British Isles Lupus Assessment Group (BILAG) index. In addition, the modified Cutaneous Lupus Erythematosus Disease Area and Severity Index (mCLASI) score was used to evaluate rash, and tender and swollen joint counts were used to assess arthritis.

Results: 360 patients received anifrolumab 300mg (IFNGS test-high, n=298; IFNGS test-low, n=62) and 366 patients were given placebo (IFNGS test-high, n=302; IFNGS test-low, n=64). Change from baseline to Week 52 compared with placebo was measured by outcomes, ordered by their stringency. More anifrolumab-treated patients achieved rash improvement using SLEDAI-2K (complete resolution: difference 13.5%, nominal $P<0.001$), BILAG (at least 1 severity grade lowering: difference 15.5%, nominal $P<0.001$), and mCLASI ($\geq 50\%$ improvement, if baseline score >0 : difference 15.6%, nominal $P<0.001$). Results were comparable in the IFNGS test-high subset (SLEDAI-2K: difference 17.0%, nominal $P<0.001$, BILAG: difference 16.1%, nominal $P<0.001$; mCLASI: difference 18.1%, nominal $P<0.001$). There was a trend toward anifrolumab-associated rash improvement in IFNGS test-low patients using BILAG (Figure). More patients receiving anifrolumab had SLEDAI-2K-defined resolution in arthritis (difference 8.2%, nominal $P=0.029$), BILAG severity lessening (difference 11.8%, nominal $P=0.002$), and $\geq 50\%$ decrease in tender/swollen joint counts, when ≥ 6 at baseline (difference 12.6%, nominal $P=0.016$). Results were comparable in the IFNGS test-high subset (SLEDAI-2K: difference 11.7%, nominal $P=0.005$; BILAG: difference 12.9%, nominal $P=0.003$; joint counts: difference 11.3%, nominal $P=0.054$). In IFNGS test-low patients, there was a trend toward anifrolumab-associated arthritis improvement when measured using BILAG, and the effect of anifrolumab on the number of swollen/tender joint counts was similar to the IFNGS test-high group, although the IFNGS test-low sample size in this analysis was very small (Figure).

Conclusion: In pooled data from the TULIP trials, anifrolumab treatment was associated with improvements in rash and arthritis using measures of different stringency. The SLEDAI-2K findings were largely driven by the subset of patients who were IFNGS test-high. However, using measures that were more sensitive to change, despite small sample sizes, IFNGS test-low patients may also have benefit.

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Figure. Patients with SLEDAI-2K-defined resolution (A) and BILAG-defined improvement (B) in rash. Patients with $\geq 50\%$ improvement in mCLASI score from baseline to Week 52 (mCLASI >0 at baseline) (C). Patients with SLEDAI-2K-defined resolution (D) and BILAG-defined improvement (E) in arthritis. Patients with $\geq 50\%$ improvement in the number of swollen or tender joints from baseline to Week 52 (≥ 6 at baseline) (F).

BILAG, British Isles Lupus Assessment Group; IFNGS, interferon gene signature; mCLASI, modified Cutaneous Lupus Erythematosus Disease Area and Severity Index; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000.

Data pooled from TULIP-1 and TULIP-2 trials. Resolution defined as: SLEDAI-2K rash component=0 (patients with SLEDAI-2K rash component ≥ 2 at baseline); SLEDAI-2K arthritis component=0 (patients with SLEDAI-2K arthritis component ≥ 4 at baseline); improvement defined as: BILAG rash, mucocutaneous baseline score A change to B, C, or D, or baseline B change to C or D; BILAG arthritis, musculoskeletal baseline score A change to B, C, or D, or baseline B change to C or D; mCLASI defined as the activity portions of CLASI that describe skin erythema, scale/hypertrophy, and inflammation of the scalp.

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OP0132

EFFECT OF IBERDOMIDE ON CUTANEOUS MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS OF A 24-WEEK, PLACEBO-CONTROLLED, PHASE 2 STUDY

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Background: Iberdomide is a high-affinity cereblon ligand that promotes proteasomal degradation of Ikaros (*IKZF1*) and Aiolos (*IKZF3*), transcription factors involved in innate and adaptive immune cell development and homeostasis, and linked to the genetic risk for systemic lupus erythematosus (SLE). A phase 2, placebo-controlled study evaluated the efficacy and safety of iberdomide in patients (pts) with moderate to severe SLE.

Objectives: To examine the effect of iberdomide on cutaneous manifestations in SLE pts.

Methods: Adult autoantibody-positive SLE pts with a SLE Disease Activity Index 2000 (SLEDAI 2K) score ≥ 6 were randomized (2:2:1:2) to oral iberdomide (0.45, 0.3, 0.15 mg) or placebo once daily (QD) for 24 weeks while continuing standard background lupus medications. The Cutaneous Lupus Area and Severity Index Activity score (CLASI-A) was assessed every 4 weeks through week 24. As prespecified, exploratory analyses, change from baseline and the proportion of pts who achieved $\geq 50\%$ reduction from baseline (CLASI-50) were evaluated for all pts, pts with baseline CLASI-A ≥ 8 , and by cutaneous lupus subtypes (acute [ACLE], subacute [SCLE], chronic [CCLE]). CLASI-A outcomes were also evaluated post hoc for subgroups with high baseline expression of *IKZF3* or the type 1 interferon (IFN) gene signatures in the blood.

Results: Of 288 randomized pts, the mean and median (range) baseline CLASI-A scores were 6.9 and 5.0 (0-49), with 28% of pts having a score ≥ 8 . 56% of pts had ACLE, 29% CCLE, and 16% SCLE. CLASI-50 responses were not significantly different comparing iberdomide to placebo in all pts and pts with baseline CLASI-A ≥ 8 at week 24, where high placebo response rates were observed (Table). Numerically greater mean improvement from baseline in CLASI-A scores in pts with baseline CLASI-A ≥ 8 was observed for iberdomide 0.45 mg vs placebo beginning at week 4, with continuous improvement through week 24. For pts with SCLE or CCLE, CLASI-50 response rates were significantly higher with iberdomide 0.45 mg vs placebo at week 24 ($P<0.03$). Treatment differences in CLASI-A between iberdomide 0.45 mg and placebo were larger for SCLE and CCLE subgroups with high baseline *IKZF3* or type 1 IFN gene signatures, with statistical significance achieved for SCLE pts but not CCLE pts (Figure).

Conclusion: Iberdomide showed beneficial effects on skin manifestations in pts with SLE. Efficacy appears to be more pronounced in pts with SCLE and CCLE skin subtypes, and in pts with high *IKZF3* or IFN gene expression signatures.

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

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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