that reported the incidence of sustained amenorrhoea (defined as at least 12 months of amenorrhoea) during i.v.CYC treatment in patients with ARD; and those that assessed sustained amenorrhoea in patients receiving GnRHa and i.v.CYC, compared to controls receiving i.v.CYC alone.

Results: 1099 articles were identified and their titles and abstracts screened, following which 81 papers were selected for full text review. 31 studies were then identified that addressed the risk of sustained amenorrhoea with i.v.CYC in n=1382 patients with ARD. The majority of these patients had systemic lupus erythematosus (1326 out of 1382 patients, 96.0%). The mean age was 24.9 (range 13-36.1) years. Sustained amenorrhoea occurred in 269 patients (19.5%, range 0-54% depending on age and cumulative cyclophosphamide dose). The rate of sustained amenorrhoea significantly positively correlated with increasing cumulative cyclophosphamide dose, and occurred in patients with a mean age ranging from 13-36.1 years at mean cumulative doses ranging from 1-20.1g. A further 3 studies assessed ARD patients given i.v.CYC +/- GnRHa, including 56 patients (mean age range 23.9-25.6 years) receiving GnRHa and i.v.CYC, and 37 controls (mean age range 25-29.4 years) given i.v.CYC only. Sustained amenorrhoea occurred in 2/56 (3.6%) patients treated with GnRHa, compared to 15/37 (40.5%) of controls. The pooled odds ratio of sustained amenorrhoea with GnRHa and i.v.CYC compared to i.v.CYC alone was 0.0543 (95%CI 0.0115-0.2576, p=0.0002). The number needed to treat was 2.7 (95%CI 2.0-4.4) and the absolute risk reduction was 37.0% (95%CI 35.6-38.4%).

Conclusion: Although the risk of POI with i.v.CYC was associated with increasing age, it was observed across all age groups and from cumulative doses of 1g or more. GnRHa markedly reduced this risk in ARD, and therefore should be considered for concomitant use with i.v.CYC in all women of child-bearing age with ARD.

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Acknowledgement: Arthritis Australia

Disclosure of Interests: Shi-Nan Luong: None declared, Anthony Isaacs: None declared, Fang En Sin: None declared, Ian Giles Consultant for: UCB, Speakers bureau: UCB

DOI: 10.1136/annrheumdis-2019-eular.2411

OP0045

ABATACEPT TREATMENT OF PATIENTS WITH EARLY ACTIVE PRIMARY SJÖGREN'S SYNDROME – A RANDOMIZED, DOUBLE-BLIND PLACEBO-CONTROLLED PHASE III STUDY (ASAP-III)

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Background: Effective systemic treatment is not yet available for primary Sjögren syndrome (pSS). Abatacept (CTLA-4-Ig) targets the CD80/CD86:CD28 costimulatory pathway required for full T-cell activation and T-cell dependent activation of B-cells. IV abatacept was shown to be safe, well tolerated, and to decrease disease activity in an open-label study of 15 pSS patients.¹

Objectives: To assess the efficacy and safety of subcutaneous (SC) abatacept vs. placebo in patients with early active pSS.

Methods: The Abatacept Sjögren Active Patients phase III (ASAP-III) study is a monocenter, investigator-initiated, double-blind, placebo-controlled trial (NCT02067910). ASAP-III included 80 adult patients with biopsy-proven pSS, fulfilling the AECG and ACR/EULAR criteria, with a disease duration of ≤7 years and moderate to high EULAR Sjögren's syndrome disease activity score (ESSDAI ≥5). Patients were randomized in a 1:1 ratio to receive weekly SC abatacept (125 mg) or placebo for 24 weeks (figure 1). After the double-blind phase, all patients were treated with abatacept in a 24-week open label phase. Concomitant use of other DMARDs was not permitted, with the exception of a stable dose of prednisone (≤10mg). Rescue therapy with prednisone or cyclophosphamide was permitted after week 12. Participants visited

our pSS tertiary referral center nine times, to be evaluated by a multidisciplinary team of rheumatologists, ophthalmologists, and oral and maxillofacial surgeons.

The primary endpoint is ESSDAI at 24 weeks. Secondary outcomes over 24 and 48 weeks include clinical, patient reported, functional, histological, laboratory, ultrasound, and microbiome parameters, and the occurrence of (serious) adverse events and treatment discontinuation.

