Background and aims Ozanimod (RPC1063) is a specific and potent small molecule modulator of $S1P_{1,5R}$ that has shown therapeutic benefit in clinical trials of relapsing multiple sclerosis and ulcerative colitis. Its metabolite, RP-101075, shares ozanimod's specificity profile at the S1P receptor family *in vitro*, and its pharmacokinetic (PK) and pharmacodynamic profile *in vivo*.
Methods The (NZB×NZW)F1 model was used in therapeutic dosing mode to assess the benefit of an $S1P_{1,5R}$ modulator in systemic lupus erythematosus (SLE), compared to cyclophosphamide.
Results As predicted for an $S1P_{1,5R}$ modulator, treatment with 0.3, 1 and 3 mg/kg RP-101075 resulted in a dose-dependent reduction in circulating T and B cells, achieving 62%–99% decrease across all doses tested. Compared to vehicle treated animals, 3 mg/kg RP-101075 reduced proteinuria over the duration of the study (34±5 vs 18±1 U*week; p<0.0001), and blood urea nitrogen (36±5 vs 21±3 mg/dL; p<0.0001). Additionally, RP-101075 reduced kidney disease in a dose dependent manner, as quantified by histological assessment of mesangial expansion, endo- and exo-capillary proliferation, interstitial infiltrates and fibrosis, glomerular deposits and tubular atrophy. In addition, RP-101075 significantly reduced expression of fibrotic and immune genes in the kidneys, with minimal effect on IFN-inducible genes. Of particular note, RP-101075 lowered the number of plasmacytoid dendritic cells, a major source of IFNα in lupus patients, and all B and T cell subsets in the spleen.
Conclusions Given that RP-101075 shares the pharmacokinetic profile of ozanimod and reduces circulating lymphocytes similarly, ozanimod warrants clinical evaluation as a potential treatment for SLE.

80 IS SPLENECTOMY A SAFE AND EFFECTIVE THERAPEUTIC OPTION IN SYSTEMIC LUPUS ERYTHEMATOSUS? A SINGLE-CENTRE STUDY

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Background and aims Thrombocytopenia is a relatively common feature in systemic lupus erythematosus (SLE) patients, although severe thrombocytopenia is rare. Splenectomy is considered an acceptable treatment option for refractory thrombocytopenia in different haematological conditions. However, its role in SLE has been controversial, due to potential surgical complications and to its possible association with SLE flares. The aim of this study was to determine safety and efficacy of splenectomy in a cohort of SLE patients.
Methods We included all patients with SLE who fulfilled ≥4 ACR criteria, and underwent splenectomy between 2000 and 2015 in a tertiary care centre in Mexico City. Patients with other rheumatic diseases (except for anti-phospholipid syndrome) were excluded. We recorded demographic, clinical and serological characteristics at the time of surgery and during follow-up.
Results Thirty-six patients were included, 91.7% were women and mean age was 33.31±12.95. Refractory thrombocytopenia was the surgical indication in 28 patients (77.7%). Laparoscopic splenectomy was performed in 80.6% of cases. Two patients had surgical complications (intra-abdominal sepsis and pancreatic fistula). There were no deaths directly associated with the procedure. Among patients with thrombocytopenia, 85.7% achieved complete remission, in a mean period of 1.65 ±3.13 months. Cumulative prednisone dose in the year after the surgery was lower than the year before (8.7±5.8 vs 4.2 ±3.2 grams, p<0.01). Mean SLEDAI score at baseline was 3.53±2.9, and it decreased at 3 and 6 months (1.15±2.07 and 1.21±2.38, p<0.01, respectively) during follow-up.
Conclusions Splenectomy is a safe procedure in SLE patients, and it represents an effective therapeutic option for refractory thrombocytopenia.

81 OUTCOMES OF MULTI-TARGET THERAPY USING MYCOPHENOLATE MOFETIL AND TACROLIMUS FOR REFRACTORY LUPUS NEPHRITIS

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Background and aims Outcomes of systemic lupus erythematosus (SLE) has significantly improved over the years. However, it can still be unfavourable when there is major organ involvement such as lupus nephritis and standard therapies fail. Outcomes of multi-target therapy using mycophenolate mofetil (MMF) and tacrolimus in SLE patients who were refractory to standard therapy was assessed.
Methods Retrospective analysis was done in patients with biopsy-confirmed lupus nephritis class III or IV who failed to achieve complete response with standard induction therapy for 24 weeks and switched to multi-target combination therapy with MMF and tacrolimus. Outcomes including renal response, urine protein/creatinine ratio (UPCR), glomerular filtration rate (GFR), serum albumin, and complements were assessed at 24 weeks.
Results A total of 20 patients, with mean age of 27.9±8.2 years and 82.8% female, who initiated MMF and tacrolimus combination therapy were included. At 24 weeks, 25.9% showed complete response and 37.0% showed partial response. When all patients were compared, the mean UPCR increased from 3.06±3.00 at baseline to 3.21±4.23 at 24 weeks and GFR declined from 96.55±37.07 mL/min/1.73m^2 to 92.00±41.12 mL/min/1.73m^2. But in subgroup comparison, UPCR decreased from 1.82±0.86 to 1.39±0.85 in patients who had shown partial response to standard induction therapy and increased from 5.61±2.93 to 8.62±4.11 in no response patients.
Conclusions Multi-target therapy combining MMF and tacrolimus can be considered in patients who had partial response to standard induction therapy in patients with lupus nephritis.

