Table 1. CLASI-50 Response Rates by Subgroups at Week 24

Subgroup	0.15 mg QD			0.3 mg QD			0.45 mg QD		
	(n=42)			(n=82)			(n=81)		
	Placebo (n=83)	0.15 mg QD vs Placebo	0.3 mg QD vs Placebo	0.3 mg QD vs Placebo	0.45 mg QD vs Placebo	0.45 mg QD vs Placebo	0.45 mg QD vs Placebo	0.45 mg QD vs Placebo	0.45 mg QD vs Placebo
	n/m (%)	n/m (%)	Str Diff in % (95% CI) P value	n/m (%)	Str Diff in % (95% CI) P value	n/m (%)	Str Diff in % (95% CI) P value	n/m (%)	Str Diff in % (95% CI) P value
All pts	37/83 (44.6)	19/42 (45.2)	0.4 (-17.33, 18.55) <i>P</i> =0.961	41/82 (50.0)	5.3 (-9.93, 20.11) <i>P</i> =0.499	45/81 (55.6)	10.9 (-4.30, 25.51) <i>P</i> =0.163	45/81 (55.6)	10.9 (-4.30, 25.51) <i>P</i> =0.163
CLASI-A ≥8	10/20 (50.0)	8/13 (61.5)	15.9 (-17.42, 45.45) <i>P</i> =0.399	13/24 (54.2)	12.1 (-17.57, 39.97) <i>P</i> =0.458	16/24 (66.7)	15.1 (-15.51, 42.49) <i>P</i> =0.368	16/24 (66.7)	15.1 (-15.51, 42.49) <i>P</i> =0.368
ACLE	23/50 (46.0)	15/30 (50.0)	4.8 (-17.22, 26.31) <i>P</i> =0.662	20/43 (46.5)	-3.3 (-22.95, 16.67) <i>P</i> =0.738	17/38 (44.7)	-3.0 (-23.20, 17.65) <i>P</i> =0.782	17/38 (44.7)	-3.0 (-23.20, 17.65) <i>P</i> =0.782
SCLE	9/17 (52.9)	5/9 (55.6)	2.6 ^a (-33.04, 36.33) <i>P</i> =0.966	3/9 (33.3)	-6.6 (-38.98, 31.86) <i>P</i> =0.999	11/12 (91.7)	38.7 ^a (4.54, 61.75) <i>P</i> =0.035	11/12 (91.7)	38.7 ^a (4.54, 61.75) <i>P</i> =0.035
CLE	5/18 (27.8)	7/14 (50.0)	22.2 ^a (-10.51, 50.00) <i>P</i> =0.198	10/23 (43.5)	23.8 (-6.89, 48.88) <i>P</i> =0.129	18/29 (62.1)	34.1 (4.43, 56.16) <i>P</i> =0.029	18/29 (62.1)	34.1 (4.43, 56.16) <i>P</i> =0.029

CI, confidence interval; Str Diff, stratified difference.^aUnstratified difference.

Figure. CLASI-A Percent Change From Baseline by CLE Subtype for All Patients and Patients with High Baseline Expression of IKZF3 or Type 1 IFN Gene Signature

Δ, treatment difference of adjusted means; CLE, chronic cutaneous lupus erythematosus; CLASI-A, Cutaneous Lupus Erythematosus Disease Area and Severity Index-activity score; IFN, interferon; SCLE, subacute cutaneous lupus erythematosus.

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OP0133

THE PREVALENCE AND RISK FACTORS OF RETINAL TOXICITY ASSOCIATED WITH LONG-TERM HYDROXYCHLOROQUINE USE

S. Do¹, J. H. Du², J. X. An³, J. Wang⁴, A. Lin⁵. ¹Western University of Health Sciences, School of Pharmacy, Pomona, United States of America; ²Kaiser Permanente Fontana Medical Center, Department of Pharmacy, Fontana,

United States of America; ³Kaiser Permanente Research & Evaluation, Department of Research and Evaluation, Pasadena, United States of America; ⁴Kaiser Permanente Fontana Medical Center, Department of Ophthalmology, Fontana, United States of America; ⁵Kaiser Permanente Southern California, Department of Rheumatology, Fontana, United States of America

Background: Hydroxychloroquine (HCQ) is commonly used for the treatment of various autoimmune diseases. The medication is generally well-tolerated. However, long-term use after 5 years may increase the risk of retinopathy. One study in 2014 has demonstrated the risk can be as high as 7.5%. Optical Coherence Tomography (OCT) has become a major modality in screening retinopathy.

