303 CLINICAL AND LABORATORY ASSOCIATIONS OF LONGITUDINAL CELL-BOUND COMPLEMENT ACTIVATION PRODUCTS IN SLE

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Introduction Cell-bound complement activation products (CB-CAPs) in a multi-analyte assay with algorithm (MAP) is a valuable biomarker for the diagnosis of SLE. Erythrocyte-bound complement activation products have been associated with SLE disease activity. The clinical and serologic phenotype of longitudinal MAP positive patients has not been well described. Herein, we evaluated the relationship between longitudinal MAP results with clinical and laboratory variables.

Methods This was a longitudinal study of adult SLE patients (2012 SLICC or 2019 ACR/EULAR criteria with a range of disease activity) with $\geq$2 routine lupus clinic visits from June 2020 to July 2022. Patients completed the polysymptomatic distress scale. The treating rheumatologist scored the PGA and SLEDAI scores at the time of the visit. Autoantibodies including ANA and anti-RNA-binding proteins were measured by ELISA. Anti-dsDNA was determined by immunofluorescence using the Crithidia luciliea assays. CB-CAPs were analyzed by flow cytometry. The multi-analyte assay panel (MAP) was determined using a 2-tier algorithm. Chi- square and ANOVA tests were used to analyze differences in demographic and disease history between persistently MAP positive, MAP negative, and patients with changing MAP positivity. Serologies and clinical variables at follow-up visits were compared using generalized linear models.

Results In this longitudinal cohort of 113 patients with 175 follow-up visits (100% SLICC SLE, 90% female, 62% Black, mean age 45) 65% were consistently MAP positive, 20% were negative, and MAP positivity changed in 15%. Patients with persistent MAP positivity were younger and more often of Black race. There was no difference in MAP positivity based on SLE disease duration. Significantly more MAP positive patients met 2019 ACR/EULAR criteria and had higher total ACR/EULAR scores. Patients who remained MAP positive were more likely to have a history of acute cutaneous lupus but there was no difference in other historical manifestations of SLE between the three groups (table 1).

When evaluating longitudinal associations, patients with persistent MAP positivity had higher total SLEDAI scores, but there was no difference in the clinical SLEDAI. Therapy was comparable across groups except for greater use of belimumab, rituximab, and cyclophosphamide in persistent MAP-positive patients. Patients who remained MAP positive reported higher rates of depression, but a similar amount of polysymptomatic distress and fatigue. A greater number of lupus-specific serologies were present in those with MAP positivity (table 2).

Conclusion Identifying endotypes of SLE is important to advancing personalized medicine. In this longitudinal cohort of SLE with a full spectrum of disease active, MAP results were static in most patients. MAP resulted changed between visits in a subset of patients; although there was not a distinct clinical, demographic or laboratory phenotype in those patients. Patients with consistent MAP positivity reported more depression and had a greater burden of disease activity as measured by the ACR/EULAR score and greater use of biologic and

