multi-centre abatacept trial³ and ETAP (tocilizumab) trial⁴. CRESS response rates were assessed at the primary endpoint visit of all four trials.

Results: Five complementary items were selected to form CRESS: systemic disease activity, patient-reported symptoms, tear gland, salivary gland and serological item. Definition of response per item is presented in Table 1. Total CRESS response was defined as response on ≥ 3 of 5 items. Since not all trials have ocular staining score or salivary gland ultrasonography (SGUS) available, the concise CRESS (cCRESS) was developed simultaneously, leaving Schirmer's test and unstimulated whole saliva flow for the tear and salivary gland items, respectively. In the ASAP-III trial, CRESS response rates were 24/40 (60%) for abatacept vs. 7/39 (18%) for placebo at week 24 ($p < 0.001$).

Table 1. CRESS items and definition of response

Items	Measurements	Definition of response
Systemic disease activity	ClinESSDAI	Score < 5 (low disease activity)
Patient-reported symptoms	ESSPRI	Decrease of ≥ 1 point or $\geq 15\%$
Tear gland*	Schirmer/OSS**	-If abnormal Schirmer (≤ 5 mm) at baseline: increase of ≥ 5 mm in Schirmer -Or if abnormal OSS (≥ 3 points) at baseline: decrease ≥ 2 points in OSS -Or if both Schirmer/OSS normal scores at baseline: no change to abnormal in both
Salivary gland*	UWS/SGUS	Increase of $\geq 25\%$ in UWS (or if score is 0 at baseline, any increase) Or decrease of $\geq 25\%$ in total Hocevar score (SGUS)
Serological	RF/IgG	Decrease of $\geq 25\%$ in RF Or decrease of $\geq 10\%$ in IgG
CRESS responder	Responder on ≥ 3 of 5 items	

Ocular Staining Score (OSS), Unstimulated whole salivary flow (UWS), Salivary gland ultrasonography (SGUS), Rheumatoid factor (RF), Immunoglobulin G (IgG)***Concise CRESS (cCRESS):** CRESS without OSS and SGUS, leaving Schirmer and UWS for tear and salivary gland items, respectively**Mean of both eyes

Figure 1 A. CRESS and cCRESS (=CRESS without OSS and SGUS) response rates in ASAP-III trial at week 12 and 24. At week 12, only CRESS without SGUS was available. B. cCRESS response rates in TRACTISS (rituximab) trial at week 24 and 48. C. CRESS without SGUS response rates in multi-centre abatacept trial at week 12 and 24. D. cCRESS without rheumatoid factor response rates in ETAP (tocilizumab) trial at week 12 and 24. E. CRESS response rates vs. ESSDAI MCII response rates in ASAP-III trial at week 24. Median baseline ESSDAI scores for abatacept were 14.0 (IQR 9.0-16.8), for placebo 13.0 (IQR 8.0-18.0). F. cCRESS response rates vs. ESSDAI MCII response rates in TRACTISS trial at week 48. Mean baseline ESSDAI scores for rituximab were 5.3, SD=4.7, for placebo 6.0, SD=4.3. G. CRESS without SGUS response rates vs. ESSDAI MCII response rates in multi-centre abatacept trial at week 24. Mean baseline ESSDAI scores for abatacept were 8.7, SD=3.4, for placebo 10.1, SD=4.0. H. CRESS without RF response rates vs. ESSDAI MCII response rates in ETAP trial at week 24. Median baseline ESSDAI scores for tocilizumab were 11.0 (IQR 8.0-13.5), for placebo 10.0 (IQR 8.0-14.8). For all trials, ESSDAI response percentages were calculated imputing missing patients as non-responders.

In the external validation trials, cCRESS response rates for TRACTISS were: 33/67 (49%) rituximab vs. 20/66 (30%) placebo at week 48 ($p=0.026$). CRESS response rates (without SGUS) for the multi-centre abatacept trial were: 41/92 (45%) abatacept vs. 30/95 (32%) placebo at week 24 ($p=0.067$). cCRESS response rates (without rheumatoid factor) for ETAP were: 10/55 (18%) tocilizumab vs. 13/55 (24%) placebo at week 24 ($p=0.482$) (Figure 1A-D). Compared to ESSDAI MCII of ≥ 3 points decrease, CRESS was able to approximately halve placebo response rates in RCTs with high baseline ESSDAI scores (> 5) (Figures 1E-H).

Conclusion: CRESS shows lower placebo response rates compared to ESSDAI MCII, which is crucial for demonstrating treatment efficacy. With the CRESS, higher response rates in abatacept and rituximab treated patients compared to placebo were found in RCTs which previously showed negative primary endpoint results. CRESS confirmed that no differences were found for almost all outcome measures between tocilizumab and placebo,⁴ with low response rates. The CRESS is a well-balanced, feasible, composite endpoint for use in clinical trials in PSS patients.

REFERENCES:

- [1] Van Nimwegen 2020;9913(19):1–11
- [2] Bowman 2017;69(7):1440–50
- [3] Baer (doi:218599)
- [4] Felten (doi:21846)

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OP0131 ANIFROLUMAB EFFECTS ON RASH AND ARTHRITIS IN PATIENTS WITH SLE AND IMPACT OF INTERFERON SIGNAL IN POOLED DATA FROM PHASE 3 TRIALS

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Background: Treatment with the type I interferon (IFN) receptor antibody anifrolumab was associated with clinical improvements in mucocutaneous and musculoskeletal disease activity in patients with systemic lupus erythematosus (SLE) in the phase 2 MUSE trial (NCT01438489) and phase 3 TULIP trials.^{1–4} Because rash and arthritis are the most common manifestations of SLE, the effect of anifrolumab on these symptoms can be examined in biomarker-defined subsets, as previously reported for the MUSE trial.²

Objectives: To evaluate the effect of anifrolumab on rash and arthritis in patients with SLE, and the impact of IFN gene signature (IFNGS) on treatment response, using disease measures of different stringency in pooled data from the phase 3 TULIP trials.

Methods: TULIP-1 (NCT02446912) and TULIP-2 (NCT02446899) were placebo-controlled, 52-week trials of intravenous anifrolumab administered every 4 weeks in patients with moderate to severe SLE.^{3,4} In this post hoc analysis, outcomes of rash and arthritis were evaluated using mucocutaneous and musculoskeletal domains of the SLE Disease Activity Index 2000 (SLEDAI-2K) and the

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.

REFERENCES:

1. Furie R, et al. *Arthritis Rheumatol*. 2017;69:376–86.
2. Merrill JT, et al. *Lupus Sci Med*. 2018;5:e000284.
3. Furie RA, et al. *Lancet Rheumatol*. 2019;1:e208–19.
4. Morand EF, et al. *N Engl J Med*. 2020;382:211–21.

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.