

Scenarios were identified using the top 13 organ involvement combinations, then patients were grouped into 7 categories based on GC dose and 10 patients per category were selected. Scenario information included: SLEDAI-2K score, organ involvement combination and GC dose.

3 rheumatologists ranked disease activity with PGA. An independent cohort was used for the validation in phase 3. We hypothesised that in patients with improvement/worsening by SLEDAI-2K, the change in SLEDAI-2K and SGI will correlate.

Results Scenario development is summarised in table 1. 131 scenarios were ranked by 3 rheumatologists leading to 393 records. Perfect LS agreement was achieved; ICC (2, k) of 0.89 (95% CI: 0.83, 0.89). A quadratic linear regression model relating GC and SLEDAI-2K was structured; $SGI\ score = SLEDAI-2K\ score + [3.65 + 0.29 * GC - 0.0027(GC * GC)]$. The weight score of GC doses was derived (Table 2). Construct Validity: 109 of the 158 patients improved, 38 remained unchanged, 11 worsened. SLEDAI-2K and SGI correlated highly ($r=0.87$) and changed in the same direction in patients with improvement/worsening proving the validity of SGI.

Conclusions We developed and validated a novel lupus disease activity index, SGI, that describes disease activity while accounting for GC dose.

12 VALIDATION OF A NOVEL DEFINITION OF LOW DISEASE ACTIVITY STATE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background and aims While a “Treat-to-target” principle is widely advocated in management of systemic lupus erythematosus (SLE), there is currently no internationally agreed definition of low disease activity in lupus. In 2015, the Asia-Pacific Lupus Collaboration presented a novel consensus definition of a safe state in lupus, the “Lupus Low Disease Activity State” (LLDAS). (<http://dx.doi.org/10.1136/annrheumdis-2015-207726>)

Methods This was a prospective study to determine whether LLDAS predicted lower flare-ups, damage and mortality. 339 SLE patients were recruited and followed for 30 months. Multivariable binomial regression was used to determine factors associated with LLDAS and Cox proportional hazard model to determine whether prior higher% of days in LLDAS would be associated with lower future flare-ups.

Results Mean patient age was 48.1 years and mean disease duration 19.6 years. Female to male ratio=16 to 1. 79 flare-ups were documented. 92.6% of patients had ever achieved LLDAS during the study period and 62.1% of patient-days were in LLDAS. No major demographic or prior disease presentations were found to be associated with the attainment of LLDAS. Patients with prior higher percentage of days in LLDAS had lower hazard of lupus flare-ups ($HR=0.420$, $p=0.015$) after adjustment for gender and age. The numbers of patient damage and death were insufficient for analysis.

Conclusions LLDAS is an independent construct achievable by most patients of different history or background. Our preliminary study shows LLDAS can predict the risk of future flare-ups though further studies are needed to determine whether it is associated less lupus-related damage and lower mortality.

Parallel Session 1: CNS lupus

13 ANTIBODY-MEDIATED NEUROPSYCHIATRIC LUPUS

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Neuropsychiatric lupus manifestations, especially the common disorders of mood and cognition, can be mediated by cytokines or by antibodies. In particular, a subset of anti-DNA antibodies has been shown to bind the N-methyl d-aspartate receptor. The antibodies preferentially bind the active configuration of the receptor, augmenting the effects of ligand binding. Meta-analysis has confirmed that high serum titers of these antibodies, present in 30%–40% of SLE patients, are associated with cognitive impairment.

In a mouse model, antibody within the circulation is not harmful to the brain unless there is a breach in blood-brain barrier integrity. If there is an insult to the hippocampal vasculature, antibody gains access to hippocampal neurons and mediates tissue damage in 2 distinct stages. First, there is immediate antibody-mediated excitotoxicity causing neuronal loss. Second, after antibody is no longer present in the brain, there is microglial activation and dendritic pruning of surviving neurons. The brain injury that ensues leads to impairment in spatial cognition.

These studies suggest there are two distinct approaches to therapy; one might modulate the initial damage by neutralising the pathogenic antibodies or maintaining blood-brain barrier integrity, the other might mitigate the later damage by inhibiting microglial cells.

14 INCREASED HETEROGENEITY OF BRAIN PERFUSION IS AN EARLY MARKER OF CENTRAL NERVOUS SYSTEM INVOLVEMENT IN ANTIPHOSPHOLIPID ANTIBODY CARRIERS

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Background and Aims The non-criteria neuropsychiatric manifestations of antiphospholipid syndrome include headache, dizziness, vertigo, seizure, depression and psychosis. There was still no objective method qualified to detect the early central nervous system involvement in non-criteria antiphospholipid syndrome. We evaluated the effectiveness of Tc-99m ECD SPECT in assessing circulatory insufficiency in the brains of patients with antiphospholipid antibodies and neuropsychiatric symptoms but without thromboembolism.

