FRI0188

EARLY RENAL IMPROVEMENTS FOLLOWING RITUXIMAB IN LUPUS NEPHRITIS

Sophie Collinson, Ben Parker, Eoghan McCarthy, Ian N. Bruce, British Isles Lupus Assessment Group Biologics Register. *Kellgren Centre for Rheumatology, NIHR Manchester Musculoskeletal Biomedical Research Centre, Manchester University Hospitals NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, United Kingdom*

Background: Rituximab (RTX) is the monoclonal antibody of choice in patients with lupus nephritis (LN) who either fail to respond to, or cannot receive standard of care (SOC) therapy. Despite its continued use in clinical practice, published clinical trials regarding its use in LN management have failed to show any clear benefit.

Objectives: We aimed to analyse renal outcomes of LN patients in a large national register.

Methods: Patients with active LN on recruitment into the BILAG-Biologics Register (BILAG-BR) were included. Active LN was defined as a BILAG A or B score in the renal domain. Patients are eligible for RTX if they have failed either MMF or cyclophosphamide. We defined renal response at 6 and 12 months as a change in BILAG score from A to B/C/D or B to C/D. Non-renal disease activity was also described.

Results: Overall 259/897 patients in BILAG-BR had active LN at baseline. Of these, 230 received RTX and 29 received SOC. 109/159 (68.6%) RTX patients and 15/19 (78.9%) of SOC patients had a renal BILAG response at 6 months ($p=0.792$) (Table 1). In those with sufficient response data at 12 months, 31/98 (31.6%) and 7/15 (46.7%) ($p=0.084$) demonstrated continued renal response in the RTX and SOC groups respectively. Both groups made improvements or remained stable in all other renal domains (UPCR, eGFR, creatinine) at 6 and 12 months. Oral steroid doses decreased in both treatment groups. Of note, baseline steroid doses in the SOC group were higher than RTX patients (30mg (20-40) vs. 12.5mg (10-25), $p<0.001$). Non-renal disease activity measures improved in both cohorts.

Variable	RTX	SOC	p
Renal BILAG response*	109/159	15/19 (78.9%)	0.792
- 6m ($n=159$ RTX, 19 SoC)	68.6%	7 (46.7%)	0.084
- 6 to 12m ($n=98$ RTX, 15 SoC)	31 (31.6%)		
UPCR (median [IQR]) mg/mmol	215 (103-388)	173 (88-352)	0.2945
- 0m ($n=160$)	149 (54-404)	66 (21-92)	0.331
- 6m ($n=92$)	71 (42-316)	18 (11-40)	0.0045
- 12m ($n=60$)			
Serum creatinine (median [IQR]) micromol/l	69 (58-97)	66 (52-90)	0.3864
- 0m ($n=239$)	70 (59-99)	70 (51-84)	0.4774
- 6m ($n=157$)	70 (59-100)	68 (60-95)	0.7651
- 12m ($n=105$)			
Oral steroid dose (median [IQR]) mg/day	12.5 (10-25)	30 (20-40)	<0.001
- 0m ($n=196$ RTX, 29 SoC)	10 (7-17.5)	12.5 (10-20)	0.1246
- 6m ($n=151$ RTX, 19 SoC)	10 (5-15)	8.5 (6.25-12.5)	0.9730
- 12m ($n=108$ RTX, 16 SoC)			
Non-renal BILAG	9 (1-12)	8 (1-10)	0.9310
- 0m ($n=230$)	1 (0-2)	1 (0-2)	0.6527
- 6m ($n=153$)	1 (0-2)	1 (0-2)	0.7803
- 12m ($n=101$)			
Non-renal SLEDAI (median [IQR])	3 (2-4)	2 (1-3)	0.0426
- 0m ($n=254$)	1 (0-2)	1 (0-2)	0.2845
- 6m ($n=183$)	1 (0-2)	1 (0-2)	0.6887
- 12m ($n=113$)			
SLICC DI ≥ 1	113 (50.2%)	14 (48.3%)	0.844
- 0m ($n=254$)			

Conclusion: In a large UK-wide, real-world, observational LN cohort we have shown that RTX does improve renal outcomes at 6 and 12 months in refractory SLE patients. RTX is a valid treatment option for many patients with renal disease in SLE.