Results: Baseline characteristics of participants are shown in table 1. Database lock for the blinded stage is planned in March 2019. Subsequently, the first intention-to-treat analyses will be performed, focusing on the ESSDAI and EULAR Sjögren Syndrome Patient Reported Index (ESSPRI), quality of life (EQ-5D), unstimulated and stimulated whole salivary flow (UWS, SWS), Schirmer test, Ocular Staining Score (OSS), serological parameters (RF, IgG), and safety parameters.

Conclusion: The ASAP-III trial was designed to assess the clinical efficacy and safety of SC abatacept in pSS patients with short disease duration and active disease. The 24-week results will be available during the EULAR congress 2019.

Figure 1. Design of the ASAP-III study.

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Table 1: Baseline characteristics of participants (n=80)

Characteristics	Value
Age (years), mean±SD	48.8±15.6
Female, n (%)	74 (93)
Disease duration (years), median (IQR)	2.0 (1.0-4.0)
Anti-Ro/SSA, n (%)	71 (89)
Previous use of DMARDs, n (%)	34 (42.5)
Use of prednisone, n (%)	1 (2)
ESSDAI, median (IQR)	13 (8-17)
ESSPRI, mean±SD	6.7±1.6
EQ-5D index, median (IQR)	0.71 (0.57-0.84)
UWS (ml/min), median (IQR)	0.05 (0.01-0.13)
SWS (ml/min), median (IQR)	0.16 (0.04-0.35)
OSS*, mean±SD	4.5±3.4
Schirmer* (mm/5 min), median (IQR)	3 (0-10)
IgG (g/L), median (IQR)	18.2 (14.4-25.9)
RF (IU/ml), median (IQR)	25 (5-71)

* Average of left and right eye.

Disclosure of Interests: Jolien F. van Nimwegen Speakers bureau: Bristol-Myers Squibb, Greetje S. van Zuiden Speakers bureau: Roche, Suzanne Arends Grant/research support from: Grant/research support from Pfizer, Esther Mossel: None declared, Robin F. Wijnsma: None declared, Alja J. Stel: None declared, Konstantina Delli: None declared, Bert van der Vegt: None declared, Eriln A. Haacke: None declared, Lisette Olie: None declared, Leonie I. Los: None declared, Janita Bulthuis-Kuiper: None declared, Gwenny M. Verstappen: None declared, Sarah A. Pringle: None declared, Fred K.L. Spijkervet: None declared, Frans G.M. Kroese Grant/research support from: Unrestricted grant from Bristol-Myers Squibb, Consultant for: Bristol-Myers Squibb, Speakers bureau: Bristol-Myers Squibb, Roche, Janssen-Cilag, Arjan Vissink: None declared, Hendrika Bootsma Grant/research support from: Unrestricted grants from Bristol-Myers Squibb and Roche, Consultant for: Roche, Bristol-Myers Squibb, Novartis, Medimmune, Union Chimique Belge, Speakers bureau: Bristol-Myers Squibb, Novartis **DOI:** 10.1136/annrheumdis-2019-eular.970

OP0046

MULTICENTRIC STUDY COMPARING CYCLOSPORINE, MYCOPHENOLATE MOFETIL AND AZATHIOPRINE IN THE MAINTENANCE THERAPY OF LUPUS NEPHRITIS: 10 YEARS FOLLOW UP

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Background: The most effective drug for the maintenance therapy of severe forms of lupus nephritis (LN) is still a matter of debate.

Objectives: To compare efficacy and safety of cyclosporine (CYA) with mycophenolate mofetil (MMF) and with azathioprine (AZA) in the long-term maintenance therapy of LN.

Methods: Ninety-six patients (pts) (93 females, mean age 31.98 ± 12.78 years) with SLE and biopsy proven LN (16 pts: class III; 64 pts: class IV; 16 pts: class V ISN/RPS). Fifty-six pts entered this study at diagnosis of LN and 40 during a course of a LN flare. Twenty-five pts (30%) had Glomerular Filtration Rate (eGFR) < 60 ml/min (MDRD) and proteinuria was 3.88 ± 2.89 gr/day. Induction therapy: 3 methylprednisolone pulses followed by oral prednisone in 92 pts and oral prednisone in 4 pts; cyclophosphamide in 74% of pts, MMF in 9.4%, AZA in 5.2%, and other immunosuppressors in 11.4%. After six months, 30 pts started maintenance therapy with CYA, 32 with MMF and 34 with AZA. At induction therapy there were not significant differences between the three groups in histological classes at renal biopsy, mean serum creatinine, eGFR and proteinuria, and type of induction therapy. The mean follow-up after the beginning of the study was 15.9 years for CYA, 10.5 for MMF, 14.1 AZA. Primary endpoint was renal response at 1, 5 and 10 years defined as complete renal response: eGFR > 60 ml/min and proteinuria < 0.5 g/die, partial response: eGFR > 60 ml/min and proteinuria ≥ 0.5 g/die, no response: eGFR < 60 ml/min. Secondary endpoint: incidence of flare and safety.