Abstract 303 Table 1 Demographics and disease history of the SLE patient cohort

	Overall Patients (N = 113)	MAP remains positive (N = 73)	MAP remains negative (N = 23)	MAP changing positivity (N = 17)	p-value
Demographics					
Age, mean (SD)	44.6 (14.3)	42.1 (15.0)	47.1 (12.9)	52.0 (10.2)	0.0227
Female	89.4% (101)	87.7% (64)	95.7% (22)	88.2% (15)	0.5485
Black race	61.9% (70)	71.2% (52)	39.1% (9)	52.9% (9)	0.0584
Ethnicity Hispanic	5.4% (6)	4.1% (3)	13.0% (3)	0.0% (0)	0.1488
SLE Disease History					
Duration of disease, mean (SD)	12.7 (9.0)	13.2 (9.0)	12.5 (9.2)	11.0 (9.4)	0.6764
1997 ACR Criteria	92.0% (104)	94.5% (69)	87.0% (20)	88.2% (15)	0.4149
2011 SLICC Criteria	100.0% (113)	100.0% (73)	100.0% (23)	100.0% (17)	na
2019 ACR/EULAR Criteria	94.7% (107)	98.6% (72)	91.3% (21)	82.4% (14)	0.0190
2019 ACR/EULAR Total Score, median (25th - 75th pctls)	21 (16–29)	24 (18–30)	18 (13–21)	19 (16–26)	0.0117
h/o Renal	45.1% (51)	45.2% (33)	34.8% (8)	58.8% (10)	0.3195
h/o Arthritis	67.3% (76)	72.6% (53)	65.2% (15)	47.1% (8)	0.1262
h/o Acute cutaneous SLE	62.8% (71)	68.5% (50)	65.2% (15)	35.3% (6)	0.0373
h/o Discoid SLE	18.6% (21)	21.9% (16)	17.4% (4)	5.9% (1)	0.3057
h/o Serositis	23.9% (27)	26.0% (19)	21.7% (5)	17.6% (3)	0.7385
h/o Neuropsychiatric	5.3% (6)	8.2% (6)	0.0% (0)	0.0% (0)	0.1762
h/o Oral ulcers	54.0% (61)	52.1% (38)	65.2% (15)	47.1% (8)	0.4480
h/o Alopecia	56.6% (64)	56.2% (41)	43.5% (10)	76.5% (13)	0.1135
h/o Hematologic	61.1% (69)	65.8% (48)	39.1% (9)	70.6% (12)	0.0504

Abstract 303 Table 2 Serologies, medications, disease activity and patient symptoms at the longitudinal follow-up visits

	All Follow-up Visits (N = 175)	MAP remains positive (N = 111)	MAP remains negative (N = 43)	MAP positive to negative (N = 10)	MAP negative to positive (N = 11)	
Serologies						
Anti-dsDNA positive	21.7% (38/175)	34.2% (38/111)	0.0% (0/43)	0.0% (0/10)	0.0% (0/11)	<.0001
Low C3 or C4	14.4% (25/174)	17.3% (19/110)	11.6% (5/43)	0.0% (0/10)	9.1% (1/11)	0.2236
Anti-Sm positive	3.0% (2/66)	5.6% (2/36)	0.0% (0/17)	0.0% (0/7)	0.0% (0/6)	0.4795
Anti-Ro60 positive	46.2% (80/173)	49.5% (54/109)	39.5% (17/43)	50.0% (5/10)	36.4% (4/11)	0.6242
Anti-U1RNP positive	29.3% (49/167)	44.8% (47/105)	0.0% (0/42)	11.1% (1/9)	9.1% (1/11)	<.0001
Anti-Cq1 positive	23.4% (41/175)	27.9% (31/111)	14.0% (6/43)	10.0% (1/10)	27.3% (3/11)	0.1785
Medications						
Hydroxychloroquine	83.3% (145/174)	84.5% (93/110)	81.4% (35/43)	70.0% (7/10)	90.9% (10/11)	0.6051
Mycophenolate	31.0% (54/174)	33.6% (37/110)	25.6% (11/43)	20.0% (2/10)	36.4% (4/11)	0.6322
Prednisone	18.4% (32/174)	22.7% (25/110)	9.3% (4/43)	10.0% (1/10)	18.2% (2/11)	0.2010
Belimumab, Rituximab, Cyclophosphamide	13.2% (23/174)	17.3% (19/110)	9.3% (4/43)	0.0% (0/10)	0.0% (0/11)	0.0451
Current Disease Activity						
PGA, mean (SD), N	0.5 (0.5), 175	0.5 (0.5), 111	0.4 (0.4), 43	0.4 (0.5), 10	0.4 (0.5), 11	0.7886
PGA >= 1.5	9.7% (17/175)	11.7% (13/111)	4.7% (2/43)	10.0% (1/10)	9.1% (1/11)	0.5701
SLEDAI, mean (SD), N	2.2 (2.5), 175	2.6 (2.7), 111	1.9 (2.2), 43	0.8 (1.7), 10	0.5 (0.9), 11	0.0120
Clinical SLEDAI, mean (SD), N	1.1 (1.8), 175	1.2 (1.7), 111	1.1 (2.1), 43	0.8 (1.7), 10	0.4 (0.8), 11	0.5125
SLEDAI Renal	7.4% (13/175)	8.1% (9/111)	9.3% (4/43)	0.0% (0/10)	0.0% (0/11)	0.3183
SLEDAI Arthritis	12.0% (21/175)	9.9% (11/111)	18.6% (8/43)	20.0% (2/10)	0.0% (0/11)	0.1466
SLEDAI Rash	17.1% (30/175)	21.6% (24/111)	9.3% (4/43)	0.0% (0/10)	18.2% (2/11)	0.0601
Patient reported symptoms						
Polysymptomatic distress score, mean (SD), N	9.3 (6.7), 159	8.8 (6.7), 99	10.8 (6.6), 40	9.1 (5.1), 10	7.8 (7.3), 10	0.3985
Fatigue (moderate/severe)	48.0% (72/150)	46.4% (45/97)	54.3% (19/35)	55.6% (5/9)	33.3% (3/9)	0.6473
Depression	36.5% (54/148)	45.7% (43/94)	21.6% (8/37)	11.1% (1/9)	25.0% (2/8)	0.0136

