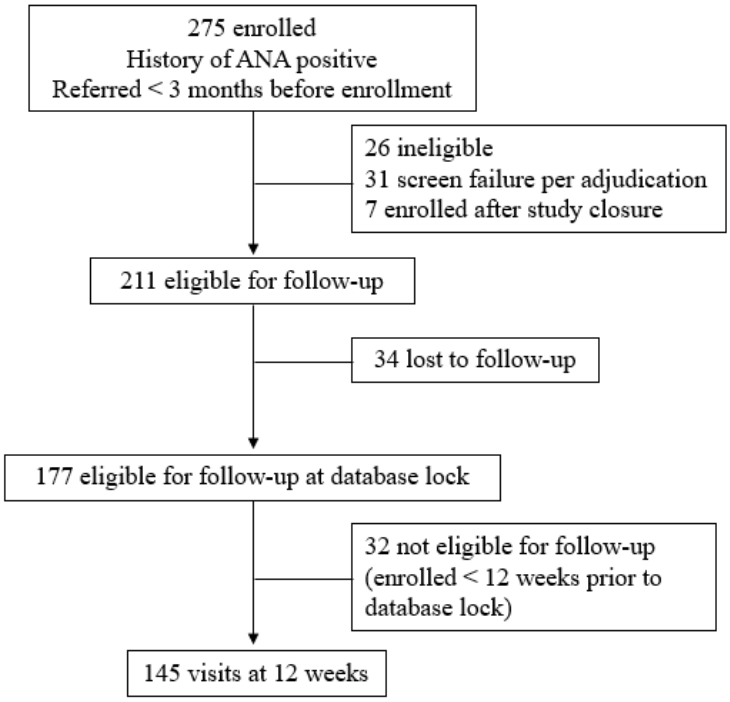
For example, a tier-1 negative subject presenting with ANA=35 units, EC4d =15 net MFI, BC4d=35 net MFI, and Anti-CCP=50 units would have an index score of:

Tier-2 index =-5.2954 + (0.9771x1) + [0.3053xLn(15) + 1.0278xLn(35)] – (2.4819x1) = -2.3

Ln: natural log



Supplementary Figure 2: **Enrollment in the study**



Supplementary Table I: **Symptoms at enrollment visit.**
There were no significant differences between the incidence of symptoms between SDLT and MAP testing arm (p>0.17) with the exception of Raynaud's (p=0.03).

Symptoms, Mild to severe	SDLT arm N=73	MAP/CB-CAPs testing arm N=72
Fever	1.4% [1/73]	4.2% [3/72]
Weight loss	2.7% [2/73]	8.3% [6/72]
Fatigue	72.6% [53/73]	77.8% [56/72]
Arthralgia	83.6% [61/73]	80.6% [58/72]
Arthritis	56.2% [41/73]	56.9% [41/72]
Muscle weakness	12.3% [9/73]	15.3% [11/72]
Myalgia	38.4% [28/73]	43.1% [31/72]
Generalized aches	49.3% [36/73]	52.8% [38/72]
Raynaud's	16.4% [12/73]	31.9% [23/72]
Sicca	37.0% [27/73]	48.6% [35/72]
Skin rash	35.6% [26/73]	33.3% [24/72]
Hair loss	47.9% [35/73]	40.3% [29/72]
Vasculitis	0.0% [0/73]	0.0% [0/72]
Neurological	11.0% [8/73]	8.3% [6/72]
Lung disease	2.7% [2/73]	2.8% [2/72]

Supplementary Table II: **Diagnostic immunology profile by randomization arm, as compared to estimates from the clinical laboratory.**

	SDLT arm [N=73]	MAP/CB-CAPs arm [N=72]	Clinical Laboratory [N=283,754]
ANA IFA ≥1:80	79.5%	80.6%	59.9%
ANA ≥20 units	58.9%	61.1%	54.1%
Anti-dsDNA [>301 U], confirmed by IIF	1.4%	1.4%	4.5%
Anti-Smith (>10 U)	1.4%	1.4%	0.6%
EC4d (>14 net MFI) or BC4d (>60 net MFI)	12.3%	5.6%	10.6%
Anti-CCP (>10 U)	1.4%	0.0%	4.7%
Anti-CENP B (>10 U)	4.1%	1.4%	3.1%
Anti-Jo1 (>10 U)	0.0%	0.0%	0.2%
Anti-SSB (>10 U)	4.1%	2.8%	2.6%
Anti-Scl 70 (>10 U)	0.0%	0.0%	0.2%
MAP/CB-CAPs (>0)	15.1%	12.5%	13.0%

