POS0701

ANIFROLUMAB, AN ANTI-INTERFERON- α RECEPTOR MONOCLONAL ANTIBODY IN SYSTEMIC LUPUS ERYTHEMATOSUS- A META ANALYSIS

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Background: Type I interferons such as Anifrolumab have been implicated in Systemic lupus erythematosus (SLE) pathogenesis on the basis of increased interferon-stimulated gene expression and genetic susceptibility. Little is known regarding its efficacy and safety profile.

Objectives: To assess the efficacy and safety of Anifrolumab in patients with SLE.

Methods: Electronic databases (PubMed, Embase, Scopus, Cochrane) were searched from inception until December 15th, 2020. Unadjusted odds ratios (OR) were calculated from dichotomous data using Mantel Haenszel (M-H) random-effects with statistical significance to be considered if the confidence interval excludes 1 and $p < 0.05$. The primary outcome of interest was British Isles Lupus Assessment Group (BILAG)-based Composite Lupus Assessment (BICLA). Secondary outcomes included the proportion of patients who achieved an SLE responder index of 4 (SRI-4) reduction of 50% or more in the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI), reductions in the glucocorticoid dose and adverse effects.

Results: A total of three studies^{1,2,3} with 839 participants (Anifrolumab=372, Placebo=467) were included in our analysis. Follow-up duration was at week 52. A statistically significant difference was observed in the Anifrolumab arm in terms of BICLA response (OR 0.44 95%CI 0.34-0.59; $p < 0.00001$, $I^2 = 4$), $\geq 50\%$ reduction in CLASI activity score (OR 0.36 95%CI 0.21-0.60; $p = 0.0001$, $I^2 = 0$), glucocorticoid reduction (OR 0.41 95%CI 0.28-0.59; $p < 0.00001$, $I^2 = 0$) and SRI-4 response (OR 0.52 95%CI 0.30-0.90; $p = 0.02$, $I^2 = 75$). However, Adverse events were less

likely in the placebo arm as compared to Anifrolumab (OR 1.54 95%CI 1.05-2.25; $p = 0.03$; $I^2 = 0$).

Conclusion: Anifrolumab was found to be more effective than placebo for the management of SLE, but may also cause more severe adverse effects.

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PREGNANCY IN SLE PATIENTS TREATED WITH BELIMUMAB: EXPERIENCE FROM 3 ITALIAN CENTERS

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Background: Belimumab (BEL) is a monoclonal antibody approved for SLE treatment but few data are available about its use before or during pregnancy.

Objectives: Our study aims to describe pregnancies in SLE patients who have discontinued BEL before conception, at positive pregnancy test or during pregnancy.

Methods: Data from prospectively-followed pregnancies (2014-2020) in SLE patients treated with BEL in 3 Italian centers where retrospectively collected, focusing on maternal disease activity, obstetric and neonatal outcome. Continuous data are expressed as median [min-max].

Results: Thirteen SLE pregnancies were analyzed (median age at conception 32 [24-41] years; 77% spontaneous, 69% primigravidae). All patients had positive ANA and anti-dsDNA antibodies; 4 had anti-Ro antibodies (31%); 4 had anti-phospholipid antibodies (aPL; 1 single, 2 double and 1 triple positivity). Seven patients (54%) had a history of lupus nephritis (LN); 2 patients (15%) had a concomitant diagnosis of antiphospholipid syndrome (1 thrombotic-APS and 1 thrombotic+obstetric-APS).

Ten (77%) pregnancies were planned and the use of BEL with regard to pregnancy was agreed with the patient during preconception counseling. At preconception visit, 8 patients were in remission while 5 had active disease (median SLEDAI 3 [0-8]).

BEL (11 intravenous, 2 subcutaneous) was stopped in 2 cases before conception, in 7 at positive pregnancy test and in 4 during pregnancy (2 at 11th week, 1 at 22nd, 1 at 24th); median duration of treatment at discontinuation was 29 [4-68] months. Other treatments during pregnancy were: oral prednisone in 12 cases (92%); intravenous methylprednisolone in 1 (8%); hydroxychloroquine in 10 (77%); chloroquine in 1 (8%); azathioprine in 5 (39%); calcineurin inhibitors in 5 (39%); low-dose acetylsalicylic acid in 10 (77%); low molecular weight heparin in 9 (69%).

