Results: In addition to upregulated mRNA levels of RLRs IFIH1 (encoding for MDA5) and DDX58 (encoding for RIG-I), which we previously observed in pDC and monocytes of IFNpos pSS patients, gene expression of IFIH1 and DDX58 was also upregulated in B cells. Upregulation of mRNA levels of the DSRs IFI16 and ZBP1 was observed in monocytes and B cells from IFNpos patients. In pDC protein expression of MDA5, ZBP-1, IFI16 was increased in IFNpos pSS, while there were no differences in RIG-I. In monocytes protein expression of MDA5 was increased and a trend was visible for RIG-I and IFI16. B cells showed increased protein expression of MDA5 and a trend was observed for RIG-I, ZBP-1 and IFI16. These data indicate upregulation of RLRs and DSRs particularly in pDC of IFNpos pSS patients. To further look into the signalling of RLRs and DSRs, phosphorylation of TBK was studied in pDC, the main IFN-I producers, of pSS patients. Increased expression of pTBK1 was observed in pDCs from IFNpos pSS. Upon treatment with BX795, PBMCs from IFNpos pSS downregulated the production of IFN-I and mRNA expression of the ISGs MxA, IFI44, IFI44L, IFIT1 and IFIT3.

Conclusions: RLRs and DSRs are upregulated in IFNpos pSS. Signalling of these receptors could be blocked using a TBK1 inhibitor, which reduced IFN-I protein production and expression of ISGs in PBMCs of IFNpos pSS patients. As patented pharmacological inhibitors, amongst others a small molecule inhibitor, are available TBK1 inhibition is indicated as a potential future treatment target for IFNpos pSS.

REFERENCE:

[1] Maria, et al. ARD 2016.

Acknowledgements: The research for this manuscript was (partly) performed within the framework of the Erasmus Postgraduate School Molecular Medicine. The authors thank patients and healthy volunteers for taking part in this study.

Disclosure of Interest: I. Bodewes: None declared, E. Huijser: None declared, C. van Helden-Meeuwse: None declared, L. Tas: None declared, R. Huizinga: None declared, V. Dalm: None declared, M. van Hagen: None declared, N. Groot: None declared, S. Kamphuis: None declared, P. van Daele: None declared, M. Versnel Grant/research support from: Research funding Domainex

DOI: 10.1136/annrheumdis-2018-eular.4641

FRI0308

CORTICOSTEROIDS COMBINED WITH DOUBLET OR SINGLE-AGENT IMMUNOSUPPRESSIVE THERAPY FOR ACTIVE PROLIFERATIVE LUPUS NEPHRITIS

B. Liu¹, Y. Yu², Y. Tang¹, S. Fu¹, P. Liang¹, A. Xu¹. ¹Nephrology; ²Guangdong Provincial Key Laboratory of Malignant Tumor Epigenetics and Gene Regulation, Breast Tumor Center, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, China

Background: Current evidence exploring whether corticosteroids (C) plus doublet immunosuppressive therapy (IT) is superior to the classical combination of C with single-agent IT for active proliferative lupus nephritis (LN) is controversial.

Objectives: We aimed to clarify the efficacy and safety of C+doublet versus single-agent IT for active proliferative LN by a meta-analysis.

Methods: We searched for randomised clinical trials that evaluated the benefits and risks of C+doublet versus single-agent IT for active proliferative LN. The primary outcome was overall response rate (ORR). The second outcomes were the change from baseline in Systemic Lupus Erythematosus Disease Activity Index (SLE-DAI) score, negative conversion ratio of anti-double-stranded DNA (anti-dsDNA), and adverse events. The quality of the evidence was evaluated with the GRADE framework. The PROSPERO registry number is CRD42017068491.