Results: At the beginning of maintenance therapy, the mean serum creatinine and eGFR were similar in the 3 groups (0.92 ± 0.26 mg/dl, eGFR 109.9 ± 49.5 ml/min in CYA, 0.86 ± 0.4 mg/dl, eGFR 119 ± 44.6 in MMF, 0.85 ± 0.3 mg/dl, eGFR 106.6 ± 43.9 ml/min in AZA). Proteinuria was higher in CYA group (CYA: 2.03 ± 1.7 g/day; MMF: 0.77 ± 0.8 g/day; AZA: 1.2 ± 1.1 g/day). At the beginning of maintenance therapy, complete, partial and no response were 26.6%, 60%, and 13.4% in CYA, 53.1%, 43.8% and 3.1% in MMF and 38.2%, 58.8% and 3% in AZA group (Fig 1). At 1 year, after 6 months of maintenance therapy, in CYA group the percentage of pts in complete remission increased to 73% (vs 65.6% in MMF and 40% in AZA), at 5 years it was 80% (vs 83% in AZA and in MMF) and 88% at 10 years vs 70% in MMF and 68% in AZA (Fig 2,3,4). The percentage of non-responsive pts was stable from 1 to 10 years in the CYA group (around 13%), it slightly increased in MMF group (from 3.1 to 13.5%) and in AZA group (from 15 to 24%). During the study, SLE flares occurred in 30% of CYA group, 41% in MMF and 32% of the AZA. The average time from the beginning of the study and the first flare was 3.95 ± 2.76 years in CYA, 3.62 ± 1.60 in MMF and 5.9 ± 2.37 in AZA. No side effects were reported in 90% of pts treated with CYA, in 81.3% with MMF and in 85.3% with AZA group.

Conclusion: This is the first study comparing these 3 drugs as maintenance therapy in the long term. After 10 years of observation, CYA, AZA and MMF have proven to be effective in consolidating and maintaining the remission of LN. Of interest are the results achieved in the CYA group. Despite worse clinical conditions at the beginning of maintenance therapy, CYA allowed a rapid achievement of LN remission in the great majority of pts compared to AZA and MMF. Remission persisted over 10 years of observation. The number and type of flares and of side effects were not different between groups.

Baseline

Figure 1

After 1 year

Figure 2

After 5 years

Figure 3

After 10 years

Figure 4

REFERENCE:

[1] Moroni G, et al. 2006

Disclosure of Interests: Lorenza Maria Argolini: None declared, Elena Elefante: None declared, Francesca Saccon: None declared, Valentina Binda: None declared, Maria Gerosa: None declared, Luigi Sinigaglia Speakers bureau: Yes, I, ve been invited speaker by Amgen, Ely Lilly, UCB, Abbvie, Roche and BMS., Piergiorgio Messa: None declared, Andrea Doria: None declared, Marta Mosca Paid instructor for: GlaxoSmithKline, Lilly, UCB, Gabriella Moroni: None declared
DOI: 10.1136/annrheumdis-2019-eular.3393

WEDNESDAY, 12 JUNE 2019

Crystals

OP0047

A GENOME-WIDE ASSOCIATION STUDY IDENTIFIED NOVEL LOCI ASSOCIATED WITH THE PROGRESSION FROM ASYMPTOMATIC HYPERURICEMIA TO GOUT

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Background: Gout is one of the commonest forms of inflammatory arthritis induced by monosodium urate (MSU) crystals that result from elevated serum uric acid (SUA) level. Thus far, we and others have performed genome-wide association studies (GWASs) of gout by comparing the genetic differences between gout cases and normouricemia controls¹⁻³ and have identified gout risk loci such as *ABCG2* and *SLC2A9*: these are similar results to those from GWASs of SUA. Meanwhile, not all hyperuricemia cases develop gout: the reason, we consider, is that there are at least two steps (Figure 1) by which normouricemic individuals develop gout.