Three flares occurred during the 3rd trimester in patients who stopped BEL at positive pregnancy test.

Live-births occurred in 92% of the pregnancies. A patient with thrombotic+obstetric-APS and LN, underwent assisted reproductive technology (embryo donation) and developed eclampsia (25th week), an urgent cesarean section was performed and the newborn died after 3 days. One pre-eclampsia occurred in a patient with history of LN, double aPL positivity and active disease. One miscarriage at 11th week occurred; no early miscarriages (<10th week) were recorded. Pregnancy complications and outcomes are reported in Table 1.

No malformations were recorded. Two newborns were transferred to the Intensive Care Unit (1 for milk protein intolerance and 1 for desaturation).

Table 1. Pregnancy complications and outcomes according to the timing of discontinuation of BEL.

	BEL STOPPED PRECONCEPTIONALLY (2)	BEL STOPPED AT POS PREGNANCY TEST (7)	BEL STOPPED DURING PREGNANCY (4)
Pre-eclampsia	0/2	0/7	1/4 (25%)
Eclampsia	0/2	0/7	1/4* (25%)
Gestational Diabetes	0/2	1/7 (14%)	0/4
IUGR	0/2	1/7 (14%)	1/4* (25%)
pPROM/PROM	0/2	0/7	1/4 (25%)
Live birth	1/2 (50%)	7/7 (100%)	4/4 (100%)
Severe pre-term birth (≤ 34 th week)	0/2	0/7	1/4* (25%)
Late pre-term birth (35 th –37 th week)	0/2	3/7 (43%)	0/4
Small for Gestational age neonate	0/2	4/7 (54%)	1/4 (25%)
Late miscarriage (>10th week)	1/2 (50%)	0/7	0/4
Perinatal death	0/2	0/7	1/4* (25%)

IUGR: IntraUterine Growth Restriction; PROM: Premature Rupture of Membrane; pPROM: pre-term PROM; *in the same patient (history of thrombotic and obstetric-APS and lupus nephritis) who underwent Assisted Reproductive Technologies (embryo donation).

Eight newborns received vaccinations according to national schedule (missing data for 3). Five newborns were breastfed, 1 received formula milk and 5 mixed-feeding. BEL was resumed in 7/13 patients after pregnancy (in 4 cases for flare), after a median period of 5 [4–22] months.

Conclusion: While more data are needed, this small series suggests that BEL might be a therapeutic option for SLE patients during pregnancy planning, similarly to other biological drugs used in chronic forms of arthritis.

Disclosure of Interests: None declared

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POS0703

CARDIAC ADVERSE EFFECTS OF LONG-TERM USE OF HYDROXYCHLOROQUINE IN SYSTEMIC LUPUS ERYTHEMATOSUS. SINGLE UNIVERSITY CENTER STUDY OF 109 PATIENTS

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Background: Hydroxychloroquine (HCQ) is a widely used drug especially in connective tissue disorders such as Systemic Lupus Erythematosus (SLE). Cardiac adverse effects of long-term use of HCQ remains controversial.

Objectives: To assess cardiac adverse effects of long-term use of HCQ in SLE.

Methods: Observational single center study of 109 patients with SLE treated with HCQ for more than 3 months. The main outcomes were cardiac structural and conduction disorders in a 12-lead electrocardiogram and/or echocardiogram at baseline and during HCQ treatment.

Results: We studied 109 patients (95 women/14 men; mean age 66.9±14.7 years). Main cardiovascular history was hypertension (n=61, 56.0%), diabetes mellitus (n=16, 14.7%) and renal impairment (n=11, 10.1%). HCQ was used for 11.7±8.9 years. Initial median SLE Disease Activity Index 2000 (SLEDAI-2K) was 7 [3.75–11]. At baseline, 27 (24.8%) patients had conduction disorders and 15 (13.7%) had structural abnormalities: Most prevalent cardiac alterations were Left Anterior Fascicular Block (LAFB) (n=9, 8.3%), left ventricular hypertrophy (n=9, 8.3%) and right bundle branch block (n=8, 7.3%). After 11.7±8.9 years of follow-up (mean HCQ cumulative dose: 1042.2±2675 g; median SLEDAI-2K 1 [0–4]), there was a significant increase in conduction disorders (n=41, 37.6%, p=0.011) and in LAFB (n=16, 14.7%, p=0.021). There was no statistically significant increase in structural abnormalities (n=21, 19.7%, p=0.629).

