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Figure. Subgroup Analysis of SRI-4 Response Between BIIB059 and Placebo at Week 24

BILAG 2004 = British Isles Lupus Assessment Group 2004; dsDNA = double-stranded DNA; LLN = lower limit of normal; LS = least-squares; OCS = oral corticosteroid; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000; SLE = systemic lupus erythematosus; SRI-4 = SLE Responder Index

SRI-4 was defined as a reduction from baseline of ≥ 2 points in SLEDAI-2K, no new BILAG-2004 Grade A domain score or no more than 1 new BILAG-2004 Grade B domain score, no worsening from baseline in Physician's Global Assessment (≥ 10%), and no violations of protocol-specified medication rules. Participants who were considered as treatment failures or discontinued treatment were considered as nonresponders at visits after treatment failure or discontinuation. Participants who completed treatment but had a missing score at a primary timepoint were classified as nonresponders for that timepoint. Results are based on a generalized linear regression model adjusted for treatment using an identity link function (linear probability model) for the LS mean differences. Only BIIB059 450 mg and placebo are included in the statistical modeling.

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POS0699

GREATER REDUCTION IN CLASI-A SCORES ACHIEVED WITH BIIB059 VERSUS PLACEBO INDEPENDENTLY OF DISEASE SEVERITY AT BASELINE

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Background: Patients with cutaneous lupus erythematosus (CLE) experience symptoms including photosensitivity, rash, pain, and skin damage that can

impact their quality of life. No targeted therapies are approved for CLE. BIIB059 is a humanized monoclonal antibody that targets blood dendritic cell antigen-2 (BDCA2), expressed exclusively on the surface of plasmacytoid dendritic cells (pDCs). The binding of BIIB059 to BDCA2 leads to rapid internalization of BDCA2 from the cell surface of pDCs, thereby inhibiting the production of pDC-derived type I interferons, cytokines, and chemokines, which are involved in CLE pathology. In Part B of the 2-part, phase 2 LILAC study (NCT02847598), the primary endpoint was met: BIIB059 significantly reduced CLE activity, as evidenced by a statistically significant dose response and statistically significant differences in least-squares mean percent changes in Cutaneous Lupus Erythematosus Disease Area and Severity Index – Activity (CLASI-A) score¹ versus placebo.²

Objectives: To determine the proportion of patients with CLE who presented at baseline with moderate or severe disease (CLASI-A ≥ 10) or with the higher category of mild disease (CLASI-A < 10 [i.e., 8 or 9]) and experienced a shift in CLASI-A score to a mild skin disease category or clear/almost clear skin status.

Methods: Adults with histologically confirmed CLE with or without systemic manifestations were enrolled if they had CLASI-A ≥ 8 at baseline, despite prior use of or intolerance to topical corticosteroids (CS) and/or antimalarials, in addition to ≥ 1 lesion diagnostic of subacute CLE (CLASI-A erythema score ≥ 2) and/or chronic CLE (CLASI-A erythema score ≥ 2 and CLASI-Damage scarring score ≥ 1). Concomitant CLE/SLE therapy was allowed if doses were initiated ≥ 12 weeks and kept stable ≥ 4 weeks before randomization and throughout the treatment period. Systemic corticosteroid doses could not exceed 15 mg/day of prednisone (or equivalent). BIIB059 (50, 150, 450 mg) or placebo was subcutaneously administered once every 4 weeks for 12 weeks, with an additional dose at Week 2. An ad hoc analysis was conducted to determine the proportion of participants (CLASI-A ≥ 10 or < 10 at baseline) with a shift in CLASI-A score to ≤ 1, ≤ 3, ≤ 6, and ≤ 8 at Week 16.

Results: In this ad hoc analysis from LILAC Part B, 106 (80.3%) and 26 (19.7%) of participants had a baseline CLASI-A score ≥ 10 and < 10, respectively. Compared with placebo, higher proportions of participants treated with BIIB059 achieved a shift in CLASI-A score from either ≥ 10 or < 10 at baseline to ≤ 1, ≤ 3, ≤ 6, and ≤ 8 at Week 16 (Figure 1). Treatment with BIIB059 resulted in higher proportions of participants achieving reduced scores, indicating shifts to more mild disease activity, compared with placebo. A score ≤ 1 (clear or almost clear skin) at Week 16 was achieved by 0.0% (0/25), 5.0% (1/20), 14.3% (3/21), and 12.5% (5/40) of participants with baseline CLASI-A ≥ 10 who were treated with placebo and BIIB059 50, 150, and 450 mg, respectively. Two of 26 participants with baseline CLASI-A < 10 achieved a score ≤ 1 (both received BIIB059 150 mg).

Conclusion: A greater proportion of participants achieved milder skin disease or clear/almost clear skin status in the BIIB059 groups as compared with the placebo group. This effect was observed in participants with moderate or severe disease as well as in those in the higher range of the mild category of disease severity at baseline, indicating the ability of BIIB059 to improve skin lesions in patients with a broad range of cutaneous disease activity.