Objectives: To evaluate the prevalence of retinal toxicity among patients using hydroxychloroquine and to determine various risk factors associated with hydroxychloroquine-associated retinal toxicity.

Methods: We performed a retrospective chart review on a cohort of adult patients with long-term use (≥ 5 years cumulative) of HCQ between January 1st, 2011 to December 31st, 2018 from the Kaiser Permanente San Bernardino County and Riverside medical center areas in Southern California, USA. Patients were excluded if they had previously been diagnosed with retinopathy prior to hydroxychloroquine use, were deceased, or had incomplete OCT exam. Our primary endpoint was the prevalence of patients who developed retinal toxicity detected by OCT, and later confirmed by retinal specialist. Potential risk factors (age, duration of therapy, daily consumption per actual body weight, cumulative dose, confounding diseases and medication) for developing retinopathy were also evaluated. Univariable and multivariable logistic regression analyses were used to determine risk factors associated with retinal toxicity.

Results: Among 676 patients exposed to more than 5 years of HCQ, the overall prevalence of retinal toxicity was 6.8%, and ranged from 2.5% to 22.2% depending on the age, weight-based dosing, duration of use and cumulative dose. Duration of therapy for 10 years or more increased risk of retinopathy by approximately 5 to 19 folds. Similarly, weight-based dose of 7 mg/kg/day or greater was associated with increased risk of retinopathy by approximately 5 times. Patients with cumulative dose of 2000 grams or more had greater than 15 times higher risk of developing retinopathy. Duration of use for 10 years or more (odds ratio 4.32, 95% CI 1.99 – 12.49), age (odds ratio 1.04; 95% CI 1.01 – 1.08), cumulative dose of more than 1500g (odds ratio 7.4; 95% CI 1.40 – 39.04) and atherosclerosis of the aorta (odds ratio 2.59; 95% CI, 1.24 – 5.41) correlated with higher risk of retinal toxicity.

Table 2. Hydroxychloroquine Treatment Exposure

	No Retinal Toxicity (N=630)		Retinal Toxicity (N=46)		p-value
	Mean	Std Dev	Mean	Std Dev	
Dose per day (mg)	326.6	96.2	337	92.8	0.479
Dose per kg/day	4.3	1.4	4.9	1.7	0.003
Duration of use					
Months	99.3	33.4	141.5	64.5	< 0.0001
Years	8.3	2.8	11.8	5.4	< 0.0001
Cumulative dose (mg)	983.2	445.2	1483.6	891.5	< 0.0001

Conclusion: The overall prevalence of retinopathy was 6.8%. Regular OCT screening, especially in patients with hydroxychloroquine use for more than 10 years, daily intake > 7 mg/kg, or cumulative dose > 1500 grams is important in detecting hydroxychloroquine-associated retinal toxicity

Prevalence of HCQ Retinopathy Stratified by Cumulative Dose (g)

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OP0134

NOVEL INTERFERON GENE EXPRESSION SCORES PREDICT REFRACTORY SEVERE CUTANEOUS DISEASE FOLLOWING RITUXIMAB THERAPY IN SLE

L. M. Carter¹, A. Alase², Z. Wigston², A. Psarras², A. Burska², M. Y. MD Yusuf², E. Hensor², J. Reynolds³, M. Wittmann², I. N. Bruce⁴, E. Vital² on behalf of The MASTERPLANS Consortium. ¹University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom; ²University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom; ³University of Birmingham, Institute of Inflammation and Ageing, Birmingham, United Kingdom; ⁴University of Manchester, Division of Musculoskeletal & Dermatological Sciences, Manchester, United Kingdom

Background: We developed and validated two continuous interferon-stimulated gene (ISG) expression scores (IFN-Score-A and IFN-Score-B) that predict clinical outcomes in SLE. IFN-Score-A includes ISGs typically present in a global interferon signature while IFN-Score-B includes additional ISGs potentially responsive to multiple IFN subtypes [1].

We have previously shown that these scores associate with treatment response following rituximab (RTX) therapy within the British Isles Lupus Assessment Group (BILAG) Biologics Register (BILAG-BR), a UK wide study of patients treated with RTX for active SLE following cyclophosphamide and/ or mycophenolate mofetil treatment failure. Specifically, multivariable analysis showed higher baseline IFN-Score-B independently predicted BILAG response at 6 months post treatment [2]. We also showed that response of cutaneous lupus to RTX can be poor even when other organs respond well, and that interferons are enriched in the skin of patients with SLE where dysregulated keratinocytes are a source of IFN κ [3]. MASTERPLANS is a consortium aimed at identifying therapeutic biomarkers in SLE.

