SLE, Sjögren's and APS – treatment

POS0705 DILEMMA OF BELIMUMAB THERAPY (DIS) CONTINUATION DURING PREGNANCY: RESULTS OF A RETROSPECTIVE STUDY IN EUDRAVIGILANCE

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Background: Active systemic lupus erythematosus (SLE) and nephritis due to SLE contribute to poor pregnancy outcomes. (1, 2) A meta-analysis has shown a relative risk of 1.51 for miscarriage in SLE patients compared to women without SLE. (3) The risk is even higher if the disease is active during pregnancy (around 3-fold increase in pregnancy loss). (4) Corticosteroids, azathioprine, hydroxychloroquine, ciclosporine and tacrolimus are considered safe treatments. (5) However, these treatment options may still not be sufficient in patients poorly responsive to conventional therapies or patients who suffer from nephritis. (6) The only biologic authorized for SLE up to this date, belimumab, is currently not recommended for use during pregnancy due to lack of data. Provided that the health of the child begins with the health of the mother, pregnant patients, face the dilemma of cessation or continuation of belimumab. If belimumab is stopped there will be a risk of SLE flare and its consequences for mother and foetus. Continuation is also not optimal because the lack of knowledge on safety for use during pregnancy.

Objectives: To compare the reported foetal outcomes in SLE patients who stopped scheduled belimumab within the first trimester (group A) and who continued scheduled belimumab during the first trimester or thereafter (group B).

Methods: All belimumab-exposed pregnancy-related reports, were extracted from the EudraVigilance (EV) database until March 11th 2021. After case review, repeated cases, uninformative reports, non-medical elective abortions and foetal chromosomal abnormalities were excluded. Included pregnancies were divided into two groups (group A and B, as described above). Foetal outcomes were divided into live birth or foetal death (due to miscarriage or still birth) and were compared between both groups. Furthermore, neonatal outcomes, such as reporting rates of pre-term birth, low birth weight and major congenital malformations (CMs) were compared.

Results: No statistical difference in foetal death was observed between group A and B (reporting rates: 46.4% and 52.4%, respectively; p-value>0.05). Occurrence of major CMs, pre-term birth and low birth weight was higher - though not statistically different- in group A (Table 1).

Table 1. Neonatal characteristics of live born children (including twin pregnancies)

Live births	Stopped (group A); (n=37)	Continued (group B); (n =10)	Total; (n=47)
Gestational age at birth, median (IQR), weeks	37.1 (35.5, 40.0)	38.2 (36.4, 39.1)	**37.6 (36.0, 39.4)**
Weight, median (IQR), grams	2749 (2268, 3200)	2975 (2700, 3175)	**2835 (2406-3175)**
Preterm birth*; n (%)	16 (43.2)	4 (40.0)	**20 (42.5)**
Low birth weight*; n (%)	9 (24.3)	0 (0.0)	**9 (19.4)**

Conclusion: Based on our data belimumab continuation during first trimester or thereafter does not result in higher reporting of foetal death. Therefore, continuation might be even preferable if the pregnancy is already exposed to belimumab. Since the analysis is based on spontaneous reports / retrospective data, additional studies are needed to confirm the results.

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POS0706 LONG-TERM HYDROXYCHLOROQUINE TREATMENT IMPROVES ESSPRI AND ESSDAI IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME

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Background: Primary Sjögren's syndrome (pSS) is a chronic, systemic autoimmune disease typically affecting the salivary and lacrimal glands and producing symptoms of dry mouth, dry eyes, fatigue and pain. Hydroxychloroquine (HCQ) have been shown to have various immunomodulatory and immunosuppressive effects, and currently have established roles in the management of rheumatoid arthritis and systemic lupus erythematosus (SLE). However, the use of HCQ in pSS is based in expert recommendations and in few studies with a low level of evidence. There are very few publications assessing HCQ use in a double-blind, randomized, and placebo-controlled studies. In Japan, HCQ is indicated for patients with SLE and cutaneous lupus erythematosus (CLE) and is off-label use for pSS patients without CLE. Recently, ESSPRI and ESSDAI have been developed by the European League Against Rheumatism (EULAR) SS study group as standardized outcome tools for measuring patients' reported symptoms and disease-specific activity. ESSDAI and ESSPRI have been proven to be valid and reliable, they have been used to select patients or as the primary or secondary outcome measures in clinical trials.

Objectives: The aim of this study was to examine the efficacy of HCQ in pSS at 8 and 52 weeks after treatment evaluated by ESSPRI and ESSDAI.

Methods: Twenty-six pSS patients (26 female, mean age 51.6 ± 13.6 years) with CLE who fulfilled the ACR/EULAR classification criteria for SS and/or the Japanese Ministry of Health and Welfare criteria for SS were studied. The clinical indexes were evaluated by ESSDAI, ESSPRI, IgG and CH50 before and after HCQ treatment at 8 and 52weeks. ESSPRI components were calculated individually and as a single factor composed of the mean of the three components (pain, fatigue, and dryness: VAS 0-10). ESSDAI (0–123) proposes the evaluation of 12 domains or organ systems (constitutional, lymphadenopathy, glandular, articular, cutaneous, pulmonary, renal, peripheral nervous system, central nervous system, muscular, hematological and biology).

Results: ESSPRI and component of fatigue and pain were significantly lower at 8 and 52 weeks after treatment than HCQ pre-treatment (ESSPRI: 4.14±1.45 vs 3.38±1.57, 3.34±1.56, p=0.005, p=0.045, fatigue: 4.68±2.12 vs 3.68±1.96, 3.58±1.87, p=0.010, p=0.036, pain: 3.32±1.94 vs 2.09±1.60, 1.79±1.51, p=0.0043, p=0.0014). However, there was no significant difference in dryness component between HCQ pre-treatment and 8 and 52 weeks after treatment (4.41 ± 2.09 vs 4.32 ± 2.06, 4.21 ± 2.39, p = 0.71, p = 0.94), and the amount of saliva produced by the gum test also showed no significant difference between pre-HCQ treatment and 52 weeks after treatment (8.21 ± 6.72 vs 8.24 ± 6.79 mL / 10 minutes, p = 0.45). There was also a significant decrease in ESSDAI and constitutional, articular, cutaneous and biological domain at 52 weeks after treatment compared to HCQ pre-treatment (ESSDAI: 9.68±6.14 vs 4.74±6.43, p=0.0004; constitutional: 1.41±1.50 vs 0.63±1.26, p=0.034, articular: 1.00±1.02 vs 0.21±0.63, p=0.0027, cutaneous: 2.86±3.27 vs 1.11±2.49, p=0.010, biological: 1.14±0.83 vs 0.79±0.86, p=0.014). An improvement of at least 1 point or 15% in ESSPRI and at least 3 points in ESSDAI compared to HCQ pr-treatment were observed in 63.6% and 31.8% at 8 weeks and 73.7% and 68.4% at 52 weeks after treatment. In addition, IgG was significantly decreased at 52 weeks after treatment compared to HCQ pre-treatment (1934 ± 613 vs 1714 ± 564 mg / dL, p=0.0005).

Conclusion: HCQ treatment improved pain such as arthritis, fatigue, constitutional and cutaneous manifestations, but was not effective for salivary function and dryness. HCQ treatment was useful in improving ESSPRI and ESSDAI, and long-term treatment increased the number of effective cases from 8 weeks to 52 weeks.

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