Disclosure of Interests: Sophie Collinson: None declared, Ben Parker Grant/research support from: GSK, Consultant for: AZ, UCB, GSK, Eoghan McCarthy: None declared, Ian N. Bruce Grant/research support from: Genzyme Sanofi, GlaxoSmithKline, Consultant for: AstraZeneca, Eli Lilly, GlaxoSmithKline, ILTOO Pharma, MedImmune, Merck Serono, Speakers bureau: GlaxoSmithKline, UCB Pharma

DOI: 10.1136/annrheumdis-2019-eular.317

FRI0189

POOLED ANALYSIS OF THE REAL-WORLD EFFECTIVENESS OF BELIMUMAB IN TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS USING MULTI-COUNTRY DATA FROM THE OBSERVE STUDIES

Christopher Collins¹, Josefina Cortés-Hernández², Mercedes García³, Johannes von Kempis⁴, Andreas Schwarting⁵, Zahi Touma⁶, Shannon Ferrante⁷, Milena Kurtinecz⁷, Kerry Gairy⁸. ¹Washington Hospital Center, Washington, United States of America; ²Vall d'Hebron Hospital, Barcelona, Spain; ³HIGA San Martín La Plata, La Plata, Argentina; ⁴Kantonsspital St. Gallen, St Gallen, Switzerland; ⁵Johannes Gutenberg-University, Mainz, Germany; ⁶Toronto Western Hospital, University of Toronto Lupus Clinic, Toronto, Canada; ⁷GSK, Collegeville, United States of America; ⁸GSK, Brentford, United Kingdom

Background: Real-world evidence of belimumab effectiveness in patients with systemic lupus erythematosus (SLE) has been reported separately for several countries through the OBSERVE (evaluation Of use of Belimumab in clinical practice SETtings) programme.

Objectives: To evaluate the effectiveness of belimumab in patients with SLE using pooled data from the individual OBSERVE studies.

Methods: This was a *post hoc* meta-analysis (GSK study 206351) of patient level data pooled from six retrospective observational cohort studies (Argentina, Canada, Germany, Spain, Switzerland, United States of America). Physicians provided data for adults (≥ 18 years; clinical diagnosis of SLE) who had initiated intravenous belimumab as part of their usual SLE care ≥ 6 months prior to enrolment and for whom reasons for belimumab initiation could be identified. Primary objective: physician-assessed overall clinical response to belimumab at Month 6, which reflected physicians' impression of change in overall clinical manifestations, categorised as worse, no improvement, and improvement of $<20\%$, $20-49\%$, $50-79\%$, and $\geq 80\%$. Secondary objectives included a description of patient characteristics at belimumab initiation (index); treatment patterns during the 6 months after index; and patient and treatment characteristics associated with an overall clinical response. Safety was not assessed.

Results: Data were pooled from all 830 patients (89.3% female; mean [standard deviation] age 41.9 [12.6] years) included in each of the OBSERVE studies. At index, most patients had moderate SLE (71.4%; physician-assessed) and serological indicators of high disease activity (82.8%; high anti-dsDNA and/or low complement). Of 345 patients for whom Safety of Estrogens in Lupus Erythematosus-National Assessment Trial-SLE Disease Activity Index baseline data were available, 60.0% had a score ≥ 10 . At index, 72.0% of patients had musculoskeletal, 59.0% had mucocutaneous manifestations, and 16.5% had renal involvement. At Month 6, 82.8% of patients had $\geq 20\%$ improvement and 48.1% had $\geq 50\%$ improvement in their overall condition; only 4.7% had none or a worse response to belimumab therapy (Figure). At index, 81.4% of patients received steroids at a mean dose of 17.6 mg/day. At Month 6, the mean change in steroid dose was -9.7 mg/day. Of those receiving a dose >7.5 mg/day (78.4% of all patients receiving steroids at index), 54.5% had a dose reduction to ≤ 7.5 mg/day at Month 6. Ineffective previous treatment was the main reason for belimumab initiation (74.3%). Prior to Month 6, 4.4% of patients ($n=12/270$) in Argentina, Spain, Germany and Switzerland discontinued belimumab, most frequently due to lack of efficacy and patient request (both 33.3%); OBSERVE US and Canada excluded patients with <6 months' belimumab treatment.

