Repeated testing was 3.5 times higher in tANA tested patients than in those tested with MAP.

Linked EHR-Medicare data revealed a greater decrease in post-test vs. pre-test mean annualized outpatient lab testing in MAP(-) (-$985, $p < 0.0001$) vs. tANA(-) (-$356, $p<0.0001$) patients. A similar analysis of outpatient lab testing in EHR-HealthCore linked data revealed similar numerical trends but did not reach significance ($p > 0.05$).

Conclusions The significantly greater likelihood of SLE diagnosis and SLE medication initiation in MAP(+) vs. tANA(+) patients is consistent with improved clinical actionability, potentially shortening time to diagnosis. MAP(-) patients experienced a greater decrease in outpatient lab testing post-test relative to tANA(-) patients, supporting the improved negative predictive value of MAP vs. tANA, and MAP patients were tested 3.5 fewer times than tANA patients, reducing valuable health-care dollars.

1803 THE CLINICAL CHARACTERISTICS OF SLE PATIENTS WITH INCREASED LEVELS OF CELL-BOUND COMPLEMENT ACTIVATION PRODUCTS

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Background Cell-bound complement activation products (CB-CAPs), including erythrocyte-bound C4d (EC4d) and B-lymphocyte-bound C4d (BC4d), in a multi-analyte assay with algorithm (MAP) represent an important addition to the diagnostic armamentarium of SLE. The clinical and serologic phenotype of SLE patients with elevated levels of CB-CAPs has not been well described. Herein, we assessed the demographics, clinical manifestations, medical therapy, and laboratory variables of SLE patients with and without elevated CB-CAPs.

Materials and Methods This was a cross-sectional study of adult SLE patients (2012 SLICC or 2019 ACR/EULAR criteria) from June 2020 to July 2022. Patients completed the polysymptomatic distress scale. The managing physician scored the PGA and SLEDAI scores. Autoantibodies including ANA and anti-RNA-binding proteins were determined by ELISA. Anti-dsDNA was measured by immunofluorescence using the Crithidia luciliea assays. CB-CAPs were determined by flow cytometry. The multi-analyte assay panel (MAP) was determined using a 2-tier algorithm. All autoantibodies, EC4d, and BC4d were tested in Exagen's clinical laboratory. Fisher's exact test and Kruskal-Wallis test were used to analyze differences in clinical and laboratory variables between CB-CAPs positive and CB-CAPs negative patients.

Results In this cohort of 185 SLE patients (90% female, 60% Black, mean age 44 years), 70% were MAP positive and 46% were BC4d and/or EC4d positive. CB-CAPs positive patients were younger, but there were no differences in sex, ethnicity, race, or mean length of disease between CB-CAPs positive and negative patients. Although almost all patients met both SLICC and ACR/EULAR classification criteria, the total ACR/EULAR classification score was greater for CB-CAPs positive patients. Higher rates of nephritis, serositis, alopecia and hematologic criteria were observed in the CB-CAPs positive patients.

Additionally, CB-CAPs positive patient demonstrated evidence of SLE disease activity with significantly higher SLEDAI

Abstract 1803 Table 1 Demographics and SLE Disease Manifestations

	BC4d and/or EC4d Pos n=85	BC4d and EC4d Neg n=100	Overall n=185	p-value
Demographics				
Mean length of disease	13.0 (8.8)	14.0 (10.0)	13.5 (9.5)	0.5
Mean age (SD)	39.8 (13.9)	47.0 (13.1)	43.7 (13.9)	0.0004
% Female	78 (92%)	89 (89%)	167 (90%)	0.6
Black (n=179)	55 (67%)	53 (55%)	108 (60%)	0.09
Ethnicity Hispanic (n=180)	6 (7%)	4 (4%)	10 (6%)	0.5
SLE History and Classification				
2012 SLICC Criteria	84 (99%)	99 (99%)	183 (99%)	1.0
2019 ACR/EULAR Criteria	84 (99%)	93 (93%)	177 (96%)	0.07
2019 ACR/EULAR Total Score [Median (IQR)]	26 (21-33)	18 (13.5-24.5)	22 (17-29)	<0.0001
Renal	47 (55%)	38 (38%)	85 (46%)	0.03
Serositis	30 (35%)	19 (19%)	49 (26%)	0.02
Alopecia	54 (64%)	47 (47%)	101 (55%)	0.03
Hematologic	61 (72%)	53 (53%)	114 (62%)	0.01
Medications				
Hydroxychloroquine	71 (84%)	82 (82%)	153 (83%)	0.8
Methotrexate	8 (9%)	14 (14%)	22 (12%)	0.4
Azathioprine	17 (20%)	15 (15%)	32 (17%)	0.4
Mycophenolate	35 (41%)	33 (33%)	68 (37%)	0.3
Prednisone > 5mg	32 (38%)	26 (26%)	58 (31%)	0.1
Belimumab, Rituximab, or Cyclophosphamide	16 (19%)	13 (13%)	29 (16%)	0.3
Physician Assessments				
PGA	0.7 (0.7)	0.5 (0.6)	0.6 (0.6)	0.08
SLEDAI	4.1 (3.9)	2.1 (2.6)	3.0 (3.4)	<0.0001
SLEDAI Renal	13 (16%)	7 (7%)	20 (11%)	0.1
SLEDAI Rash	21 (25%)	13 (13%)	34 (18%)	0.06
Patient Assessments				
Polysymptomatic Distress Score (n=167)	8.1 (6.9)	10.0 (6.7)	9.1 (6.8)	0.09
Widespread pain index (n=167)	3.6 (4.5)	4.7 (4.2)	4.2 (4.3)	0.1
	n(%)	n(%)	n(%)	
Fatigue (mod-severe) (n=151)	33 (49%)	45 (54%)	78 (52%)	0.6
Depression (yes) (n=147)	31 (46%)	38 (48%)	69 (47%)	1.0

