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.

REFERENCES:

[1] Marder W, Fisseha S, Ganser MA, Somers EC. Ovarian damage during chemotherapy in autoimmune diseases broad health implications beyond fertility. Clin Med Insights Reprod Health 2012;6:9-18.

[2] Marder W, McCune WJ, Wang L, Wing JJ, Fisseha S, McConnell DS, et al. Adjunctive GnRH-a treatment attenuates depletion of ovarian reserve associated with cyclophosphamide therapy in premenopausal SLE patients. Gynecol Endocrinol 2012;28(8):624-7.

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OP0045 ABATACEPT TREATMENT OF PATIENTS WITH EARLY ACTIVE PRIMARY SJÖGREN'S SYNDROME – A RANDOMIZED, DOUBLE-BLIND PLACEBO-CONTROLLED PHASEFRED K.L. SPIJKERVETY. K. ONNO TENGE.J. ARENDS III-STUDY (ASAP-III)

Jolien F. van Nimwegen[1], Greetje S. van Zuiden[1], Suzanne Arends[1], Esther Mossel[1], Robin F. Wijnsma[1], Alja J. Stel[1], Konstantina Delli[2], Bert van der Vegt[3], Erlin A. Haacke[1,3], Lisette Olie[4], Leonie I. Los[4], Janita Bulthuis-Kuiper[1], Gwenny M. Verstappen[1], Sarah A. Pringle[1], Fred K.L. SpijkervetFrans G. M. Kroese[2], Frans G.M. Kroese[1], Arjan Vissink[2], Hendrika Bootsma[1]. *[1]University Medical Center Groningen, University of Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands*; *[2]University Medical Center Groningen, University of Groningen, Oral and Maxillofacial Surgery, Groningen, Netherlands*; *[3]University Medical Center Groningen, University of Groningen, Pathology and Medical Biology, Groningen, Netherlands*; *[4]University Medical Center Groningen, University of Groningen, Ophthalmology, Groningen, Netherlands*

Background: Effective systemic treatment is not yet available for primary Sjögren syndrome (pSS). Abatacept (CTLA-4-Ig) targets the CD80/CD86:CD28 co-stimulatory 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.

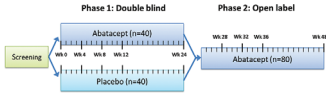

Figure 1. Design of the ASAPIII study.

REFERENCE:

[1] Meiners, et al. Ann Rheum Dis 2014;73:1393-6.

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.

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OP0046 MULTICENTRIC STUDY COMPARING CYCLOSPORINE, MYCOPHENOLATE MOFETIL AND AZATHIOPRINE IN THE MAINTENANCE THERAPY OF LUPUS NEPHRITIS: 10 YEARS FOLLOW UP

Lorenza Maria Argolini[1,2], Elena Elefante[3], Francesca Saccon[4], Valentina Binda[5], Maria Gerosa[1,2], Luigi Sinigaglia[2], Piergiorgio Messa[5], Andrea Doria[4], Marta Mosca[3], Gabriella Moroni[5]. *[1]University of Milan, Clinical Sciences and Community Health, Milan, Italy*; *[2]ASST Istituto Gaetano Pini – CTO, Clinical Rheumatology, Milan, Italy*; *[3]Rheumatology Unit, University of Pisa, Clinical and Experimental Medicine, Pisa, Italy*; *[4]University of Padua, Rheumatology, Padova, Italy*; *[5]Fondazione Ca' Granda IRCCS Ospedale Maggiore Policlinico Milano, Nephrology, Milan, Italy*

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