weeks), with 4 having CR and 6 PR. The median response duration (MRD) was 12 weeks.

Conclusion: Our study provided preliminary but promising clinical evidence for iguratimod in treating refractory LN patients. A large randomized clinical trial is needed to establish its safety and efficacy for refractory LN.

REFERENCES:

- [1] Yan Q, Du F, Huang X, Fu Q, Chen S, Dai D, et al. Prevention of immune nephritis by the small molecular weight immunomodulator iguratimod in MRL/lpr mice. *PLoS One*. 2014;9(10):e108273.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.875

FRI0216B

SELECTIVE IRAK4 INHIBITOR DAMPENS MYD88 SIGNALING AND AMELIORATES INFLAMMATION AND FIBROSIS IN A MOUSE MODEL OF LUPUS NEPHRITIS

Dania Rabah¹, Ramon Bonegio², Agnes Gardet¹, Holly Legault¹, Ian Rifkin², Ti Wang¹, Chris Roberts¹, Jeffery Vessels¹, Norm Allaire³, Andrea Bertolotti-Ciarlet⁴, Kevin Guckian¹. ¹Biogen, Cambridge, United States of America; ²Boston University, Boston, United States of America; ³Cystic Fibrosis Foundation Therapeutics, Lexington, United States of America; ⁴Takeda, Cambridge, United States of America

Background: IRAK4 is an important signaling mediator of the innate immune system. IRAK4 initiates MyD88-dependent signaling from most TLRs and from IL-1Rs, resulting in downstream production of pro-inflammatory cytokines¹.

Objectives: Inhibition of IRAK4 kinase activity is a promising therapeutic approach for the treatment of autoimmune diseases, such as lupus. To this end, we identified a potent and highly selective inhibitor of IRAK4 kinase activity, BIIB-IRAK4i.

Methods: Recombinant kinase assays and DiscoverX kinomeScan were used to measure BIIB-IRAK4i kinase inhibition and selectivity, respectively. BIIB-IRAK4i-mediated proximal and distal pharmacodynamics effects (PD) were measured in both cell lines and whole blood assays. The ability of BIIB-IRAK4i to inhibit cytokine production induced by TLR ligands was measured *in vitro* and *in vivo*. Acute antibody-mediated lupus nephritis mouse model, which is a TLR-7 dependent and characterized by severe glomerular proliferative lesions with crescent formation, was used to determine the efficacy of BIIB-IRAK4i.

Results: BIIB-IRAK4i displayed equipotent proximal inhibition of MYD88 signaling and distal inhibition of cytokine production *in vitro*. BIIB-IRAK4i led to potent inhibition of cytokine production in whole blood assays stimulated with various synthetic TLR ligands as well as more physiological stimuli such as immune complexes, a hallmark of lupus pathogenesis. BIIB-IRAK4i inhibited TLR9-mediated cytokine production with same potency *in vitro* and *in vivo*. In addition, BIIB-IRAK4i decreased both inflammation and fibrosis in an acute antibody-mediated lupus nephritis mouse model. BIIB-IRAK4i inhibited crescent formation as well as markers of tubulointerstitial fibrosis, which are both associated with decreased survival and adverse outcomes in human lupus nephritis.

Conclusion: Our study highlights that pharmacological inhibition of IRAK4 can reverse two key components of lupus nephritis; the inflammatory and the fibrotic response.

REFERENCES:

- [1] O'Neill LA and Bowie AG. The family of five: TIR-domain-containing adaptors in Toll-like receptor signaling. *Nat Rev Immunol*. 2007 May;7(5):353-64.

Disclosure of Interests: Dania Rabah Shareholder of: Employee and shareholder of Biogen, Employee of: Biogen, Ramon Bonegio Grant/research support from: Merck, Chugai Pharmaceuticals, Astra Zeneca, Aurinia Pharmaceuticals, Consultant for: Merck, Chugai Pharmaceuticals, Agnes Gardet Shareholder of: Biogen, Employee of: Biogen, Holly Legault Shareholder of: Biogen, Employee of: Biogen, Ian Rifkin Grant/research support from: Chugai, Merck, Biogen, Kyowa Kirin, Consultant for: Eisai, Ti Wang Shareholder of: Biogen, Employee of: Biogen, Chris Roberts Shareholder of: Biogen, Employee of: Biogen, Jeffery Vessels Shareholder of: Biogen, Employee of: Biogen, Norm Allaire Shareholder of: Biogen, Employee of: Biogen, Andrea Bertolotti-Ciarlet Shareholder of: Biogen, Takeda, Employee of: Biogen, Takeda, Kevin Guckian Shareholder of: Biogen, Employee of: Biogen