Conclusion: This study provides important insights into global real-world outcomes in a large number of patients with SLE treated with belimumab. After 6 months of treatment, most patients demonstrated clinical improvements in SLE; results were consistent across the pooled population and for patients with high disease activity. Belimumab was steroid sparing; most patients receiving steroids at belimumab initiation decreased their steroid dose after 6 months of belimumab treatment.

Figure. Overall improvement in disease activity at Month 6 ($n=830$)

Acknowledgement: Study funded by GSK. Gosia Carless, PhD, Fishawack Indicia Ltd, UK, provided editorial assistance funded by GSK.

Disclosure of Interests: Christopher Collins Grant/research support from: Exagen, Consultant for: Exagen, AbbVie, Speakers bureau: Exagen, AbbVie, Novartis, Josefin Cortés-Hernández Grant/research support from: GSK, Speakers bureau: GSK, Mercedes García Grant/research support from: GSK, Speakers bureau: GSK, Johannes von Kempis: None declared, Andreas Schwarting Grant/research support from: GSK, Pfizer, AbbVie, Novartis, Roche, Speakers bureau: GSK, Novartis, Zahi Touma Grant/research support from: GSK Canada, Consultant for: UBC, Pfizer, Janssen, Inc, Shannon Ferrante Shareholder of: GSK, Employee of: GSK, Milena Kurtinecz Shareholder of: GSK, Employee of: GSK, Kerry Gairy Shareholder of: GSK, Employee of: GSK
DOI: 10.1136/annrheumdis-2019-eular.7637

FRI0190 INCIDENCE OF ANTIMALARIALS-INDUCED RETINOPATHY IN INFLAMMATORY RHEUMATIC DISEASES, USING OCT AND VISUAL FIELD TEST : A SYSTEMATIC REVIEW AND META-ANALYSIS

CAGNY Hélène DE¹, Jacques Morel^{1,2}, Bernard Combe^{1,2}, Cecile Gaujoux-Viala^{3,4}, Cédric Lukas^{1,2}. ¹University of Montpellier, Montpellier, France; ²University hospital, Rheumatology, Montpellier, France; ³University of Nîmes, Nîmes, France; ⁴University hospital, Rheumatology, Nîmes, France

Background: Antimalarials (AM) are frequently used as first-line therapy in mild inflammatory diseases, because of a good benefit/risk ratio. Recently, their benefit on long term cardiovascular risk in RA patients has been demonstrated [1, 2]. Their most severe side effect is retinopathy, which can potentially lead to blindness, but remains reversible if detected early, provided the treatment is stopped. This complication has been described early [3], but its incidence remains uncertain. A recent update of the American Association of Ophthalmology (AAO) recommendations on screening for chloroquine and hydroxychloroquine retinopathy, suggests to screen patients under AM treatment, with a frequency depending on risk factors, and with the systematic and minimal use of Optical Coherence Tomography (OCT) and Visual Field (VF) test, completed by others tests if required [4].

Objectives: We aimed at estimating the exact incidence of AM-induced retinopathy, based on available published literature about this issue, with particular reference to detection performed with OCT and VF test.

Methods: A systematic literature search was conducted in Pubmed, Cochrane and Embase databases until April 6th 2018, completed by a manual search in references from the resulting selected articles. We first selected all publications about the incidence of AM-associated retinopathy in patients treated for inflammatory diseases and included them in the systematic literature search. Among them, and in order to minimize heterogeneity of results, we focused on those which had used at least OCT and VF test, as recommended by the AAO, to perform a meta-analysis. Analysis was conducted using MetaXL for Microsoft Excel, applying the Inverse of Variance method.

Results: Among the 3890 articles of potential interest, we selected 91 articles appropriately addressing the topic and included them in the systematic literature search. They were published between 1964 and 2018, with variable population sizes (10 to 3580 patients). Patients were treated with hydroxychloroquine, chloroquine or both for an inflammatory disease (usually lupus or rheumatoid arthritis). Mean treatment duration ranged from 1 to 14.1 years. Most of them were retrospectively designed, and diagnostic methods were diverse. For the aforementioned meta-analysis, we used data from 16 articles published between 2010 and 2018, in which every patient had at least OCT and VF Test. We found a pooled estimate of incidence of 6.05% (IC 95% [5.18 – 7.31]), with a I2 heterogeneity coefficient of 80%.

Conclusion: We found a pooled incidence of approximately 6% of AM-induced retinopathy when OCT and VF test are used. However diagnostic criteria are not consensually well-defined, leading to heterogeneous data.

