**Background** Lupus nephritis is a major risk for overall morbidity and mortality in SLE (Systemic lupus erythematosi s), and despite potent anti-inflammatory and immunosuppressive therapies still ends in Chronic Kidney Disease (CKD) or End Stage Renal Disease (ESRD) for too many patients. Renalase is a novel, kidney secreted cytokine-like protein that promotes cell survival.

**Aim of the work** studying the relationship between level of Human Serum Renalase (RNLS) with LN and its role in the disease activity and progression.

**Methods** For the current cross-sectional study 23 healthy controls and 48 patients with LN were screened and 30 subjects were selected. These patients were subdivided into two equal groups according to disease activity measured by SLEDAI (SLE Disease Activity Index). Human Serum Renalase (RNLS) concentration was measured by a highly sensitive, commercial sandwich enzyme immunoassay which uses (RNLS) antibody to capture Renalase from serum. Assessment before and after treatment was done for 17 patients who received prednisone, and immunosuppressive therapy were recruited and followed up for three months to evaluate the serum renalase levels before and after treatment.

**Results** The level of renalase was significantly higher in LN patients compared to healthy controls, (P value<0.001). Moreover, patients with active LN had higher serum renalase levels compared to patients with inactive LN (P value<0.005) Serum renalase levels were positively correlated with SLEDAI, 24 hour urine protein excretion, ds-DNA and ESR and CRP but inversely correlated with serum C3 and the class (especially in proliferative type (Class III, IV, more than class V). Renalase amounts decreased significantly after three-months of standard therapy. Also we found there is insignificant difference of renlase level according to treatment by MMF(mycophenolate mofetil) and Cyclophosphamide during and after activity (P value=0.655, 0.550)

**Conclusions** Serum renalase levels were correlated with disease activity in LN. Serum renalase might serve as a potential indicator for disease activity in LN.

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**Abstracts**

**214 RELATIONSHIP BETWEEN SERUM LEVEL OF RENALASE AND LUPUS NEPHRITS ACTIVITY**

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Results Among 323 participants, 89% were female, 39% Asian, 11% African American, 22% Hispanic of any race, and 29% White. Mean age was 45±14; mean age at diagnosis 29 ±12. Nearly half of respondents had a college degree. SDI at the baseline study visit ranged from 0 to 10 points, mean 1.8 ±2.0; 70% of the cohort had SDI>0. The regression model showed strong evidence (p=0.01) for interaction of age of diagnosis with race/ethnicity. As seen in the figure 1, SDI scores in racial/ethnic minorities were much higher among those diagnosed at younger ages; this relationship was not seen among whites.

Conclusions In this multi-ethnic cohort of SLE patients, the association of diagnosis age and disease damage varied according to race/ethnicity, with whites diagnosed at younger ages accumulating less damage than those in other racial/ethnic groups diagnosed at comparable ages. Future research should examine if these differences are due to phenotypic differences among the groups, diagnostic delays, or other access to care issues.

Funding Source(s): Centers for Disease Control and Prevention (U01 DP005120)
sided bootstrapped confidence interval, which is well below the 10 ms threshold of regulatory concern (ICH-E14 guidance).

**Conclusions** Evobrutinib was well-tolerated in healthy volunteers, with predictable PK and no prolongation of QT interval (QTcF). Evobrutinib is undergoing clinical investigation in SLE and other autoimmune diseases.

**Funding Source(s):** Merck KGaA, Darmstadt, Germany

**INHIBITION OF BRUTONS TYROSINE KINASE (BTK) PREVENTS INFLAMMATORY MACROPHAGE DIFFERENTIATION: A POTENTIAL ROLE IN SLE**

**Background** Brutons tyrosine kinase (BTK) mediates B cell receptor (BCR) and Fc receptor (FcR) signaling in several hematopoietic cell lineages, including B cells, macrophages and neutrophils. The BTK inhibitor evobrutinib silences B cells and prevents innate immune activation via FcR and has been shown to be efficacious in a preclinical model for SLE. Macrophages can have pro-inflammatory and anti-inflammatory properties and thus they play a crucial role in exacerbation versus control of autoimmune disease. BTK function has been implied downstream of certain cytokine receptors that control macrophage differentiation. The aim of this preclinical study was to investigate the effect of BTK inhibition on the differentiation and activation of monocytes and macrophages.

**Methods** Monocytes were isolated from the peripheral blood of healthy volunteers. BTK activation was analyzed by Western blot following a 30 min BTK inhibitor treatment and a subsequent granulocyte-macrophage colony-stimulating factor (GM-CSF) stimulation time course. Survival of GM-CSF differentiated M1 cells was analyzed by flow cytometry following AnnexinV/PI staining. Expression levels of interleukin (IL)-1ß and IL-10 were determined by quantitative polymerase chain reaction following 48 hours of GM-CSF stimulation and BTK inhibitor treatment. Tumor necrosis factor alpha (TNF-) levels in cell culture supernatants were measured by ELISA following overnight lipopolysaccharide stimulation and BTK inhibitor treatment. The uptake of apoptotic cells by M2 macrophages was analyzed by flow cytometry.

**Results** BTK was activated downstream of the GM-CSF receptor. In line with this finding, in vitro GM-CSF differentiated M1 macrophages underwent apoptosis upon BTK inhibition using evobrutinib. Monocytes treated with GM-CSF in the presence of BTK inhibitor secreted less TNF- and expressed...