Background and aims Ozanimod (RPC1063) is a specific and potent small molecule modulator of S1P<sub>1,5R</sub> 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<sub>1,5R</sub> modulator in systemic lupus erythematosus (SLE), compared to cyclophosphamide.

Results As predicted for an S1P<sub>1,5R</sub> 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 IFN 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.

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

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.