Conclusion: This preliminary analysis suggests that assessment of IFN activity has a role in predicting response to RTX. A novel IFN score (Score B) was more predictive than classic ISGs (Score A). These results add to a body of work showing that IFN-Score-B predicts clinically significant outcomes independently of overall IFN activity. Future work will analyse this biomarker in a larger cohort of patients and integrate with other putative clinical and biological predictors of response.

REFERENCE:

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Acknowledgement: We would like to thank the Medical Research Council, National Institute of Health Research, UK for funding the MASTERPLANS project.

Disclosure of Interests: Adewonuola Alase: None declared, Zoe Wigston: None declared, Agata Burska: None declared, Elizabeth Hensor: None declared, Md Yuzaiful Md Yusof: None declared, John Reynolds: None declared, The Masterplans Consortium: None declared, Miriam Wittmann Consultant for: consultancy honoraria from Abbvie, Celgene, Janssen, L'Oreal, Novartis and Pfizer, 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, Edward Vital Grant/research support from: He has received honoraria and research grant support from Roche, GSK and AstraZeneca.

DOI: 10.1136/annrheumdis-2019-eular.5750

FRI0180 OFF-LABEL USE OF RITUXIMAB IN RHEUMATIC DISEASES, A SWISS TERTIARY CENTRE EXPERIENCE

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Background: Rituximab (RTX), a monoclonal antibody targeting CD20, is licenced for the treatment of rheumatoid arthritis (RA) for many years and more recently for ANCA-associated vasculitis. RTX is frequently used off-label to treat other auto-immune diseases (AID), especially connective tissue diseases (CTD). There are no published data about off-label use of RTX in AID in Switzerland.

Objectives: To describe off-label use of RTX in a real-life setting, when treating AID.

Methods: Retrospective cohort study of all patients treated with RTX in the Rheumatology Department between 2005 and 2017. Clinical efficacy of RTX after 12 and 24 months of treatment was evaluated with a semi-quantitative scale (no response (NR), partial (PR) and complete response (CR)). RTX discontinuation rate was also analysed using Kaplan-Meier method and log rank test to evaluate the difference between survival curves. Adverse events (AE), serious AE (SAE) were included in the safety analysis. Occurrences of hypogammaglobulinemia and anti-rituximab antibodies (ADA) were also reported.

Results: 178 patients treated with RTX could be identified: 28% for CTD, 63% for RA and 10% for other AID.

Rituximab was used off-label in 73% of the patients according to official Swiss indications. No significant differences in terms of clinical response were observed in off-label indication after 12 months (NR: 15%/13%, PR:48%/52%, CR:37%/35%, n=108/31) and 24 months (NR:13%/9%, PR:37%/35%, CR:51%/57%, n=79/23) of treatment when compared with prescriptions following official Swiss indications, respectively. RTX discontinuation rate (HR 1.03 95% CI 0.71-1.49) was also similar between both groups.

Clinical response after RTX treatment did not differ significantly between patients with CTD and RA after 12 months (NR:10%/12%, PR:50%/52%, CR:40%/36%, n=42/n=84) and 24 months (NR:7%/9%, PR:32%/44%, CR:61%/47%, n=28/n=64), respectively. Detailed results are available in Table 1. Survival curves of rituximab treatment from CTD group closely matched that from RA group (HR 0.96 95% CI 0.65-1.44). Causes of RTX treatment discontinuation in patients with CTD (n=27) and RA (n=72) consisted of lack of efficiency (63%/56%), adverse event (19%/35%) and remission (19%/10%), respectively.

SAE (n=113) occurred in 33% of the patients and consisted mainly of infectious SAE (43%) and perfusion-related AE (6%). 6 patients died during RTX treatment. Low IgG levels were observed in 34% (50/149) of the patients graded as mild (20%), moderate (11%) or severe (3%). The nadir of IgG levels occurred after 4.5(3.5) years (mean (SD)) of RTX treatment. ADA were observed in 6/51 patients.

