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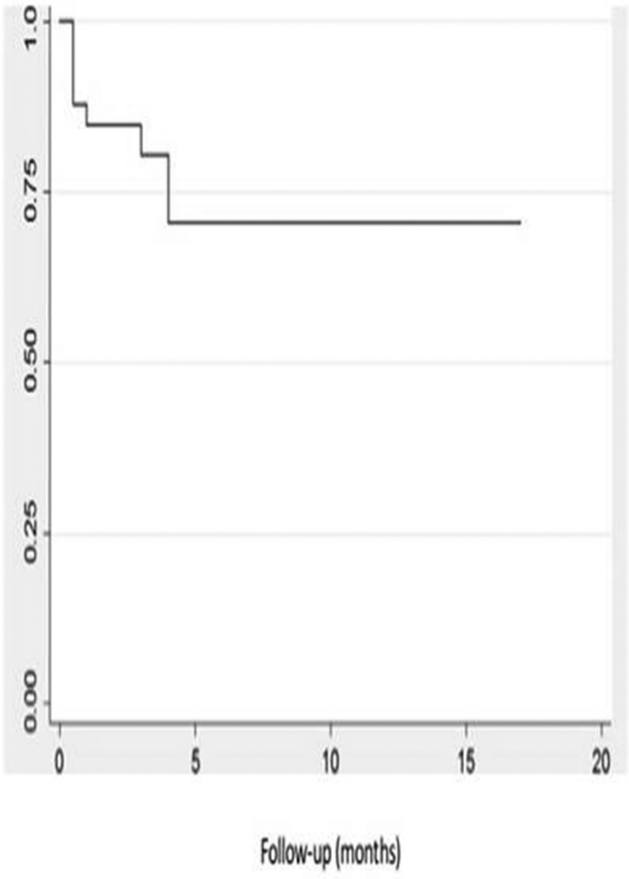
Background and aims Clinical trials have demonstrated a safety profile of belimumab in SLE patients. Safety of belimumab under daily clinical practice is less well known. Our objective

was to investigate safety of belimumab in patients with active SLE in daily clinical practice.

Methods We included patients with diagnosis of SLE (ACR criteria) treated at Medicarte IPS from March 2015 to October 2016. Medicarte is a referral centre for the integral medical care and pharmaco-surveillance of patients under biologic therapies in 13 cities in Colombia. Clinical information was obtained from electronic records. Adverse events (AE) were carefully evaluated during treatment.

Results Thirty three patients (all female) with active SLE were included. Mean age was 38.0±11.8 years, and mean disease duration was 10.6±9.2 years. Main refractory manifestations were musculoskeletal (100%), renal (45%), and mucocutaneous (42%). Background medications included MMF (87%), antimalarials (84%), MTX (72%), azathioprine (39%) and RTX (33%). Mean follow-up under belimumab treatment was 7.9 ±5.6 cycles. Mean prednisone doses were 12.0±11 mg/d. Only 8 (24%) out of 33 patients developed any AE. With a mean exposure time of 5.72 months, AE incidence rate, expressed as events per 100 p/months was 4.2 (Figure 1). The most common AE were: infusion reactions (3), urinary (2), and respiratory infections (1), herpes zoster (1) and mild pancytopenia (1). None of the patients stopped belimumab due AE

Conclusions Belimumab was safe in clinical practice setting; only a few number of mild side AE were recorded. None of the patients discontinued belimumab treatment due AE.



Abstract 85 Figure 1

86 MESENCHYMAL STEM CELLS INDUCE LYMPHOCYTES APOPTOSIS INDEPENDENT OF BIM AND BCL-XL IN LUPUS MICE

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Background and aims Mesenchymal stem cells (MSCs) have recently been used successfully in humans to control a lot of diseases. However, the mechanisms involved in their immunomodulatory effects remain a matter of debate. Here we explored whether lymphocytes apoptosis involved in the therapeutic effects of UC-MSCs in lupus mice.

Methods $1^{\wedge}$ 10^{6} of human UC-MSCs were injected into B6. lpr mice via tail vein and 6, 24 hours and 4 weeks later, all the mice were sacrificed, the apoptosis of lymphocyte in peripheral blood and spleen tissues as well as the expressions of Bim and Bcl-xl were detected by FACS, the immune cell subpopulations and cytokines in serum were also examined at 6 and 24 hours, respectively. The curative effects were assessed 4 weeks later.

Results UC-MSCs ameliorated disease progression of lupus mice at 4 weeks, increasing the percentage of Treg while downregulating Tfh, plasma cells and Th1 cells, decreasing spleen weight and repairing kidney lesion. UC-MSCs promoted lymphocyte apoptosis in peripheral blood and spleen at 6 and 24 hours, and reduced serum TGF-β1 levels, but did not affect Bim and Bcl-xl expressions in CD4+ and CD8+ T cells. Meanwhile, the percentage of Treg was significantly increased in the MSCT group at both 6 and 24 hours. Reductions in the proportions of plasma cells, Th1, Th2 cells were also evident at 24 hours after MSCs infusion.

Conclusions UC-MSCs exhibit extensive pro-apoptosis properties against lymphocytes in B6.lpr mice, which may offer a form of immunomodulatory therapy for lupus.

87 SELECTIVE AND ORALLY AVAILABLE SMALL MOLECULE INHIBITORS OF TLR7 AND 8 FOR THE TREATMENT OF LUPUS

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Background and aims The toll-like receptors (TLRs) are critical participants in vertebrate innate immune recognition of pathogen-associated molecular patterns (PAMPs). Diverse ligands act as "danger signals" detected by this component of the innate immune system. TLR7 and 8 are located in the endosomes of specific immune subpopulations, and are activated by single-stranded RNA from viruses or by autologous RNA fragments bound to immune complexes, inducing the generation of cytokines such as interferons (specifically IFN-alpha) and IL-6. Strong genetic evidence supports variants in TLR7 as contributors to development of systemic lupus erythematosus (SLE).

Methods *In vitro* and *in vivo* assays were used to guide development of potent and specific small molecule inhibitors.