DOI: 10.1136/annrheumdis-2019-eular.3385

SLE, Sjögren's and APS – clinical aspects (other than treatment)

FRI0217

PREGNANCY OUTCOME IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS IN TERTIARY UNIVERSITY HOSPITAL IN EGYPT

Fatma Ibrahim Abdelrahman¹, Mohammed A. Mortada². ¹Zagazig University, Rheumatology and Rehabilitation, zagazig, Egypt; ²Zagazig University, Rheumatology and Rehabilitation, zagazig, Egypt

Background: Pregnant systemic lupus erythematosus (SLE) patients have various risks to their fetus and themselves because a severe disease flare may be life-threatening, and some of the medications that are used to treat SLE adversely affect fetus.⁽¹⁾

Objectives: To evaluate the pregnancy outcome in SLE patients and to determine the predictive factors for adverse fetal and maternal outcomes.

Methods: The study was conducted on the pregnant SLE patients attending Rheumatology department, Zagazig University hospitals in the period from January 2013 to January 2018. The data was collected retrospectively; demographic, laboratory and serological data on all patients, age at the onset of SLE, disease duration, systems affected, their disease activity using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), treatment received immunosuppressive regimen (dose and duration) before and during pregnancy, SLE flare during pregnancy, the fetal and the maternal outcomes.

Results: Fifty-two pregnancies were observed in 49 SLE patients with mean age of (27.5±5.6), mean SLE disease duration (3.7±2.2) and mean SLEDAI (5.4±6.1). 39 (75%) pregnancies with successful live births and 13(25%) fetal losses were observed. 36 of the live births (92.3%) were full-term and 3 (7.7%) were preterm births. Fetal losses included six spontaneous abortions, 3 stillbirths and 4 therapeutic abortions; 2 of them due to observed fetal anomalies and one due to life threatening lupus flare. We found SLEDAI significantly higher in patients with lost pregnancies ($p<0.0001$) than successful pregnancies. Proteinuria during pregnancy was a predictive factor for adverse fetal outcomes (odds ratio [OR] 19.7; $P<0.0001$), also the presence of antiphospholipid antibodies (OR 15.3; $P<0.0001$), low C3 and C4 (OR 15.3; $P<0.0001$), anti-RO antibodies (OR 11.1; $P=0.02$), anti-LA (OR 4.7; $P=0.03$), chronic hypertension (OR 54.8; $p<0.0001$) and SLE flares (OR 32; $p=0.003$). SLE flares occurred in 10 pregnancies (19.2%), mostly during the second trimester (60%). Renal involvement (70%) was the most common SLE flare during pregnancy. SLE flares during pregnancy were highly associated by nephritis prior to pregnancy (adjusted OR 9; $P=0.04$) and the presence of antiphospholipid antibodies (adjusted OR 12; $p=0.01$).

Conclusion: Favorable pregnancy outcome was observed in Egyptian SLE patients; particularly in those with longer period of remission. Planned pregnancy is very important to reduce undesirable fetal and maternal outcomes in SLE patients. The presence of lupus nephritis, chronic hypertension, antiphospholipid syndrome, active disease at the onset of pregnancy, and proteinuria were highly associated with bad outcome.

REFERENCES:

- [1] Phansenee, S., Sekararathi, R., Jatavan, P., & Tongsong, T. (2018). Pregnancy outcomes among women with systemic lupus erythematosus: a retrospective cohort study from Thailand. *Lupus*, 27(1), 158–164.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.8173

FRI0218

IMMUNOPHENOTYPIC SUBGROUPS OF SLE DEFINED BY AUTOANTIBODIES, GENE EXPRESSION AND FLOW CYTOMETRIC ANALYSIS

Marta Aguilar-Zamora^{1,2}, Hui Lu³, Zoe Betteridge³, Katie Dutton⁴, MD Yuzaifal MD Yusuf⁴, Antonios Psarras⁴, The Masterplans Consortium^{3,4}, Neil Mchugh³, Edward Vital⁴. ¹Hospital Universitario Dr. Peset, Rheumatology, Valencia, Spain; ²Fundación Valenciana de Reumatología, Valencia, Spain; ³University of Bath, Bath, United Kingdom; ⁴University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM), Leeds, United Kingdom

Background: SLE may be stratified according to a range of different immune assessments but the relationships between these are less well defined. MASTERPLANS is an MRC-funded consortium that seeks to identify immunophenotypic subgroups of patients that predict response to therapy.