Objectives: To investigate how IFN-Score-A and -B associated with skin disease and response to RTX.

Methods: Pre-treatment whole blood samples were collected in TEMPUS tubes from subjects undergoing first RTX treatment within BILAG-BR. IFN-Scores were derived using a custom Taqman array as previously described [1]. Clinical response was defined as improvement in BILAG-2004 disease activity, with a maximum of one domain showing persistent BILAG-2004 grade B disease, and no new BILAG grade A or B disease flares at 6 months. The mucocutaneous domain of BILAG was then analysed separately.

Results: 147 patients were studied, of whom 90 had follow up data available. Baseline BILAG-2004 grade A/B disease activity predominantly affected the mucocutaneous domain in 74/147 (50.3%), musculoskeletal in 61 /147 (41.5%) and renal domain 66/147 (37.4%).

At 6 months 59/90 (65.6%) achieved an overall treatment response. Responders showed significantly higher mean IFN-Score-B compared with non-responders (-1.8 vs -2.4, $p = 0.04$). Among those with active grade A/B BILAG-2004 mucocutaneous disease at baseline, 38/50 (76%) showed improvement within this domain at 6 months. However, among overall non-responders, 7/31 (22.6%) had new or residual BILAG-A mucocutaneous disease at 6 months post RTX, indicating it to be a substantial component of overall treatment failure. In contrast, persistent grade A musculoskeletal disease was seen in 9.7% of non-responders. BILAG-A mucocutaneous disease is characterised by severe manifestations including extensive rashes covering > 18% of body surface area, severe bullous lupus or panniculitis and disabling deep mucosal ulceration. Neither IFN-Score-A nor IFN-Score-B were significantly associated with the severity of mucocutaneous disease at baseline. However, individuals with persistent or new BILAG-A mucocutaneous disease at six months following RTX displayed significantly lower baseline IFN-Score-B than those with improving or residual less severe disease (-3.0 vs -2.1, $p = 0.04$) after RTX.

Conclusion: Low IFN score-B status identified an endotype of severe mucocutaneous SLE which was resistant to RTX therapy in the BILAG-BR cohort. We previously showed that high IFN-score-B independently predicts overall therapeutic response to rituximab. Further work will aim to refine IFN status as overall and organ specific biomarkers in SLE.

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OP0135

SAFETY AND EFFICACY OF SUBCUTANEOUS BELIMUMAB AND INTRAVENOUS RITUXIMAB COMBINATION IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME: A PHASE 2, RANDOMISED, PLACEBO-CONTROLLED 68-WEEK STUDY

X. Mariette¹, C. Baldini², F. Barone³, H. Bootsma⁴, K. Clark⁵, S. De Vita⁶, K. Lerang⁷, P. Mistry⁸, F. Morin⁹, R. Punwaney¹⁰, R. Seror¹, P. L. Van Daele¹¹, A. Van Maurik¹², N. Wisniacki¹³, D. Roth¹⁴. ¹Université Paris-Saclay, Rheumatology, Paris, France; ²University of Pisa, Rheumatology Unit, Department of Clinical and Experimental Medicine, Pisa, Italy; ³University of Birmingham, College of Medical and Dental Sciences, Rheumatology, Birmingham, United Kingdom; ⁴University of Groningen, University Medical Center Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands; ⁵GlaxoSmithKline, Clinical Science, Stevenage, United Kingdom; ⁶Azienda Ospedaliera Universitaria di Udine, Rheumatology Clinic, Department of Medical Area, Udine, Italy; ⁷Oslo University Hospital, Department of Rheumatology, Oslo, Norway; ⁸GlaxoSmithKline, R&D Biostatistics, Stevenage, United Kingdom; ⁹Centre de Recherche Musculo-Squelettique, Centre de Recherche Musculo-Squelettique, Trois Rivières, Canada; ¹⁰GlaxoSmithKline, Pharmaceutical Research and Development, Philadelphia, PA, United States of America; ¹¹Erasmus Medical Center, Department of Internal Medicine and Department of Immunology, Rotterdam, Netherlands; ¹²GlaxoSmithKline, Clinical Pharmacology and Experimental Medicine, Stevenage, United Kingdom; ¹³GlaxoSmithKline, Discovery Medicine, Stevenage, United Kingdom; ¹⁴GlaxoSmithKline, Research and Development, Collegeville, PA, United States of America