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SLE, Sjögren's and APS – treatment

AB0457 AUDIT ON HYDROXYCHLOROQUINE RELATED RETINOPATHY SCREENING IN RHEUMATOLOGY PATIENTS IN SVUH

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Background: Hydroxychloroquine (HCQ) is a medication commonly used to treat rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and other rheumatological conditions. A known adverse effect associated with long-term use of these medications is vision loss resulting from irreversible retinal toxic effects. Recent guidelines emphasized on routine ophthalmological examination and to adhere on real weight-based dosages.

Objectives: This audit conducted to evaluate adherence rate on standard recommendation on HCQ related retinopathy screening in rheumatology patients in St Vincent's University Hospital (SVUH).

Methods: Patient were on HCQ and attended rheumatology clinics at SVUH with rheumatic diseases selected randomly from on 01/08/2017 and end on 01/04/2018. A total sample size of 56 patients received a questionnaire that included information on HCQ dose, duration and actual body weight. Other information included precipitant factors and ophthalmology examination reports were retrieved retrospectively form patient's chart. Standards were measured against recommendations on screening for HCQ retinopathy published by American Academy of Ophthalmology, 2016 Revision.

Results: Total 56 patients on HCQ with different rheumatic disease studied. Out of 56 patients studied, 6/56 (10.7%) were <25 years (young), 45/56 (80.4%) were 25-65 years (middle age), and 5/56 (8.9%) were >65 years (elderly). Sex distribution showed that 7/56 (12.5%) were males and 49/56 (87.5%) were females. Around 35.7% (20/56) were in HCQ dose >5mg/kg, and 64.3% (36/56) were on standard HCQ dose (<=5mg/kg of real body weight. The were 44.6% (25/54) patients on HCQ for a period <5 years, the rest, 55.4% (32/56) were on HCQ for a period of 5-20years, and none of these patients were on it for >20 years duration. There were only 1/56 (1.8%) patient with history of HCQ toxicity, 98.2% (55/56) showed no history of HCQ related toxicity. None of the 56 patients had any of the following influencing factors: renal impairment, Tamoxifen usage, coagulopathies, hepatic impairment, or pre-existing retinal/macular disease. However, there were 8.9% (5/56) of this group their age was > 65years (verses 51/56 91.1% were <65years age. Only 69.6% (39/56) of these patients underwent retinal baseline screening, were 17/56 (30.4%) did not receive any baseline screening after commencing HCQ therapy. Frequency of follow up retinal screening were done annually in 19/56 (33.9%), 5 yearly in 6/56 (10.7%). However, it was not done in 21/56 (37%) and it was not due in 9/56 (16.1%). Out of those who underwent the screening at any time, 32/56 (57.1%) showed normal examination results, only 1/56 patient (1.8%) showed abnormal results. Rest of the patient data either were not available, or examination were not done.

Conclusion: Above data emphases the need to adhere on standards HCQ retinal screening as baseline and follow up. Furthermore, adherence on real weight calculated dose rather than estimated/average body weight.

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AB0458 A PHASE II RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PROOF OF CONCEPT STUDY OF ORAL SELETALISIB IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME (PSS)

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Background: Seletalisib is a potent, selective oral inhibitor of phosphoinositide-3 kinase delta (PI3Kδ). Preclinical data have shown that the PI3Kδ pathway is upregulated within salivary glands of patients with PSS and contributes to disease pathogenesis.[1]

Objectives: To assess the efficacy and safety of seletalisib in patients with PSS.

Methods: In this Phase II, double-blind, proof of concept study (NCT02610543), patients with PSS having an EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) score ≥5 were randomised 1:1 to seletalisib once daily or placebo (PBO) in addition to current PSS therapy for 12 weeks. The primary endpoint was change from baseline in ESSDAI at Week 12. The study was designed to have 80% power to detect a difference of 3.8 points in change from baseline in ESSDAI between seletalisib and PBO at Week 12 and required 58 patients to complete treatment. Other endpoints included EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI), salivary gland biopsy changes, Schirmer's I test, immunoglobulin concentrations and incidence of treatment-emergent adverse events (TEAEs).

Table 1. Change from baseline to Week 12 for secondary and exploratory endpoints (full analysis set)

	Seletalisib n=13, LS mean (SE)	PBO n=14, LS mean (SE)	Difference (95% CI)
ESSPRI score[a]	–2.13 (0.68)	–0.57 (0.56)	–1.55 (–3.39, 0.28)
Stimulated salivary flow rate, mL/min[a]	–0.08 (0.11)	–0.11 (0.08)	0.02 (–0.27, 0.31)
Schirmer's I test score[b]	–0.9 (3.3)	0.5 (2.6)	–1.41 (–10.35, 7.52)
Immunoglobulin G, g/L[a]	–2.36 (0.71)	1.17 (0.64)	–3.53 (–5.55, –1.51)
Immunoglobulin M, g/L[a]	–0.33 (0.10)	0.07 (0.09)	–0.40 (–0.68, –0.12)
Immunoglobulin A, g/L[a]	0.03 (0.13)	0.06 (0.12)	–0.03 (–0.40, 0.34)