Methods Patients with a history of positive antiphospholipid antibodies and neuropsychiatric symptoms but without thromboembolism composed the case group; patients without antiphospholipid antibody served as the control group. Subjects with autoantibodies to extractable nuclear antigens were

excluded from this study. All patients underwent Tc-99m ECD SPECT and were classified by the number of positive antiphospholipid antibodies they carried. The heterogeneity of brain perfusion was defined as the coefficient of variation. Analysis of variance (ANOVA) was used to evaluate the differences between groups.

Results Total 60 adult patients were included in this study. There were 54 patients in the case group and 6 patients in the control group. The mean age was 38.3 ± 11.5 years. There were 52 women and 8 men. There was no significant difference in mean brain perfusion between groups ($p=0.69$). However, Tc-99m ECD SPECT demonstrated significant heterogeneity of brain perfusion in relation to the number of antiphospholipid antibodies ($p=0.01$).

Conclusions This is the first study to show that Tc-99m ECD SPECT can detect the increased heterogeneity of brain circulation in non-criteria antiphospholipid antibody carriers with neuropsychiatric manifestations.

15 THE ROLE OF INTRACISTERNAL DEPOSITED IGG IN THE PATHOGENESIS OF NEUROPSYCHIATRIC SYMPTOMS OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background and Aims Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterised by high levels of autoantibodies and multi-organ tissue damage including damage of the central system. Nerve system disease in SLE includes neurologic and psychiatric events, collectively termed neuropsychiatric SLE (NPSLE). Currently, the pathogenesis of NPSLE is unclear. We investigated pathogenesis of NPSLE in this study.

Methods To understand the pathogenesis of NPSLE, we analysed the medical records of 1131 patients with SLE, and conducted experiments by using lupus-prone mice and mice with intracisternal injections of lupus serum containing high level of autoantibody and mice with gene deficiency.

Results There are 59 patients with NPSLE clinical manifestation including headaches, seizure disorder, cognitive dysfunction, cerebrovascular disease, etc. MRI examination in 14 patients with NPSLE indicates 50% normal and 50% abnormal signals. Lupus-prone mice spontaneously develop meningitis. Meningitis was developed in normal mice with intracisternal injection of lupus serum but not healthy serum; IgG is a major contributor in this meningitis. Monocyte/macrophage, complement and selectin are involved in the development of meningitis induced by lupus serum. This meningitis is dependent on dose of IgG but not associated with kinds of autoantibodies and systemic disease activity. Severity of meningitis induced by lupus serum IgG was significantly reduced in TNF deficient mice compared to wild mice.

Conclusions The deposited IgG or IgG contained immune complex in brain tissue exerts an important role in the pathogenesis of meningitis. This finding will promote development of effective therapeutic strategy to patients with NPSLE.

Parallel Session 2: Cell targeting in SLE

16 HIGH SALT PROMOTES SYSTEMIC LUPUS ERYTHEMATOSUS BY TET2-INDUCED DNA DEMETHYLATION AND DRIVING THE DIFFERENTIATION OF TFH CELLS

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Background and Aims Systemic lupus erythematosus (SLE) is an autoimmune disorder that is characterised by the presence of autoantibodies and immune dysregulation. The pathogenesis of SLE has not been elucidated. The induction of epigenetic changes by environmental factors such as diet may also be relevant. A high-salt diet is considered an important contributor to cardiovascular and renal diseases, and recent research has indicated that a high-salt diet can induce autoimmunity.

Methods In this study, the effects of high salt on various immune cells and in MLR/lpr mice were observed, and the underlying mechanisms were investigated by flow cytometry, high-throughput sequencing, DNA methylation map, ChIP-PCR.

Results In this study, high salt (sodium chloride, NaCl), under physiological conditions, was demonstrated to increase the differentiation of Tfh. A high-salt diet markedly increased lupus features in MRL/lpr mice. The mechanism is NaCl-induced DNA demethylation via the recruitment of the hydroxytransferase Ten-Eleven Translocation 2 (TET2). Gene silencing of TET2 obviously diminished NaCl-induced Tfh cell polarisation *in vitro*. In addition, the gene expression of sh2d1a, map3k1, spn and stat5b was enhanced after NaCl treatment, consistent with the findings in lupus CD4⁺T cells. However, only spn was directly regulated by TET2, and spn was not the sole target for NaCl.

Conclusions High-salt treatment promotes SLE in mice and the underlying mechanism might be NaCl enhancing Tfh cell differentiation by TET2 inducing global and gene specific DNA demethylation. Our findings not only explain the epigenetic mechanisms of high-salt induced autoimmunity but also provide an attractive molecular target for intervention strategies of SLE.

Parallel Session 4: Lupus reflections across the continents: are we addressing the needs of our patients?

17 CAPABILITIES OF EUROPEAN LUPUS GROUPS: MEMBERS OF LUPUS EUROPE

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Background Lupus patient organizations (POs) are becoming increasingly important stakeholders in political and medical healthcare decision-making processes. LUPUS EUROPE is an umbrella organization of national lupus groups in Europe.

Objectives To identify the different structures and capabilities among European lupus groups.