REFERENCES:

- [1] Rempnault C, Combe B, Barnette T, et al. Metabolic and cardiovascular benefits of hydroxychloroquine in patients with rheumatoid arthritis: a systematic review and meta-analysis. *Ann Rheum Dis* 2017.
- [2] Mathieu S, Pereira B, Tournadre A, et al. Cardiovascular effects of hydroxychloroquine: a systematic review and meta-analysis. *Ann Rheum Dis* 2017.
- [3] Hobbs H, Sorsby A, Freedman A: Retinopathy following chloroquine therapy. *Lancet* 1959; II: 478.
- [4] Marmor MF, Kellner U, Lai TY, et al, American Academy of Ophthalmology Statement. Recommendations on screening for chloroquine and hydroxychloroquine retinopathy (2016 revision). *Ophthalmology*. 2016;123:1386-1394.

Disclosure of Interests: Hélène DE CAGNY: None declared, Jacques Morel: None declared, Bernard Combe Consultant for: Abbvie, Bristol-Myers Squibb, Gilead, Janssen, Eli Lilly, MSD, Novartis, Pfizer, Roche-Chugai, Sanofi, UCB, Cecile Gaujoux-Viala Consultant for: Speaking and/or consulting fees from AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Merck-Serono, Medac, Nordic Pharma, Novartis, Pfizer, Roche, Sandoz, Sanofi and UCB Pharma., Speakers bureau: Speaking and/or consulting fees from AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Merck-Serono, Medac, Nordic Pharma, Novartis, Pfizer, Roche, Sandoz, Sanofi and UCB Pharma., Cédric Lukas: None declared

DOI: 10.1136/annrheumdis-2019-eular.5146

FRI0191 TREATMENT OF REFRACTORY POOR APL-RELATED OBSTETRIC OUTCOMES WITH TNF-ALPHA BLOCKERS: MATERNAL-FETAL OUTCOMES IN A SERIES OF 18 CASES

Jaume Alijotas-Reig¹, Enrique Esteve-Valverde², Elisa Llorba³, Josep M⁸ Gris⁴. ¹Systemic Autoimmune Diseases Unit. Department of Internal Medicine-1. Vall d'Hebron University Hospital. Barcelona. Professor of Medicine. Department of Medicine. Faculty of Medicine. Universitat Autònoma de Barcelona., Barcelona, Spain; ²Staff. Department of Internal Medicine. Althaia Network Health. Manresa, Barcelona, Spain; ³Head. Obstetric and Gynecology Department. Sant Pau University Hospital. Universitat Autònoma de Barcelona., Barcelona, Spain; ⁴Staff. Reproductive Medicine Unit. Obstetric Department. Vall d'Hebron University Hospital. Barcelona. Universitat Autònoma de Barcelona, Barcelona, Spain

Background: No absolute data on the treatment of antiphospholipid antibodies (aPL) related to refractory obstetric complications exist to date. TNF- α play a major role in this disorder.

Objectives: To assess the effectiveness of TNF- α blockers in 18 aPL-positive women with recurrent infertility after therapy with low-molecular-weight heparin (LMWH) plus aspirin (LDA) plus hydroxychloroquine (HCQ).

Methods: Prospective case-series of 12 women fulfilling Sydney criteria for obstetric antiphospholipid syndrome (OAPS) and 6 with incomplete forms (OMAPS). All women tested positive for aPL at least twice. Non-criteria aPL were tested in 15/18. Complement, TNF- α and IL-10 were also evaluated. Women were closely monitored for fetal well-being and possible malformations throughout gestation and the postpartum period.

Results: Sixteen patients were started on adalimumab and 2 on certolizumab. Twelve women completed gestation: 9 at term and 3 pre-term. Differences in laboratory categories and outcomes were observed when OAPS and OMAPS were compared. First trimester miscarriage or implantation failure occurred in 6 cases, all of the OAPS group. Malformations were not seen in the newborns.

Conclusion: Overall, good obstetric results were obtained in 70% of previous LMWH-LDA+HCQ refractory cases. TNF- α blockers were well tolerated without adverse effects. The combination of LMWH plus LDA plus TNF- α blockers appears to be a promising treatment for refractory obstetric complaints related to aPL; nevertheless, outcome differences between OAPS and OMAPS do exist.