Results: The analysis included 10 trials with 1587 unique patients. Compared with C+single agent IT, C+doublet IT was statistically significant with higher ORR (relative risk [RR], 1.22; 95% confidence interval [CI], 1.09 to 1.35; $p < 0.0001$; moderate certainty). In subgroup analysis, C+doublet IT without biologics resulted into significant higher ORR than C+single agent IT (RR, 1.30; 95% CI, 1.13 to 1.50; $p < 0.0001$; moderate certainty), while C+doublet IT including biologics improved ORR only for refractory severe LN (RR, 1.46; 95% CI, 1.09 to 1.96; $p = 0.012$; very-low certainty). A larger change from baseline in SLE-DAI score (standardised mean difference, -0.49 ; 95% CI, -0.68 to -0.30 ; $p < 0.0001$; moderate certainty) and a higher negative conversion ratio of anti-dsDNA (RR, 1.34; 95% CI, 1.06 to 1.69; $p = 0.014$; high certainty) were observed with C+doublet IT than with C+single agent IT. The rates of adverse events were similar between the two regimens (high to moderate certainty).

Conclusions: Compared with single-agent IT, the combination of corticosteroids with doublet IT improved clinical outcomes for active proliferative LN. C+doublet

IT including biologics may be a better regimen for refractory severe LN. There is imperative that prospective biomarker-driven trials to identify patients for whom C+doublet IT is most efficacious.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.1950

FRI0309

THE IMPACT OF BELIMUMAB AND RITUXIMAB ON HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

I. Parodis¹, A.H. Lopez Benavides¹, A. Zickert¹, S. Pettersson^{1,2}, S. Möller¹, E. Welin Henriksson¹, A. Voss³, I. Gunnarsson¹. ¹Department of Medicine, Rheumatology Unit; ²Division of Physiotherapy, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Stockholm, Sweden; ³Rheumatology Unit, Odense University Hospital, Odense, Denmark

Background: Accumulating evidence supports an impaired health-related quality of life (HRQoL) in patients with systemic lupus erythematosus (SLE). The impact of modern therapeutic interventions on patients' perception of HRQoL has not been explored in depth.

Objectives: The aim of this study was to investigate the effects of two biologic treatments – belimumab and rituximab – on SLE patients' HRQoL, fatigue and functional ability.

Methods: Patients with SLE from the Karolinska University Hospital treated with either belimumab (n=34) or rituximab (n=35) were included. Data were collected prospectively at treatment initiation and at months 3, 6, 12 and 24; these included the Medical Outcome Study short form-36 (SF-36) version 2, functional assessment of chronic illness therapy (FACIT)-Fatigue scale version 4, EuroQol research foundation 5-dimension (EQ-5D) health questionnaire, and Stanford health assessment questionnaire disability index (HAQ-DI).

Results: Substantial reductions compared to Swedish norms were observed across all SF-36 subscales at baseline (figure 1). SF-36 mental component summary scores were higher in patients who were on antimalarial agents (mean: 42.7; SD ± 11.8 ; n=29) compared to patients who were not (mean: 34.0; SD ± 14.7 ; n=32; $p = 0.019$). Accordingly, patients who were on antimalarial agents performed better in SF-36 social functioning (mean: 63.7 versus 46.5; $p = 0.022$) and mental health (mean: 68.7 versus 53.4; $p = 0.023$) compared to patients who were not. Belimumab-treated patients reported gradual improvements in the SF-36 physical summary component (significant from month 12; $p = 0.023$) and FACIT-Fatigue (significant by month 24; $p = 0.001$), no changes in EQ-5D scores, and improvements in HAQ-DI by month 6 ($p = 0.014$). Rituximab-treated patients reported rapid improvements in the SF-36 mental summary component and FACIT-Fatigue by month 3 ($p = 0.031$ and $p = 0.007$, respectively), which declined at month 12, as well as improvements in EQ-5D at month 6 ($p = 0.016$) and HAQ-DI at month 3 ($p = 0.033$), which were not maintained at later time points.

Conclusions: HRQoL was considerably impaired in SLE patients compared to population-based norms at baseline, and was not fully compensated during follow-up. Patients' perceptions of HRQoL showed treatment-specific patterns over time, and could prove useful when evaluating the effects of biologics in SLE. Early evaluation of belimumab might underestimate improvements in HRQoL and fatigue. In severe SLE, antimalarial agents may have favourable effects on mental HRQoL aspects.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3006