- The belief that HCQ is "Very important" (12.9% "low") rather than "important" (22.1% "low") or "not important / useless" (33.1% "low").
 - Taking many different medications (9.8% "low" for Patients indicating more than 7 medications vs 19.8% for those listing 3 or less)
 Childhood onset of the SLE was associated with a lower adherence (30.0% "low" vs. 17.4% for later onset SLE ($p < .001$))

658 patients (29.6%) reported having experienced side effects. 42.6% of them stopped taking HCQ (patient led 161, doctor led 110, unclear 9). Amongst those continuing HCQ despite experiencing side effects, the proportion of non adherent patients increased to 24.7%, compared to 15.2% in the group of patients that have not experienced side effects ($p = .0001$). The 232 patients who talked with their Doctor and felt listened to appear to adhere better (22.0% low adherence) than the 84 who did not feel heard (31.0% low adherence), but the significance is only directional ($p < .015$)

523 patients have used HCQ in the past. 206 (39.4%) consider the decision to stop HCQ as doctor initiated, 272 (52.0%) as patient initiated, and 36 (6.9%) as a joint decision.

When stopping was patient initiated, 59.9% was due to experiencing a significant side effect attributed by the patient to HCQ, 6.7% due to concern of a potential side effect, 11.2% "tested" stopping and noticed no difference, 10.0% were not convinced that it worked, 8.2% felt their lupus was less active, 2.6% wanted to reduce pill consumption. (Side effects attributed to HCQ may relate to age, disease activity or other factors).

Conclusion: Doctors can help HCQ adherence by boosting patient's confidence in the importance of HCQ. Better patient education may contribute to avoid up to 40% of patient initiated decision to stop HCQ treatment.

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AB0372

PREGNANCY OUTCOME IN WOMEN WITH SJÖGREN SYNDROME IS OFTEN COMPLICATED BY PLACENTA INSUFFICIENCY

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Background: Chronic inflammatory rheumatic diseases are often associated with a negative effect on pregnancy outcome. Most obstetrical complications are placenta-mediated such as preterm delivery and growths restrictions. In women with Sjögren syndrome, data on placenta-mediated complications are scarce and conflicting (1,2).

Objectives: To analyse neonatal outcome in women with Sjögren syndrome with focus on preterm delivery and growth restriction.

Methods: We retrospectively analysed 23 pregnancies of 16 patients with Sjögren syndrome that were followed at our centre with regard to pregnancy outcome, medication and disease characteristics. Small for gestational age was defined as birthweight percentile $< 10^{\text{th}}$. Preterm delivery was defined as delivery before 37, early term as delivery between 37-39 and term as delivery between 39-42 weeks of gestation.

Results: Of 23 pregnancies, one ended in a miscarriage and 22 resulted in live births including one set of twins. Treatment used during pregnancy was hydroxychloroquine (20 pregnancies), prednisone (8), azathioprine (5) and cyclosporine (2). Concomitant treatment with low-dose aspirin was used in 9 pregnancies.

Of the 22 live births, 17 were born at early term and 5 at term. There were no preterm deliveries. Median birth weight was 2820g (range 2095-3845g). Nine newborns (40.9%) were small for gestational age (SGA). Maternal treatment during these pregnancies was hydroxychloroquine in all cases and additional low-dose aspirin in three cases. Elevated CRP levels during pregnancy were found in 57% of the cases with SGA outcome. Only one woman with an SGA infant had positive anti-phospholipid antibodies.

Regarding delivery mode, most patients had caesarean sections.

Conclusion: In our cohort of women with Sjögren syndrome the prevalence of small for gestational age infants was high despite maternal treatment with hydroxychloroquine. Inflammatory markers could help to identify the patients

at risk for placental insufficiency, yet prospective studies of larger cohorts are needed.

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AB0373

TREATMENT OF SLE WITH THE IMMUNOPROTEASOME INHIBITOR KZR-616: RESULTS FROM THE FIRST 4 COHORTS OF THE MISSION STUDY, AN OPEN-LABEL PHASE 1B DOSE ESCALATION TRIAL

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Background: Non-specific proteasome inhibitors, such as bortezomib (BTZ), target the constitutive proteasome and immunoproteasome and are approved treatments for multiple myeloma¹. BTZ has also been used to treat systemic lupus erythematosus (SLE) and lupus nephritis (LN); however, treatment emergent adverse events (TEAEs), such as gastrointestinal (GI) effects, hematologic abnormalities, asthenia and peripheral neuropathy, limit its use as a long-term treatment option for chronic autoimmune disease². KZR-616 is a first-in-class selective immunoproteasome inhibitor and is highly active in murine SLE³. Subcutaneous (SC) administration of KZR-616 (30 and 45 mg weekly [QW]) was demonstrated as safe and well-tolerated, and successfully achieved target levels of immunoproteasome inhibition in healthy volunteers^{4,5}.

Objectives: We report the preliminary safety and efficacy of KZR-616 in the first 4 cohorts of the Phase 1b portion of Study KZR-616-002 in patients with active SLE (NCT03393013).