cytotoxic therapy. Combining longitudinal MAP scores with traditional assessment of SLE assessments activity may provide useful prognostic information and allow identification of a higher risk cohort of patients. Larger longitudinal studies are on-going to evaluate the relationship between individual CB-CAPs and markers of disease activity.

304 DYSREGULATED SERUM CYTOKINES IN ASSOCIATION WITH CLINICAL MANIFESTATIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease affecting multiple organ systems, making clinical trial design challenging. Biomarkers that can identify patients with specific clinical manifestations could allow for more targeted approaches in clinical development. Utilizing biomarker data from a phase III study of ustekinumab in participants with active SLE,[1] we sought to explore the dysregulation of cytokines in association with disease characteristics at baseline.

Methods The phase 3 randomized, placebo-controlled study enrolled 516 autoantibody-positive participants with SLE whose disease remained active despite standard-of-care therapy.[1] Participants were randomized in a 3:2 ratio to receive ustekinumab or placebo through week 48. Baseline serum levels of inflammatory cytokines were assessed using the Meso Scale Discovery platform (IFNγ, p40, TNFα, IL-10, IL-15, IL-16), Quanterix's single molecule array (Simoa) technology (IFNα), and the high-sensitivity Single Molecule Counting Erenna Immunoassay (IL-17F and IL-22) in a biomarker subgroup with similar baseline characteristics as the overall study population (n=201). Samples from demographically matched healthy subjects (n=30) were procured independently as a control group for biomarker analyses. In this post hoc exploratory analysis, statistical significance is defined as fold change >1.5 and $p<0.05$.

Results Compared to healthy subjects, trial participants with SLE had significantly elevated serum levels of IFNα, IFNγ, IL-12/23 p40, TNFα, IL-10, IL-15, and IL-16, but not IL-17F or IL-22. Among participants with SLE, elevated serum IFNα levels were associated with higher levels of anti-dsDNA (>75 IU/mL) and with the presence of other autoantibodies, including anti-RNP, -SSA, -SSB, and -Sm. Similar associations with each autoantibody were found with IFNγ except for anti-SSA. Clinically, both IFNα and IFNγ were found to be associated with higher overall baseline disease activity, as measured by SLEDAI-2K scores (>10 vs ≤10) and with active lupus nephritis. Skin disease was not associated with IFNα levels. However, lower IFNγ levels were found in participants with more severe skin manifestations (CLASI>6 vs ≤6). No clear difference in either IFNα or IFNγ levels were observed in patients with more arthritis activity (active joint count >6 vs ≤6).

Conclusion Inflammatory cytokines are dysregulated in individuals with SLE participating in a phase 3 clinical trial, similar