Conclusion: Off-label prescription of rituximab to treat AID was frequent. RTX discontinuation rate was comparable in patients treated for CTD and RA in our population.

Table 1

	Off-label prescription*	Partial or complete response after 12 months of RTX treatment	Partial or complete response after 24 months of RTX treatment	Rituximab discontinuation rate (95% CI), all causes, at :		
	n (%)	n=139 (%)	n=102 (%)	1 year	2 years	4 years
Connective tissue disease (n=49)	49/49 (100)	38/42 (90)	26/28 (93)	0.23 (0.13-0.37)	0.40 (0.27-0.55)	0.56 (0.42-0.71)
Overlap syndrome (n=14)		12/12 (100)	9/9 (100)			
Systemic lupus erythematosus (n=12)		8/10 (80)	7/8 (88)			
UCTD (n=8)		4/6 (67)	2/2 (100)			
Sjögren's syndrome (n=6)		6/6 (100)	4/4 (100)			
Dermato-, polymyositis (n=5)		5/5 (100)	2/3 (67)			
MCTD (n=3)		2/2 (100)	1/1 (100)			
Systemic sclerosis (n=1)		1/1 (100)	1/1 (100)			
Rheumatoid arthritis (n=112)	66/112 (59)	74/84 (88)	58/64 (91)	0.27 (0.20-0.36)	0.35 (0.27-0.44)	0.55 (0.46-0.65)
Other auto-immune diseases (n=17)	15/17 (88)	7/13(54)	6/10 (60)	0.35 (0.18-0.62)	0.76 (0.55-0.93)	-

RTX: rituximab; AE: adverse event, MCTD: Mixed connective tissue disease; UCTD: Undifferentiated connective tissue disease.

*off-label prescription according to Swiss Agency for Therapeutic Products (Swissmedic)

Disclosure of Interests: Alexandre Dumusc: None declared, Thomas Huegle Grant/research support from: AbbVie, Lilly, Novartis and Pfizer, Speakers bureau: AbbVie, Lilly, Novartis and Pfizer, Pascal Zufferey: None declared

DOI: 10.1136/annrheumdis-2019-eular.6923

FRI0181 THE PLUTO STUDY: INTRAVENOUS BELIMUMAB IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Belimumab (BEL), a monoclonal antibody targeting the B-lymphocyte stimulator, is approved in adults with active systemic lupus erythematosus (SLE). This is the first clinical trial of belimumab in pediatric patients with childhood-onset SLE (cSLE).

Objectives: PLUTO, a Phase 2, randomised, double-blind trial (BEL114055; NCT01649765), evaluated the efficacy, safety and pharmacokinetics (PK) of intravenous (IV) BEL vs placebo (PBO), plus standard of care (SoC), in cSLE.

Methods: Patients with cSLE 5–17 years of age were randomised to BEL 10 mg/kg IV or PBO every 4 weeks, plus SoC. Primary endpoint: SRI4 at Week 52. Major secondary endpoints: PRINTO/ACR 30 and 50 cSLE evaluation criteria for improvement at Week 52; cSLE core response variables at Week 52; and sustained SRI4 and ParentGA (patient well-being) responses (Weeks 44–52). Other endpoints: components of SRI4 at Week 52; and frequency of severe flares using the

modified SELENA-SLEDAI Flare Index. Safety and PK were assessed. Analyses were performed on the intent-to-treat population. The study was not powered to test for differences between groups; p-values were not calculated.

