compared to 39.4% of those diagnosed within a year. Respondents diagnosed after a year were more likely to report insurance not covering costs, long wait times for appointments with primary care physicians (PCP), and lack of nearby doctors treating lupus.

Conclusion Multiple factors associated with lupus diagnosis delays, including delayed access to specialists, onerous health care costs, and health insurance obstacles. An ongoing shortage of rheumatologists may further magnify the delay in diagnosis and explain the apparent long wait times for specialists, misdiagnosis, and increasing costs. Further practitioner education, rheumatology provider recruitment, and studies examining reasons for lupus diagnosis delays may help us better understand and reduce inequities in reaching a prompt lupus diagnosis.

It is important to recognize the limitations of the study; the convenience sample study design lacks the rigor of random sampling, some questions may have introduced recall bias, and socioeconomic status and disease burden at time of diagnosis weren't addressed in this survey.

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1400 – Lupus-targeted therapeutics

1401

EFFECTS OF ANIFROLUMAB ON RENAL DISEASE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background The type I interferon (IFN) receptor antibody, anifrolumab, has shown efficacy in patients with systemic lupus erythematosus (SLE) in the phase 3 TULIP-1 and TULIP-2 trials. Type I IFN dysregulation is associated with lupus nephritis (LN) pathogenesis. Pooled TULIP data were analyzed to assess baseline characteristics of patients with and without renal involvement and to evaluate the effects of anifrolumab on renal disease.

Methods TULIP-1 and TULIP-2 were randomized, placebo-controlled trials of intravenous anifrolumab in patients with moderate to severe SLE despite standard therapy, which excluded patients with severe active LN. Renal involvement at baseline was defined as any of the following: British Isles Lupus Assessment Group (BILAG)-2004 renal score A–C; SLE Disease Activity Index 2000 (SLEDAI-2K) renal score >0; urine protein–creatinine ratio (UPCR) >0.5 mg/mg. Baseline characteristics were evaluated in patients with and without renal involvement, and the following endpoints were compared for the anifrolumab 300 mg and placebo groups: cumulative UPCR (area under the curve, AUC) through Week (W)52; percentage of patients with UPCR >0.5 mg/mg at baseline who improved to UPCR ≤0.5 mg/mg at W52; cumulative glucocorticoid (GC) use (AUC) through W52; and percentage changes in complement C3/C4 from baseline to W52.

Results Of the 726 patients in TULIP-1/2 (anifrolumab, n=360; placebo, n=366), 99 had renal involvement at baseline (anifrolumab, n=45; placebo, n=54), 57 of whom had

Abstract 1401 Table 1 Renal endpoints in TULIP-1 and TULIP-2

Endpoint (baseline to Week 52)	Placebo	Anifrolumab 300 mg
UPCR AUC^a		
n	54	45
LS mean (SE)	271.8 (54.8)	217.7 (60.0)
LS mean difference (SE), 95% CI	−54.1 (54.3), −161.9, 53.6	
Improvement from >0.5 to ≤0.5 mg/mg UPCR^b		
n	33	24
Patients with improvement (%)	36.3	41.2
Difference,% (SE), 95% CI	4.9 (13.3), −21.1, 30.9	
Glucocorticoid AUC^a		
n	54	45
LS mean (SE)	3524.5 (339.0)	3314.2 (365.2)
LS mean difference (SE), 95% CI	−210.3 (332.6), −870.7, 450.1	
Change in C3/C4 (%)^c		
C3		
n	31	21
Mean (SE)	20.3 (6.2)	26.6 (5.0)
C4		
n	19	14
Mean (SE)	29.1 (12.0)	38.7 (13.8)

AUC, area under the curve; CI, confidence interval; LS, least squares; UPCR, urine protein–creatinine ratio; SE, standard error; n, number satisfying baseline inclusion criteria for subgroup.

^aPatients with baseline renal involvement; analysis of covariance.

^bStratified Cochran–Mantel–Haenszel.

^cPatients with renal involvement and abnormal C3/C4 at baseline.

UPCR >0.5 mg/mg (anifrolumab, n=24; placebo, n=33). Patients with vs without renal involvement had a lower mean age (37.8 vs 42.4 years) and were more likely to be male (14.1% vs 6.1%), Asian (16.2% vs 9.6%), IFN gene signature high (89.9% vs 81.5%), and anti-dsDNA positive (69.7% vs 40.4%); have a SLEDAI-2K score ≥10 (91.9% vs 68.4%); and be receiving GC ≥10 mg/day (67.7% vs 49.1%) or mycophenolate (26.3% vs 11.5%) at baseline. Among patients with baseline renal involvement, anifrolumab treatment was associated with a greater improvement vs placebo in cumulative UPCR (AUC) through W52 (table 1). More patients improved from UPCR >0.5 mg/mg at baseline to ≤0.5 mg/mg at W52 with anifrolumab vs placebo (table 1). Among patients with renal involvement, cumulative GC use (AUC) through W52 was lower with anifrolumab vs placebo and there were greater improvements in C3/C4 from baseline to W52 (table 1).

Conclusions TULIP data suggest renal benefit with anifrolumab in patients with SLE with mild/stable renal disease, supporting further investigation into anifrolumab's efficacy in patients with active LN.