Abstract 1803 Table 2 Serologies

	BC4d and/or EC4d Pos	BC4d and EC4d Neg	Overall	
	n=85	n=100	n=185	p-value
MAP Positive (n=184)	77 (92%)	52 (52%)	129 (70%)	<0.0001
ANA (ELISA) positive	80 (94%)	71 (71%)	151 (82%)	<0.0001
Anti-dsDNA (Crithidia luciliae) positive	46 (54%)	20 (20%)	66 (36%)	<0.0001
Low C3 or C4	32 (38%)	11 (11%)	43 (23%)	<0.0001
Anti-Sm positive (n=159)	13 (19%)	4 (4%)	17 (11%)	0.008
Anti-U1RNP positive (n=181)	36 (44%)	22 (22%)	58 (32%)	0.002
Anti-RNP70 positive	24 (29%)	14 (14%)	38 (21%)	0.02
Anti-Cq1 positive	26 (31%)	14 (14%)	40 (22%)	0.007
APLA positive				
ACL IgM+, ACL IgG+, B2GP IgM+ or B2GP IgG+ (n=172)	16 (21%)	8 (9%)	24 (14%)	0.03
Anti-Ro60 positive	45 (53%)	40 (40%)	85 (46%)	0.1
Anti-Ro52 positive	26 (31%)	18 (18%)	44 (24%)	0.06
Anti-La/SSB positive	9 (11%)	6 (6%)	15 (8%)	0.3

scores. Numerically more CB-CAPs positive patients had SLEDAI rash and met SLEDAI renal criteria. There was no difference in medication use or features of polysymptomatic distress such as widespread pain, fatigue, or depression (table 1).

Serologic activity emerged as a hallmark of CB-CAPs positivity. CB-CAPs positive patients were more likely to have positive ANA, anti-Sm, anti-U1RNP, anti-RNP70, anti-C1q and anti-phospholipid antibodies than those who were CB-CAPs negative (table 2). Serologic markers of disease activity including elevated levels of anti-dsDNA and decreased C3 or C4 also tracked with CB-CAPs positivity (table 2).

Conclusion Narrowing the heterogenous clinical and immunologic features of SLE into endotypical subgroups is a crucial step toward precision medicine and personalized care in SLE. CB-CAPs positive patients represent an important subset of patients who are characterized by greater serologic activity and internal organ pathology. Moreover, the cumulative burden of SLE activity is greater in those with CB-CAPS positivity, as measured by the ACR/EULAR criteria score. CB-CAPs positivity could provide both diagnostic and prognostic information with implications for improved disease monitoring. Further studies are needed to assess the effects of targeted therapeutics and the long-term outcomes of the CB- CAPs positive endotype.

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1901 THE TOLEROGENIC EFFECTS OF IL-2 ON T REGULATORY CELLS (TREGS) ARE TGF-β DEPENDENT

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Background We and others have previously shown that IL-2 is essential for TGF-β to allow conversion of naïve $CD4^+CD25^-$ T cells into $CD4^+CD25^+Foxp3^+$ Tregs. To further those studies, we recently used IL-2- loaded nanoparticles (NPs) coated with anti-CD2 antibody (Ab) to target both T cells and NK cells in lupus mice, identifying a key role of a population of TGF-β-producing NK cells in the induction of the $CD4^+$ and $CD8^+$ $Foxp3^+$ Tregs that prevented disease.

Methods Anti-CD2 Ab-coated NPs made of polylactic-co-glycolic acid (PLGA) and encapsulating IL-2 or IL-2/TGF-β were used to inhibit a lupus-like disease characterized by a human anti-mouse graft versus host disease (GVHD) that develops after transfer of human PBMCs into immunodeficient NOD SCID mice.

Research NPs containing only IL-2 protected mice from autoimmune disease similarly to NPs containing both IL-2 and TGF-β. Remarkably, the blockade of TGF-β signaling with an ALK-V inhibitor not only abolished the protective effects of the NPs but also reduced the survival of the diseased mice.

Conclusions In the absence of TGF-β, IL-2 induces pathogenic T effector cells instead of promoting the induction of protective Tregs. This key role of TGF-β in the induction of Tregs has relevance for the ongoing clinical trials that employ low-dose IL-2 or IL-2 muteins in SLE and other autoimmune diseases to expand functional Tregs. Since lymphocyte production of TGF-β is decreased in SLE, our study suggests that in the immunotherapeutic management of SLE, one needs to correct the deficits of both IL-2 and TGF-β to optimally induce and expand functional Tregs.

2001 α-KETOGLUTARATE-DEPENDENT KDM6 HISTONE DEMETHYLASES EPIGENETICALLY REGULATE INTERFERON STIMULATED GENE EXPRESSION IN LUPUS

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The authors have declared that no conflict of interest exists.

Objective To investigate the hypothesis that interferon (IFN) stimulated gene (ISG) expression in systemic lupus erythematosus (SLE) monocytes is linked to changes in metabolic reprogramming and epigenetic regulation of ISG expression.

Methods Monocytes from healthy volunteers and SLE patients at baseline or following IFNα treatment were analyzed by extracellular flux analysis, proteomics, metabolomics, chromatin immunoprecipitation and gene expression.

Treatment of SLE monocytes or pristane-treated C57BL/6 mice with GSKJ4 assessed the effects of histone demethylases KDM6A/B on ISG expression.