Methods: SLE patients (per SLICC Classification Criteria) with SLEDAI ≥ 4 despite stable background immunosuppressant, anti-malarial, and/or corticosteroid (≤ 20 mg prednisone equivalent) therapy in this open-label multicentric dose-escalation trial received KZR-616 at doses of 45mg (Cohort 1), 60mg (Cohort 2), or 30mg with escalation to 60mg (Cohorts 2a and 2b) SC weekly through Week 13 (W13) with 12 weeks of follow-up. Efficacy measures included SLEDAI, Cutaneous Lupus Erythematosus Disease Area and Severity Index, 28 tender and swollen joint counts, Physicians Global Assessment, Patient Global Assessment, and Patient Assessment of Pain, in evaluable patients (those who received ≥ 1 month of KZR-616).

Results: As of 16 January 2020, 33 patients had enrolled and received at least 1 dose of KZR-616. The majority of TEAEs have been mild or moderate with no reported peripheral neuropathy, prolonged GI-related AEs, and no clinically significant laboratory AEs. There were 3 treatment emergent SAEs, one each of thrombotic microangiopathy (Cohort 2), localized herpes zoster (Cohort 2a), and systemic inflammatory response syndrome (Cohort 2a) with the latter 2 patients completing the full 13 weeks of treatment after resolution. When compared to baseline, improvement in all measures of disease activity were seen at W13 and maintained or improved during the follow-up period, and 94% of evaluable patients had improvements on at least 2 measures/assessments of disease activity. A single patient with active class IV/V nephritis was enrolled on prednisone 10 mg, leflunomide 10 mg, and hydroxychloroquine 200mg/day; nephrotic-range proteinuria at baseline (3.85 g/day) decreased to 0.6 g/day 4 weeks after the last dose of KZR-616.

Conclusion: Weekly subcutaneous administration of KZR-616 at 45 and 60 mg was safe and well-tolerated. Evidence of disease suppression at W13 in active SLE patients on stable background therapy was observed. In addition, one study participant with active proliferative nephritis was enrolled with significant reduction in proteinuria. The Phase 2 portion of this study in active proliferative LN is open for enrollment.

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AB0374

LUPUS LOW DISEASE ACTIVITY STATE AND MAINTAINING DRUG THERAPY: A RETROSPECTIVE INVESTIGATION

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune multisystemic disease, that can begin with a wide range of clinical manifestations, and requires immunosuppressive therapies (1). A treat-to-target strategy leads to a high rate of clinical remission among patients (2). Several "remission" definitions have been provided in the last years and Lupus Low Disease Activity State (LLDAS) seems one of the best tools to evaluate it in clinical practice (3).

Objectives: To evaluate the prevalence of SLE signs and symptoms at onset and the drugs used to induce and maintain the clinical remission, evaluated by LLDAS, in a real-life cohort of SLE patients.

Methods: Thirty female SLE patients (mean age 52±15 years; mean age at disease onset 34±16 years, mean disease duration 18±13 years) in clinical remission have been enrolled (EULAR/ACR 2019 criteria) (4). Remission was defined by LLDAS (SLEDAI-2K < 4 and no activity in major organ systems, no hemolytic anemia; no new features of activity compared with previous assessment, physician global assessment (PGA) ≤ 1, prednisone dose ≤ 7.5 mg/day, well tolerated and stable therapy with maintenance doses of immunosuppressive drugs). Clinical and serological manifestations, SLEDAI-2K and pharmacological treatments were recorded at baseline and during follow-up.

Results: Mucocutaneous involvement (57%), arthritis (30%), serositis (30%), nephritis (27%), leukopenia (23%), thrombocytopenia (20%), hemolytic anemia (13%), antiphospholipid syndrome manifestations (16%), neuro-psychiatric lupus symptoms (6%) were present in various combinations at disease onset. Baseline mean SLEDAI-2K was 10.5±2.5. Patients were treated with different dosages of glucocorticoids (100%), hydroxychloroquine (HCQ, 73%), cyclofosfamide (20%), mycophenolate mofetile (MMF, 13%), azathioprine (AZA, 13%), methotrexate (MTX, 13%), cyclosporine A (CSA, 6%), rituximab (3%), abatacept (ABA, 3%). Glucocorticoids were prescribed together with a single DMARD in 50% of cases and with two DMARDs in the remaining 50% of patients. Patients reached LLDAS remission after a mean time of 14±12 years, with a mean remission duration of 4.2±3.2 years (mean SLEDAI-2K at last visit 1±1; Mean PGA 0.4±0.1). Maintenance therapies during remission were prednisone ≤ 5 mg/day and/or HCQ ≤ 400 mg/day and/or CSA ≤ 200 mg/day and/or MTX ≤ 10 mg/weekly and/or MMF ≤ 2 g/day and/or AZA ≤ 100 mg/day. In particular, only prednisone 7%, only HCQ 3%, prednisone + HCQ 53%, prednisone + single DMARD (different from HCQ) 7%, prednisone + HCQ + DMARDs 30%.

