Conclusions: TUS differed between study arms, favouring RTX. This encourages further research into SGUS as an imaging biomarker in PSS clinical trials.
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AB0445 HYDROXYCHLOROQUINE'S IMPACT IN RENAL BIOPSY AND OUTCOMES OF LUPUS NEPHRITIS

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Background: Given its immunomodulatory effects, hydroxychloroquine use is recommended in systemic lupus erythematosus (SLE). It is associated with a lower rate of appearance and of relapse of lupus nephritis (LN). LN is classically classified using ISN/RPS classification, but others indexes, such as the ones described by Austin and Hill, allow for the quantification of SLE activity in the kidney tissue.
Objectives: To analyze the association between the use of hydroxychloroquine and the activity of LN in the kidney biopsy.
Methods: Retrospective single center study of consecutive SLE and biopsy proven LN patients, diagnosed from 2010 to 2016. We evaluated the following outcomes: clinical remission, renal function and proteinuria at end of follow-up (g/24h). Complete remission was defined as a reduction of proteinuria to <0,5g/24h, inactive urinary sediment and serum creatinine <115% of baseline; partial remission same parameters, except proteinuria <1g/24h if initial value <3h/24h, or reduction to <3g/24h if initial value >3g/24h. Kidney biopsies were evaluated by the INS/RPS LN classification and the morphological indexes described by Austin and Hill, obtained after histomorphological review of renal biopsies. The studied predictor was the use of hydroxychloroquine. Statistical analysis was performed with STATA software, using one-way ANOVA, Qui2 and Pearson/Sperman test were appropriate.
Results: During 6 years, there were 46 biopsy-proven LN cases, 84,8% (n=39) woman, median 35 years old (27–42,5) and 57,6% (n=19) caucasian. 39 patients were already known to have SLE, 7,44 (1,13–12,3) years previously. Of those 39 patients, 46% were under hydroxychloroquine and 77% under other immunosuppression.
The median follow-up was 31,9 (13,2–45,6) months. Based on biopsy findings, 35 patients were started on immunosuppression – induction in 50% of cases with MMF and in 50% with cyclophosphamide; maintenance in 81% with MMF, the rest with azathioprine. Complete remission was achieved in 58% of patients, 27% achieving partial remission. We observed 4 LN relapses. At the end of FUP, we saw a 96% (n=44) patient survival, with a median serum creatinine of 0,8 mg/dl (0,7–0,99), eGFR 99,8 ml/min (71,2–116,8) and proteinuria of 0,6 g/24h (0,2–1,6). From those 46 patients, 30 were under immunosuppressive therapy at time of LN presentation, and 60% (n=18) were also under hydroxychloroquine. Table 1 summarizes the clinical findings:
With the use of hydroxychloroquine, we observed a lower histomorphological activity, as represented by a lower Hill biopsy index, and tendency towards lower Activity index. We also saw a tendency towards lower proteinuria.
Conclusions: Our data reinforces the recommendations of using hydroxychloroquine for its adjuvant role in SLE patients, as we saw a lower histomorphological activity in kidney biopsy, and a trend towards lower proteinuria.
Disclosure of Interest: None declared
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AB0446 ADDITIVE INHIBITION OF INTERFERONS, B AND T CELL ACTIVATION AND TFH-RELATED CYTOKINE CXCL13 BY LEFLUNOMIDE AND HYDROXYCHLOROQUINE SUPPORTS RATIONALE FOR COMBINATION THERAPY IN PSS PATIENTS