Table 1. Main cardiac abnormalities at baseline and after follow-up.

	Baseline	After follow-up	p
Conduction disorders, n (%)	27 (24.8)	41 (37.6)	0.011
Left anterior fascicular block	9 (8.3)	16 (14.7)	0.021
Right bundle branch block	7 (6.4)	8 (7.3)	1.0
Atrioventricular block	4 (3.6)	11 (10.1)	0.092
Incomplete right bundle branch block	4 (3.6)	5 (4.6)	1.0
Short PR interval	2 (1.8)	4 (3.7)	0.5
Prolonged QT corrected interval	2 (1.8)	4 (3.7)	0.625
Left bundle branch block	1 (0.9)	5 (4.6)	0.125
Atrial Fibrillation	1 (0.9)	5 (4.6)	0.219
Structural abnormalities, n (%)	15 (13.7)	21 (19.7)	0.629
Ventricular hypertrophy	9 (8.3)	9 (8.3)	1.0
Atrial enlargement	6 (5.5)	13 (11.9)	0.096

Main cardiac abnormalities at baseline and after 11.7±8.9 years of follow-up are summarized in Table 1. Time of occurrence of cardiac adverse effect in relation to HCQ cumulative dose is shown in Figure 1.

Figure 1. Time of occurrence of cardiac adverse effect in relation to hydroxychloroquine cumulative dose.

Conclusion: Conduction disorders were more prevalent than structural abnormalities. Patients with SLE treated with HCQ had a significant increase in LAFB. Use of electrocardiogram and/or echocardiogram may be helpful in monitoring cardiac adverse effects.

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LONG-TERM CLINICAL OUTCOMES OF PATIENTS WITH LUPUS NEPHRITIS TREATED WITH AN INTENSIFIED B-CELL DEPLETION PROTOCOL: A PROSPECTIVE STUDY

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Background: B cells play a key role in the pathogenesis of Lupus Nephritis (LN).

Objectives: we aim to investigate the safety and efficacy of an intensified B-cell depletion induction therapy (IBCDT) without immunosuppressive maintenance regimen compared to standard of care in biopsy-proven LN.

Methods: Thirty patients were administered an IBCDT (4 weekly Rituximab 375mg/m² and 2 more doses after 1&2 months; 2 infusions of 10mg/kg cyclophosphamide (CYC), 3 methylprednisolone pulses), followed by oral prednisone (tapered to 5mg/day by the 3rd month). No immunosuppressive maintenance therapy was given. Thirty patients matched for LN class and age were selected as controls: 20 received 3 methylprednisolone pulses days followed by oral prednisone and mycophenolate mofetil (MMF) 2-3g/day, while 10 were given the Euro Lupus CYC.

Results: At 12 months, complete renal remission was observed in 93% of patients on IBCDT, in 62.7% on MMF, and in 75% on CYC (p=0.03); the dose of oral prednisone was lower in the IBCDT group (mean±SD 2.9±5.0mg/dl) than MMF (10.5±8.0mg/day, p<0.01) or CYC group (7.5±9.0mg/day, p<0.01). Mean follow-up after treatment was 44.5 months (IQR 36–120months), 48.6 months (IQR36–120months), and 45.3 (IQR36–120months) for IBCDT, MMF and CYC, respectively. At their last follow-up visit, we observed no significant differences in proteinuria and serum creatinine, nor in the frequency of new flares among the three groups.

Conclusion: In biopsy proven LN, the IBCDT without further immunosuppressive maintenance therapy was shown to be as effective as conventional regimen of MMF or CYC followed by a 3-year maintenance MMF regimen. Moreover, the use of IBCDT was associated with a marked reduction of glucocorticoid cumulative dose.

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