Conclusion: After reaching the clinical remission by a treat to target strategy, the administration of low dose of prednisone and HCQ in the majority of SLE patients (63%) seems useful to prevent new SLE flares. The retrospective design and the absence of a control group of patients with active disease limit this study.

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AB0375

SAFETY AND BENEFICIAL EFFECTS OF HYDROXYCHLOROQUINE ON PREGNANCY OUTCOMES IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The use of hydroxychloroquine (HCQ) has long been established in Systemic Lupus Erythematosus (SLE) and especially as applicable drug during pregnancy. Recently, beneficial effects and safety of HCQ have been re-discussed in the light of a change in the summary of product characteristics in some countries. More current studies are required to provide patients with evidence-based advice regarding this essential drug when counselling for pregnancy.

Objectives: To examine the impact of HCQ on pregnancy outcomes of SLE women.

Methods: Pregnancies of women with SLE from an outpatient pregnancy clinic were prospectively evaluated before and throughout gestation. Maternal and fetal outcomes in women without HCQ therapy (group A) were compared to pregnancies under HCQ treatment from 1st trimester on (group B). A multiple logistic regression was performed with adjustment for confounding factors.

Results: We enrolled 184 live births from singleton pregnancies in 145 women (n=77 with HCQ and n=107 w/o HCQ). One neonatal death (group B) occurred after severe preeclampsia at 24 weeks of gestation (w/g) linked to noncompliance in a woman with high-risk aPL profile. One child (group B) was born with mycophenolate mofetil embryopathy.

Women in the HCQ group had a significantly lower rate of preterm births [aOR 0.31 (95%-CI: 0.15-0.64), p = 0.026]. Regarding preeclampsia, we found a tendency towards less incidence with the use of HCQ [aOR 0.49 (95%-CI: 0.23-1.03), p = 0.24]. These improved outcomes are opposed by a higher frequency of risk factors in group B (lupus nephritis, high-risk aPL profile, slightly more hypertension) and a tendency towards more severe SLE (expressed in terms of increased use of Azathioprine) (Table 1). Nevertheless, women with HCQ

Table 1. Patient characteristics & pregnancy outcomes

		All pregnancies (n=184)	No HCQ in pregnancy (n=107)	HCQ during pregnancy (n=77)
SLE disease & therapy characteristics	Age (years), median (IQR)	31.0 (28.0-34.0)	31.0 (29.0-34.0)	30.0 (27.0-33.0)
	Hypertension, n (%)	29 (15.8%)	16 (15.0%)	13 (16.9%)
	Preconception counselling, n (%)	122 (66.3%)	69 (64.5%)	53 (68.8%)
	Disease duration (years), median (IQR)	6.7 (2.9-10.3)	7.0 (3.0-10.0)	6.7 (2.1-11.0)
	Lupus nephritis ¹ , n (%)	51 (27.7%)	25 (23.4%)	26 (33.8%)
	High-risk aPL profile ² , n (%)	39 (21.3%)	21 (19.8%)	18 (23.4%)
	SLEDAI ¹ , median (IQR)	2.0 (0-4.0)	2.0 (0.0-4.0)	2.0 (2.0-4.0)
	Anti-dsDNA, n (%)	102 (55.7%)	47 (44.3%)	55 (71.4%)
	Anti-SSA/Ro and/or Anti-SSB/La, n (%)	91 (49.7%)	55 (51.9%)	36 (46.8%)
	Azathioprine ¹ , n (%)	38 (20.7%)	18 (16.8%)	20 (26.0%)
Obstetrical history	Low dose Aspirin ³ , n (%)	74 (41.1%)	34 (32.7%)	40 (52.6%)
	Nulliparous, n (%)	113 (61.4%)	63 (58.9%)	50 (64.9%)
	Previous fetal loss, n (%)	39 (21.2%)	22 (20.6%)	17 (22.1%)
	Previous (pre-)eclampsia or HELLP, n (%)	14 (7.6%)	8 (7.5%)	6 (7.8%)
	Previous congenital heart block, n (%)	1 (0.54%)	-	1 (1.3%)
Pregnancy outcome	(mild-moderate) flare ⁴ , n (%)	44 (29.5%)	30 (34.9%)	14 (22.2%)
	Preterm birth ⁵ , n (%)	46 (25%)	30 (28.0%)	16 (20.8%)
	Preeclampsia, n (%)	24 (13%)	15 (14.0%)	9 (11.7%)
	Intrauterine growth restriction, n (%)	3 (1.7%)	1 (1.0%)	2 (2.6%)
	Congenital heart block, n (%)	1 (0.54%)	-	1 (1.3%)

¹last visit before pregnancy, ²according to the 2019 EULAR recommendations, ³until 16 w/g,

⁴increase in SLEPDAI ≥ 4 or increase in prednisolone ≥ 5mg/d, ⁵< 37 w/g