Results: 93 patients were included (BEL, n=53; PBO, n=40). Groups (BEL vs PBO) were balanced at baseline for age (mean [standard deviation] 13.5 [2.59] vs 14.8 [2.17] years, respectively) and SELENA-SLEDAI score (10.3 [3.34] vs 10.4 [3.63], respectively). Compared with PBO, there were more SRI4 responders (including all 3 components of SRI4), and PRINTO/ACR 30 and 50 responders in the BEL group (**Figure**). Likewise, more BEL than PBO recipients had sustained improvement of SRI and patient well-being (ParentGA) (**Figure**). Changes in cSLE core response variables are shown in the **Table**. Severe flares were 62% less frequent with BEL vs PBO (hazard ratio 0.38 [95% CI 0.18, 0.82]). PK: BEL exposures in cSLE were similar to adult SLE studies. 9/53 (17%) BEL patients had ≥1 serious adverse event vs 14/40 (35%) PBO patients. One PBO patient died of acute pancreatitis.

Conclusion: The benefit:risk profile of BEL IV plus SoC in cSLE is generally consistent with BEL in adult SLE. The 10 mg/kg IV dose used in adults may be an appropriate dose in cSLE.

Acknowledgement: The authors would like to acknowledge all investigators (PRINTO, PRCSG and otherwise affiliated) for the PLUTO study. Study funded by GSK. Gosia Carless, PhD, Fishawack Indicia Ltd, UK, provided editorial assistance funded by GSK.

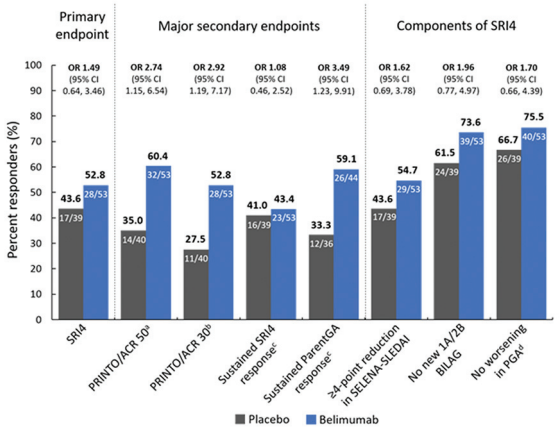
Disclosure of Interests: Nicolino Ruperto Grant/research support from: The Gaslini Hospital, where NR works as full-time public employee, has received contributions (> 10.000 USD each) from the following industries in the last 3 years: BMS, Eli-Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties., Consultant for: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Speakers bureau: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Carlos Abud-Mendoza: None declared, Diego O Viola: None declared, Inmaculada Calvo Grant/research support from: received research grants from Pfizer, Roche, Novartis, Clementia, Sanofi, MSD, BMS and GSK, Consultant for: Advisory boards: Novartis, AbbVie, Speakers bureau: AbbVie, Roche, Novartis, SOBI, Deborah M Levy Consultant for: received consulting fees and/or honoraria from AbbVie and Janssen, Julia Calderon Gallegos: None declared, Manuel Ferrandiz: None declared, Vyacheslav Chasnyk: None declared, Vladimir Keltsev: None declared, Jordi Anton Grant/research support from: JA has received grant/research support, consulting fees and/or honoraria from AbbVie, Alexion, BMS, ChemoCentryx, Gebro, GSK, Novartis, Novimmune, Pfizer, Roche, Sanofi and Sobi, Consultant for: JA has received grant/research support, consulting fees and/or honoraria from AbbVie, Alexion, BMS, ChemoCentryx, Gebro, GSK, Novartis, Novimmune, Pfizer, Roche, Sanofi and Sobi, Maria Gastanaga: None declared, Michael Shishov: None declared, Alina Boteanu: None declared, Michael Henrickson: None declared, Damon Bass Shareholder of: GSK, Employee of: GSK, Ken Clark Shareholder of: GSK, Employee of: GSK, Anne Hammer Shareholder of: GSK, Employee of: GSK, Beulah Ji Shareholder of: GSK, Employee of: GSK, Antonio Nino Shareholder of: GSK, Employee of: GSK, David Roth Shareholder of: GSK, Employee of: GSK, Herbert Struemper Shareholder of: GSK, Employee of: GSK, Mei-Lun Wang Employee of: former employee of GSK, Alberto Martini Consultant for: I do not have any conflict of interest to declare since starting from 1 March 2016 I became the Scientific Director of the G. Gaslini Hospital; therefore, my role does not allow me to render private consultancies resulting in personal income.