Supplementary Table III: **Laboratory testing ordered in patients randomized to SDLT arm**

The results are expressed as the percentage of patients for whom specific markers were ordered

Marker	percent patient test ordered	Positive %, N
Anti-dsDNA	73% [53/73]	6% [3/53]
Complement C3 C4	66% [48/73]	6% [3/48]
Anti-SSB	70% [51/73]	6% [3/51]
Anti-Smith	64% [47/73]	2% [1/47]
Anti-Scl70	55% [40/73]	5% [2/40]
Anti-CCP	47% [34/73]	6% [2/34]
Anti-Jo-1	36% [26/73]	0% [0/26]
Anti-Centromere	22% [16/73]	13% [2/16]

Supplementary Table IV: Change in SLE likelihood at 12 weeks among all patients (n=145), patients negative (n=125) and positive for MAP/CB-CAPs (n=20).

Fisher Exact test [2x3] p values are provided. Clinicians were blinded to MAP/CB-CAPs test results in the group of subjects randomized to SDLT arm.

	SDLT arm	MAP/CB-CAPs testing arm	Fisher Exact 3x2
All patients			
Lower Likelihood (decrease ≥1 point)	37% [27/73]	56% [40/72]	p=0.074
Similar Likelihood (no change 0 point)	52% [38/73]	39% [28/72]	
Higher Likelihood (increase ≥1 point)	11% [8/73]	6% [4/72]	
Negative MAP/CB-CAPs results			
Lower Likelihood (decrease ≥1 point)	37% [23/62]	60% [38/63]	p=0.002
Similar Likelihood (no change 0 point)	52% [32/62]	40% [25/63]	
Higher Likelihood (increase ≥1 point)	11% [7/62]	0% [0/63]	
Positive MAP/CB-CAPs results			
Lower Likelihood (decrease ≥1 point)	36% [4/11]	22% [2/9]	p=0.274
Similar Likelihood (no change 0 point)	55% [6/11]	33% [3/9]	
Higher Likelihood (increase ≥1 point)	9% [1/11]	44% [4/9]	

Supplementary Table V: **Initiation of prednisone or HCQ in patients randomized to SDLT arm by positive vs negative marker status**

Initiation of prednisone or HCQ did not associate with any of the markers (p>0.13).

Marker	Prednisone Started	HCQ Started
Anti-dsDNA [pos vs neg]	0% [0/3] vs 12% [6/50]	0% [0/3] vs 26% [13/50]
Complement C3 C4 [pos vs neg]	33% [1/3] vs 9% [4/45]	33% [1/3] vs 22% [10/45]
Anti-SSB [pos vs neg]	0% [0/3] vs 8% [4/48]	67% [2/3] vs 21% [10/48]
Anti-Smith [pos vs neg]	0% [0/1] vs 9% [4/46]	100% [1/1] vs 24% [11/46]
Anti-CCP [pos vs neg]	0% [0/2] vs 13% [4/32]	0% [0/2] vs 19% [6/32]
Anti-CENP	0% [0/2] vs 7% [1/14]	50% [1/2] vs 29% [4/14]

Supplementary Table VI: **Patient reported outcome [EQ-5D-5L] pre-test and post-test**.

Results are expressed as mean [SEM] at each study visit and change from enrollment.

	Pre-test enrollment	Change 12-week
SDLT arm		
All patients (n=47)	0.779±0.013	-0.030±0.019
MAP/CB-CAPs negative (n=39)	0.780±0.018	-0.034±0.020
MAP/CB-CAPs positive (n=8)	0.774±0.046	-0.008±0.050
MAP/CB-CAPs testing arm		
All patients (n=56)	0.779±0.012	+0.004±0.018
MAP/CB-CAPs negative (n=48)	0.775±0.144	-0.011±0.018
MAP/CB-CAPs positive (n=8)	0.805±0.096	+0.099±0.046