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Background: T and B cell-driven immunity is critically involved in immunopathology of pSS. Recently we demonstrated synergistic T and B-cell activation upon T cell triggering and TLR7/9-driven B cell activation in pSS patients, accompanied by synergistic induction of immunoglobulins and IFN-γ- and IL-17-producing T cells[1]. In addition, TLR7/9-expressing activated pDCs associated with increased type I IFNs and IFN-inducible genes are increased pSS patients. Several studies have shown that the DMARDs leflunomide and hydroxycholoroquine inhibit immune activation in pSS but only show moderate efficacy. However, LEF and HCQ target different pathways with overlapping, but also potentially additive mechanisms, where LEF primarily targets T and B cells and HCQ TLR7/9-driven B cell and pDC activation.
Objectives: To assess the additive effects of LEF and HCQ on CD4 T- and B-cell activation and production of interferons IFN-α and IFN-γ, Tfh-related cytokine CXCL13, as well as IgG and IgM *in vitro* employing SEB/TLR9-triggered PBMC.
Methods: PBMCs of healthy individuals (n=9) and of pSS patients (n=8) were cultured with antigen (SEB), TLR9 and their combination, in presence or absence of LEF, HCQ and their combination in clinical relevant concentrations. Proliferation of T and B cells and release of IFN-α, IFN-γ, CXCL13, IgG and IgM were measured.
Results: In line with robust T and B cell activation, IFN-γ, IFNα, CXCL13, IgG and IgM production was achieved by a combination of SEB and TLR9 (all at least $p<0.001$). LEF dose dependently inhibited B and T cell proliferation, Interferon, CXCL13 and immunoglobulin production. HCQ dose dependently inhibited B cell proliferation, IFN-α, CXCL13, and immunoglobulin production. T cell proliferation and IFN-γ production were inhibited by HCQ only at higher concentrations. At several suboptimal concentrations LEF and HCQ additively inhibited T cell proliferation both in healthy individuals and in pSS patients. (Figure 1). Significant additive effects were seen for all outcome measures except IFN-α. Since IFNa was already robustly inhibited by HCQ alone (eg.for pSS 90% at 3.3 μM, $p<0.001$), only trends towards additive effects were observed.

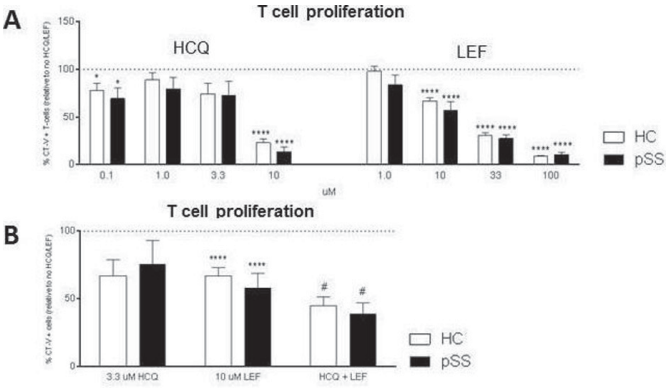

Figure 1. HCQ and LEF additively inhibit T cell activation. T cell proliferation is dose dependently inhibited by LEF and by HCQ at 0.1 and 10 μM **(A).** Significant additive inhibition of T cell proliferation is achieved by combination of suboptimal concentrations of LEF and HCQ both in HC and pSS patients **(B).** *and **** indicates statistical significance of p<0.05 and p<0.0001 resp. vs control, # indicates statistical significance of p<0.05 of the combination vs each of the single drugs.

Conclusions: LEF and HCQ robustly inhibited proliferation of T and B cells, cytokine production and immunoglobulin production with clear additive efficacy in both healthy individuals as in pSS patients. These data support the potential surplus value of combination therapy with LEF and HCQ for patients with pSS.
References:
[1] Bikker et al. Interleukin-7 and Toll-Like Receptor 7 induce synergistic B cell and T cell activation. PLoS ONE 9(4): e94756.
Disclosure of Interest: None declared
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AB0447 ANTIMALARIALS IMPROVE SURVIVAL OF SYSTEMIC LUPUS ERYTHEMATOSUS ON CHOLESTEROL: RESULTS OF A FIFTEEN-YEAR CHINESE MULTICENTER RETROSPECTIVE STUDY IN JIANGSU PROVINCE

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Abstract AB0445 – Table 1

Hydroxychloroquine use	Class II	Class III	Class IV	Class V	Hill Biopsy Index	Activity Index	Chronicity Index	End of FUP eGFR (ml/min)	End of FUP serum creatinine (mg/dl)	End of FUP proteinuria (g/24h)
Yes (n=18)	39%	28%	28%	22%	0,86 (0,2 – 1,8)	1 (0 – 4,25)	0,75 (0 – 3,25)	99,8 (81,9 – 112,1)	0,74 (0,7 – 0,8)	0,3 (0,1 – 0,6)
No (n=12)	8%	17%	58%	33%	1,52 (0,98 – 2,01)	7,25 (1,38 – 9)	2,25 (0,13 – 5,25)	98,6 (56,4 – 120,3)	0,78 (0,7 – 1,3)	0,75 (0,15 – 2,6)
p-value	0,09	NS	NS	NS	0,03	0,07	NS	NS	NS	0,09