I perform consultancy activities on behalf of the Gaslini Institute for the companies listed below:

AbbVie, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, EMD Serono, Janssen, Novartis, Pfizer, R-Pharm.

The money received for these activities are directly transferred to the Gaslini Institute's bank account. Before March 2016, I was the head of the Pediatric Rheumatology Department at the G. Gaslini Hospital, where the PRINTO Coordinating Centre is located. For the coordination activity of the PRINTO network, the Gaslini Hospital received contributions from the industries listed in this section. This money has been reinvested for the research activities of the hospital in fully independent manners besides any commitment with third parties., Daniel J Lovell Consultant for: Consulting fees and/or honoraria from Astra Zeneca, Wyeth Pharma, Amgen, Abbott, Pfizer, F. Hoffmann-La Roche, Novartis, UBC, Takeda, GSK, Boehringer, and Celgene, Hermine Brunner Grant/research support from: Bristol-Myers Squibb, Pfizer, Consultant for: Pfizer, Bristol-Myers Squibb, Janssen, Novartis, Lilly, Roche, GlaxoSmithKline, Sanofi, Speakers bureau: Novartis, Roche

Figure. Primary and major secondary endpoints at Week 52 (N=93)



[a]At least 50% improvement in 2 of 5 cSLE core response variables, with no more than 1 of the remaining worsening by more than 30%; [b]at least 30% improvement in 3 of 5 cSLE core response variables, with no more than 1 of the remaining worsening by more than 30%; [c]Weeks 44–52; [d]Defined as increase of <0.30 points from baseline

ACR, American College of Rheumatology; BILAG, British Isles Lupus Activity Group; CI, confidence interval; OR, odds ratio; ParentGA, parent global assessment; PGA, Physician's Global Assessment; PRINTO, Pediatric Rheumatology International Trials Organisation; SELENA-SLEDAI, Safety of Estrogens in Systemic Lupus Erythematosus-National Assessment Trial-Systemic Lupus Erythematosus Disease Activity Index; SRI, SLE Responder Index

Table. Percent change from baseline in cSLE core response variables at Week 52

PRINTO/ACR variable	Placebo (n=40)	Belimumab (n=53)
ParentGA, median (range)	−23.6 (−95, 600)	−53.9 (−100, 900)
n	38	47
PGA, median (range)	−47.9 (−100, 61)	−76.1 (−100, 117)
n	40	53
SELENA-SLEDAI, median (range)	−50.0 (−100, 58)	−50.0 (−100, 150)
n	39	53
PedsQL (physical functioning), median (range)	12.5 (−53, 575)	10.5 (−100, 280)
n	40	53
Proteinuria, median (range)	7.1 (−91, 570)	−2.1 (−85, 1682)
n	40	53

PedsQL, Pediatric Quality of Life Inventory; PGA, Physician's Global Assessment

DOI: 10.1136/annrheumdis-2019-eular.4884

FRI0182 FREQUENCY OF HYDROXYCHLOROQUINE RETINOPATHY IN THE HOPKINS LUPUS COHORT

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Background: The Kaiser-Permanente study projected hydroxychloroquine (HCQ) retinopathy rates of 40% after 20 years of use (1).

Objectives: We have prospectively followed SLE patients in the Hopkins lupus cohort to compare.

Methods: Patients in the Hopkins cohort are seen quarterly for assessment of disease activity and lupus complications. Yearly ophthalmology examinations are requested. Patients, if insurance allows, are referred to the Wilmer Retina group. Four tests are performed: OCT, ERG, MP-1 and FAF.