LS, least squares; SE, standard error

[a] Mixed model for repeated measures analysis

[b] Analysis of covariance

Results: The study was terminated early due to slow recruitment, which led to study power decreasing to 36%. Twenty of 27 patients randomised (seletalisib n=13, PBO n=14) completed treatment. Demographic characteristics were generally similar between groups. Mean (SE) change from baseline in ESSDAI at Week 12 was seletalisib –5.4 (1.7) vs PBO –2.8 (1.5); treatment difference vs PBO (95% CI) was –2.59 (–7.30, 2.11; p=0.266). The percentages of patients achieving a ≥3 point reduction in ESSDAI were seletalisib 66.7% vs PBO 54.5%. Post-hoc Bayesian analyses of treatment difference showed an 86.5% probability of being superior to PBO and a 48.8% probability of a >3 point difference from PBO. Clinically notable improvements in some secondary endpoints were also observed in the seletalisib group (Table 1). Minor salivary gland biopsies had broadly similar histological features across groups at baseline. At

Week 12, seletalisib treatment led to a reduction in the size and cellular organisation of mononuclear inflammatory cell foci vs PBO (Table 2). TEAEs were reported by 13/13 (100.0%) seletalisib and 13/14 (92.9%) PBO patients; most frequently reported: diarrhoea (5/13 [38.5%] vs 0/14 [0%]) and headache (3/13 [23.1%] vs 2/14 [14.3%]). Serious TEAEs were reported by 3/13 (23.1%) vs 1/14 (7.1%), and discontinuations due to TEAEs by 5/13 (38.5%) vs 1/14 (7.1%) seletalisib and PBO patients, respectively.

Table 2. Change from baseline at Week 12 in characteristics of mononuclear inflammatory cell foci from paired minor salivary gland biopsies

	Seletalisib n=7 Mean (SD)	PBO n=11 Mean (SD)
Average focus area, mm^2	–0.02 (0.02)	0.01 (0.06)
Focus score, number foci present/4 mm^2 biopsy tissue	–0.43 (0.99)	0.20 (2.73)
Percentage infiltration	–1.3 (1.4)	2.5 (8.0)
Percentage of germinal centres	–13.5 (14.3)[a]	–0.9 (15.8)[b]
Percentage of T/B cell segregation	–17.6 (8.6)[c]	–12.7 (32.3)[d]
Percentage of foci with follicular dendritic cells	–23.2 (17.1)[e]	15.1 (40.7)

SD, standard deviation

[a] n=3; [b] n=7; [c] n=4; [d] n=9; [e] n=6

Conclusion: Although this Phase II PSS study was terminated early due to slow recruitment, seletalisib demonstrated a trend to clinical improvement in patients with PSS and acceptable safety and tolerability. Histological analyses demonstrated encouraging effects of seletalisib on the organisation and extent of salivary gland lymphocytic infiltration in patients with PSS.

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AB0459 IMMUNOGLOBULINS COMBINED WITH STANDARD THERAPIES FOR THE PREVENTION OF RELAPSES IN REFRACTORY OBSTETRICAL ANTIPHOSPHOLIPID SYNDROME: A SERIES OF 103 CASES

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Background: Optimal standard therapy in obstetrical antiphospholipid syndrome (APS) (aspirin and LMWH) is effective in 72- 80% of pregnancies (1). Intravenous immunoglobulins (IVIG) are not more efficient than standard therapy (2, 3) and seems to be reserved to high risk pregnant APS patients (4) and/or refractory cases (5).
Objectives: The main aim of this study was to analyse the outcome of pregnancies in APS patients with recurrent obstetrical event despite conventional treatment, who received IVIG.
Methods: We have performed a retrospective multicentre open-labelled study (2010-2018).
Results: 103 patients (107 pregnancies) with obstetrical APS from 8 international centres were included. In all cases, the previous standard treatment was inefficient. Obstetrical APS was present in 73%, while 27% had obstetrical and thrombotic APS. Median age was 28 years. Triple antiphospholipid antibody (tAPL) positivity was found in 51% of patients and lupus anticoagulant (LA) in 60%. IV IG use was associated with favourable outcome in 101/107 pregnancies (94%). In multivariate analysis, previous history of prematurity and Ig use were associated with live-birth pregnancy (odds-ratio 0.12 95%CI 0.03-0.37, p 0.005). The dosages of IV IG were variable: 0.4g/kilo day-2g/kilo day but without differences on outcomes between patients (p 0.8). There were no differences in outcomes of pregnancies between patients with tAPLand/or LA positivity and patients with other antibodies profiles (p 0.8).
Conclusion: IVIG could be effective in cases of refractory obstetrical APS but prospective studies are necessary.

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