82 ETHANOL PREVENTS DAMAGE OF SKIN, KIDNEY AND JOINT IN LUPUS-PRONE MICE BY REGULATING LIPID RAFTS

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Background and aims Ethanol has been elaborated to have a beneficial effect on destructive arthritis. Nevertheless, the

effect of ethanol on the development of systemic lupus erythematosus (SLE) remains controversial. This study was performed to determine the potential role of moderate ethanol consumption in SLE pathological progression and clarify its functional mechanism.

Methods We used MRL/lpr mice to assess whether ethanol drinking has any impact on the development of SLE and investigated whether ethanol regulates pathologic progression of SLE through inhibiting lipid rafts.

Results We found that 10% ethanol *in vivo* delayed disease progression and organ damage and prolonged survival. *In vitro* ethanol treatment not only inhibited the aggregation, proliferation, adhesion molecule expression and IFN-γ secretion of T cells, but also decreased lipid raft clustering on T cells. In addition, ethanol inhibited SLE serum-induced skin inflammation and monocyte differentiation into dendritic cells (DCs). Furthermore, ethanol treatment of monocytes that were in the process of differentiating into DCs decreased lipid raft clustering.

Conclusions These data strongly support the viewpoint that ethanol delays the disease progression of SLE by inhibiting lipid raft clustering and suggest that moderate drinking of ethanol may have a protective value for patients with SLE.

83 BIIB059, A MONOCLONAL ANTIBODY TARGETING BDCA2, DEMONSTRATES EVIDENCE OF PROOF OF BIOLOGICAL ACTIVITY IN SUBJECTS WITH CUTANEOUS LUPUS

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Background and aims Type I interferons (IFN-I) are central to the pathogenesis of systemic lupus erythematosus (SLE). BDCA2 is a plasmacytoid dendritic cell (pDC)-specific receptor that, upon engagement, inhibits the production of IFN-I and other inflammatory mediators. In this first-in-patient phase 1b study, biological activity of BIIB059, a humanised anti-BDCA2 monoclonal antibody, was evaluated in SLE subjects with active cutaneous lupus (CLE).

Methods 12 adult SLE subjects with active CLE received a single IV administration of either BIIB059 20 mg/kg (n=8) or placebo (n=4). A panel of IFN-responsive genes (IRG) was assessed from whole blood. Cellular infiltration and expression of MxA and IFITM3 were evaluated in skin biopsies from active lesions at baseline and week 4. CLE disease activity was determined using the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI). Safety data were also collected.

Results BIIB059 decreased the expression of IRG in blood and MxA and IFITM3 proteins in skin. CD45+ cells were reduced in skin biopsies of BIIB059-treated subjects. The reduction in inflammatory cells as well as MxA and IFITM3 expression at week 4 correlated with improvement in CLASI activity score at week 12. BIIB059 was well tolerated with no withdrawals due to AEs.

Conclusions The study, confirming the major role played by pDCs in the production of IFN-I in the blood and skin in CLE, supports further development of BIIB059.

84 PROSPECTIVE SINGLE CENTRE STUDY OF EFFECTIVENESS OF UPFRONT RITUXIMAB AND MYCOPHENOLATE WITH MINIMUM STEROID IN SLE

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Background and aims Treatment options for SLE have significant morbidity and mortality. Side effects from corticosteroid usage limit patient adherence and treatment efficacy. B cell depletion appears to target a critical pathophysiological pathway in SLE. Trails with rituximab has shown mixed results.

We aim to analyse our experience of using rituximab and mycophenolate upfront on presentation with minimum oral steroids.

Methods 12 patients with SLE, seen between Jan 2015 to march 2016, were included in the study. All patients completed 6 months of follow-up. Patients were treated with 2 doses of rituximab (1 g) and methyl prednisolone (500 mg) on days 1 and 15, and maintenance treatment of mycophenolate mofetil (2000mg) and low dose prednisolone (<7.5 mg) which was tapered off.

Results 10 were females and 2 males. Mean age of the patients is 24.5. 9 had lupus nephritis, 1 mesenteric vasculitis, 1 CNS vasculitis and 1 severe cutaneous vasculitis with pancytopenia. Average SLEDAI improved from 14 to 4. 6/9 LN attained complete renal remission and 2 partial remission. one patient died due to infection and renal disease 15 days after infusion. 2 vasculitis and one NPSLE patient improved completely. Two patients had infection requiring hospitalisation with in 8 weeks of infusion and one patient had severe bradycardia during the infusion and received only 1000 mg rituximab. Steroid was stopped by 6 months in 6 patients and in the dose was below 5 mg in rest.

Conclusions Early Rituximab and mycophenolate is an effective option for treating severe lupus and has steroid sparing property.

85 SAFETY OF BELIMUMAB IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN CLINICAL PRACTICE SETTING

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Background and aims Clinical trials have demonstrated a safety profile of belimumab in SLE patients. Safety of belimumab under daily clinical practice is less well known. Our objective