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Figure. Percentage of Participants With Baseline CLASI-A ≥ 10 and < 10 Achieving a Decrease to CLASI-A Score Thresholds ≤ 1, ≤ 3, ≤ 6, and ≤ 8 at Week 16

CLASI-A = Cutaneous Lupus Erythematosus Disease Area and Severity Index – Activity

The denominator is the number of participants who had a CLASI-A score ≥ 10 or < 10 at baseline and a nonmissing CLASI-A score at Week 16. Participants who were treatment failures or who discontinued treatment were considered nonresponders at visits after the treatment failure or discontinuation. Participants who completed treatment but had a missing score at the primary timepoint were classified as nonresponders for that timepoint.

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POS0700

TREATMENT OF INTERSTITIAL LUNG DISEASE IN PATIENTS WITH PRIMARY SJOGREN SYNDROME: A SINGLE-CENTER RETROSPECTIVE ANALYSIS

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Background: Interstitial lung disease (ILD) is one of the main contributor to morbidity and mortality in patients with primary Sjogren syndrome (pSS), and whether immunosuppressive treatments are effective for pSS-ILD is uncertain. Cyclophosphamide (CYC) and rituximab (RTX) are effective in stabilizing pulmonary function in patients with ILD caused by systemic sclerosis, inflammatory myositis, and rheumatoid arthritis^{1,2}. Reports regarding the treatment response for cyclophosphamide or rituximab in pSS-ILD patients are lacking.

Objectives: To investigate whether add-on CYC or RTX in addition to steroid and oral DMARDs leads to greater improvement in pulmonary function test than conventional treatment in patients with pSS-ILD with impaired baseline pulmonary function.

Methods: pSS-ILD patients with ILD confirmed by a chest computed tomography were screened. Those with impaired baseline pulmonary function test (FVC<80% and DLCO<80%) and available results of pulmonary function tests at 6th-18th month post-treatment were retrospectively enrolled. The patients were clustered into two groups: steroid and oral DMARDs alone (steroid/oDMARD group), and add-on CyC and/or RTX (Add-on CyC/RTX group).

Results: This study enrolled 22 patients. The median age of these patients was 65. Among them, 68% were female and 18% were smokers. The median baseline FVC was 63.5% and the median DLCO was 54.4%. The predominant CT pattern was NSIP (54%), followed by UIP (22%), LIP (13.6%) and OP (9%) (table 1).

Five patients received steroid and oral DMARDs alone (hydroxychloroquine +/- azathioprine), while 17 patients received add-on CYC and/or RTX (8 patients received CYC, 3 received RTX, and 6 received CYC and RTX). There was no significant difference in baseline characteristic between these two groups (table 1).

With a median follow-up period of 9.8 months (interquartile range 7.6 - 13.4 months) after treatment, the FVC improved significantly from 61.3% to 65.5%

($p=0.013$) in CYC/RTX group, while the FVC improvement was not significant in steroid/oDMARD group (figure 1A). In CYC/RTX group, patients with non-UIP pattern (NSIP, LIP and OP) on chest CT had significant FVC improvement ($p=0.021$), contrasting to the patients with UIP pattern on chest CT (figure 1B).

Conclusion: In pSS patients with ILD and impairment of pulmonary function at baseline (FVC<80%, DLCO<80%), FVC improved significantly in patients received add-on cyclophosphamide and/or rituximab therapy.

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Table 1. Baseline characteristics of patients with Sjögren's syndrome and interstitial lung disease

	Total (n = 22)	Steroid/oDMARDs (n = 5)	Add-on CYC/ RTX (n = 17)	Comparison between two groups (p-value)
Age, year, median (IQR)	65.1 (61.7 - 69.1)	64 (64.6 - 67.4)	65.6 (61.6 - 69.2)	0.88
Female sex, n (%)	15 (68%)	4 (80%)	12 (70%)	1.00
Smoking, n (%)	4 (22%)	0 (0%)	4 (21%)	0.54
Baseline FVC, % of predicted value, median (IQR)	63.6% (53.8 - 68.2)	63.9% (63.7 - 67.5)	61.3% (50.2 - 68.2)	0.43
Baseline DLCO, % of predicted value, median (IQR)	54.4% (39.4 - 66.4)	69.1% (57.8 - 75.5)	52.1% (38.5 - 58.1)	0.12
CT pattern, n (%)	NSIP - 12 (54%) UIP - 5 (22%) LIP - 3 (13.6%) OP - 2 (9%)	NSIP 1 (20%) UIP 1 (20%) LIP 2 (40%) OP 1 (20%)	NSIP - 11 (65%) UIP - 4 (24%) LIP - 1 (6%) OP - 1 (6%)	-
UIP pattern, n (%)	5 (22%)	1 (20%)	4 (24%)	1.00

CYC, cyclophosphamide; oDMARDs, oral DMARDs; RTX, rituximab

Figure 1. FVC change before and after the immunosuppressive treatment

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