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Trial Registration NCT02446912 and NCT02446899

1402

AUGMENTED GLUCOSE DEPENDENCY OF AUTOREACTIVE B CELLS PROVIDES A TREATMENT TARGET FOR LUPUS

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Background Lupus is an autoimmune disease characterized by antibodies directed against nuclear components that induce immune complex-mediated injury to multiple organs. Underlying lupus is the induction of T-cell-dependent activation and clonal expansion of autoreactive B cells in germinal centers resulting in their differentiation into plasma cells that secrete pathogenic autoantibodies. Heightened glucose metabolism is inherent to immune/inflammatory disorders, but little is known of its role in lupus etiology. Present treatments for lupus rely heavily on broad-spectrum immunosuppressive agents, and there is a need for targeted therapies that effectively counteract this systemic autoimmune disorder.

Methods Here we examined the metabolic and gene expression profiles of key autoimmune populations in mouse models of spontaneous lupus and their responses to treatment with the glycolysis inhibitor 2-deoxyglucose (2DG) in drinking water. Therapeutic efficacy in terms of survival after long- vs. short-term 2DG-exposed times was assessed on BXS^B.Yaa and NZBWF1 lupus-prone mice. Furthermore, a chimeric antigen receptor (CAR)-T immunotherapy was used to determine whether a targeted removal of an identified B cell subset can improve disease outcomes.

Results We found greater glucose uptake and glycolysis rate in spontaneous germinal center B cells (GCB) compared to that in follicular helper T cells (Tfh). The differential dependency on glucose oxidation between GCB and Tfh was determined, rendering GCB highly susceptible to oxidative stress-induced apoptosis triggered by glycolysis inhibition via 2DG. Short-term glycolytic inhibition selectively targeted GCB, sparing other autoreactive populations, including Tfh. This reduction of GCB is, in turn, responsible for improving kidney function and lifespan of treated mice. Moreover, we identified a subset of GCB, which express TNFSF17 and exhibit a higher reliance on glucose metabolism than TNFSF17⁺ GCB. Their depletion through its ligand TNFSF13-based CAR-T treatment significantly decreased mortality from lupus.

Conclusions Differential metabolic requirement for glucose between autoreactive GCB and Tfh dictates different sensitivity to apoptosis via glycolytic inhibition, and this provides a metabolic niche for targeted lupus treatment. Combining therapies that selectively dampen GCB metabolism for survival with T cell-based immunotherapy could provide new effective treatments for lupus.

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1403

THE EIF4 TRANSLATIONAL INHIBITOR PATEAMINE A IMPROVES IMMUNOLOGICAL AND NEUROLOGICAL FUNCTIONS IN BXS^B.YAA LUPUS MICE

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Background Systemic Lupus Erythematosus (SLE) is an autoimmune disease characterized by loss of tolerance and activation of the immune response. Clinical manifestations are heterogeneous and several organs can be affected including skin, joints, central nervous system and kidney. Traditional

treatments include the use of hydroxychloroquine, glucocorticosteroids, immunosuppressive and more recently, biological drugs such as belimumab or rituximab. In the last decade new alternatives have been proposed based on targeting interferon and cytokines. Mouse models have been extremely helpful to test the efficacy of new SLE therapies. In this work we analyze the therapeutic potential of a natural compound, Patemina A (PatA) to treat SLE. Pat A is an inhibitor of the translation initiation process with immunosuppressive properties that has been tested successfully in cancer mouse models.

Methods To test Pat A efficiency in SLE we used the BXS^B.Yaa lupus model. Animals were treated for 8 weeks starting at the initial stages of disease (12 weeks). Sera was collected every three weeks and disease signs were followed. At the final point we performed serological analyses (cytokines and autoantibodies), flow cytometry on spleen to evaluate different cell populations, kidney histological and functional assays and behavioral tests to evaluate neuropsychiatric changes.

Results Our data shows that Pat A treatment increases the survival rate and is able to reduce circulating levels of proinflammatory cytokines and autoantibodies. We also observed improvement of cognitive functions (learning/memory, and depression behavioral tests) together with a reduction of proinflammatory cytokines locally in the hippocampus.

Conclusion These data suggests that translation inhibition improves lupus disease signs at the immunological and neurological levels opening a new line of research based on translation inhibition to treat lupus and possibly other autoimmune diseases with an inflammatory component, and may be a complement for present day treatments.

1404

A PEPTIDE MIMETIC OF THE KINASE INHIBITORY REGION OF SUPPRESSOR OF CYTOKINE SIGNALING-1 ATTENUATES LYMPHOCYTE ACTIVATION AND LUPUS PROGRESSION IN MRL/LPR LUPUS MODEL

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Background Lupus progression is driven by the aberrant activation of T and B lymphocytes which promote a dysregulated cytokine milieu and produce pathogenic antibodies. Many cytokines, including interferon gamma (IFN- γ), utilize the janus kinase/signal transduction and activation of transcription (JAK/STAT) pathway for signal propagation. Suppressor of Cytokine Signaling-1 (SOCS-1) is an inducible, intracellular protein which regulates the JAK/STAT pathway and IFN γ signaling. We have previously shown that a peptide mimicking the kinase inhibitory region of SOCS1 (SOCS1-KIR) inhibited IFN- γ signaling and inflammation-mediated disease progression.

Using MRL/lpr mice, which spontaneously develop SLE-like disease, we test the hypothesis that SOCS1-KIR administration inhibits T and B lymphocyte activation leading to an amelioration in lupus pathology.