PO.3.73 SOLUBLE CD200 CONCENTRATION IN SERUM IS INCREASED IN SLE PATIENTS AND CORRELATES WITH ANTI-DSDNA

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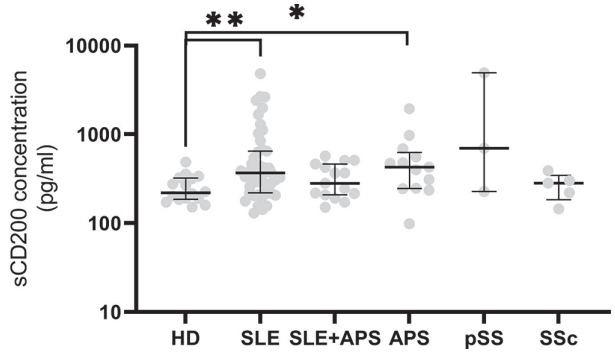
Purpose Immune inhibitory receptors are important in maintaining immune homeostasis and preventing autoimmunity. We recently showed that the function of immune inhibitory CD200 Receptor (CD200R) changes in systemic lupus erythematosus (SLE) patients. In a subset of SLE patients, CD200R function switches from inhibiting to potentiating Toll-like receptor (TLR)-7/8-induced interferon gamma production. In this study, we aim to clarify the role of CD200 in the pathophysiology of systemic autoimmune disease and study its potential as a marker for disease. We investigate the expression of CD200R and its ligand CD200 in SLE and other interferon related systemic autoimmune diseases. In addition, we determine the concentration of soluble CD200 (sCD200) in systemic autoimmune disease. sCD200 can be both a functional ligand for CD200R, or a decoy ligand that competes for CD200R binding with cell-bound CD200. Lastly, we correlated sCD200 and sCD200R with disease manifestations in SLE patients.

Methods We studied CD200R and CD200 expression in patients with SLE, antiphospholipid syndrome (APS), primary Sjögren's syndrome (pSS), and systemic sclerosis (SSc). We determined CD200 and CD200R expression in different cell subsets with flow cytometry. In addition, we measured sCD200 and sCD200R with ELISA in serum from SLE patients, and correlated concentrations with clinical disease manifestations.

Results We found an increased CD200R expression on monocytes of patients with SLE compared to healthy donors, while CD200 expression is decreased. CD200R expression is increased on T-cells and granulocytes from SLE, pSS and APS patients compared to healthy donors.

In addition, sCD200 concentration is elevated in serum from patients with SLE and APS compared to serum from healthy donors. sCD200 positively correlates with anti-dsDNA concentrations in SLE patients (r=0.45, p 0.002), but not with SLEDAI, renal involvement or complement (C3/C4) concentrations.



Abstract PO.3.73 Figure 1 Soluble (s)CD200 concentration is increased in serum from patients with SLE and APS compared to healthy donor serum. *p<0.05, **p<0.005

Conclusions CD200R expression is increased on monocytes, T cells and granulocytes of SLE patients and other interferon-related auto-inflammatory diseases. sCD200 concentration in serum was increased in SLE and APS patients, which correlates with anti-dsDNA concentrations in SLE.

Our study shows that differences in CD200/CD200R expression are not specific for SLE, but present in other interferonopathies. Therefore, they might be related to common underlying disease mechanisms in systemic autoimmunity. For future studies, it would be of interest to investigate the CD200R:CD200 axis in relation to the interferon signature, or formation of neutrophil extracellular traps (NETs).

Thursday 06 October 2022 from 13:00 to 14:10

PO.4 E- POSTER SESSION 4: disease activity measurements, flare and remission, epidemiology, etiology, genetics, epigenetics

PO.4.75 THE ANTI-BDCA2 ANTIBODY BIIB059 IMPROVES JOINT AND SKIN MANIFESTATIONS IN PATIENTS WITH SLE AND BOTH ACTIVE ARTHRITIS AND RASH

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Purpose BIIB059, a humanised monoclonal antibody targeting BDCA2, significantly reduced total active joint count versus placebo at Week 24 in patients with SLE in Part A of a Phase 2 study (NCT02847598). Changes in both joint and skin disease activity were assessed post hoc in a subset of patients with both arthritis and rash at baseline.

Methods Adults with SLE diagnosis, active arthritis and skin manifestations were randomised to receive BIIB059 450 mg or placebo subcutaneously. This post-hoc analysis included patients with both arthritis and rash based on baseline SLEDAI-2K, or BILAG-2004 musculoskeletal and mucocutaneous Grades A or B at baseline. In contrast to the previously reported primary analysis, there was no additional requirement for either skin disease activity or joint counts at baseline. The proportions of patients who improved in both domains (defined as absence of arthritis and rash by SLEDAI-2K, or improvement by ≥1 grade in BILAG-2004 musculoskeletal and mucocutaneous systems) were assessed at Week 24. Total joint count (evaluated by 28-joint assessment) and CLASI-A scores were assessed at baseline and Week 24.

Results The total numbers of patients included in this analysis were 61 and 52 (SLEDAI-2K), and 54 and 44 (BILAG-2004) for the BIIB059 and placebo treatment groups, respectively. At baseline, mean total joint count ranged between 11 and 12, and mean CLASI-A score ranged between 10 and 11 in both subpopulations. At Week 24, the proportions of patients with neither arthritis nor rash by SLEDAI-2K were

Abstract PO.4.75 Table 1 Proportions of patients who had arthritis and rash by SLEDAI-2K or BILAG-2004 musculoskeletal and mucocutaneous grades A or B at baseline and improved in joint and skin symptoms at week 24

	Placebo	BIIB059 450 mg
Pts with both arthritis and rash at baseline (SLEDAI-2K), n*	52	61
Pts with no arthritis at Week 24, n (%)	13 (25.0)	31 (50.8)
Pts with no rash at Week 24, n (%)	6 (11.5)	18 (29.5)
Pts with neither arthritis nor rash at Week 24, n (%)	5 (9.6)	14 (23.0)
LS mean, % (SE)	9.6 (4.3)	25.2 (6.4)
LS mean difference, % (95% CI)†		15.6 (1.4, 29.8)
OR (95% CI)†		2.8 (0.9, 8.3)
P-value†		0.071
Pts with BILAG-2004 Grade A or B in both musculoskeletal and mucocutaneous organ domains at baseline, n*	44	54
Pts who improved from baseline Grade A or B in musculoskeletal domain at Week 24, n (%)	22 (50.0)	38 (70.4)
Pts who improved from baseline Grade A or B in mucocutaneous domain at Week 24, n (%)	16 (36.4)	29 (53.7)
Pts who improved from baseline in both musculoskeletal and mucocutaneous scores at Week 24, n (%)	15 (34.1)	27 (50.0)
LS mean, % (SE)	27.8 (8.4)	52.9 (8.8)
LS mean difference, % (95% CI)†		25.1 (5.0, 45.2)
OR (95% CI)†		2.6 (1.0, 6.3)
P-value†		0.043

*Analyses were based on generalised linear regression adjusted for treatment, baseline corticosteroid usage level, region and baseline SLEDAI-2K score (for SLEDAI data) or baseline BILAG (for BILAG data) using a logit link function
†BIIB059 versus placebo
BILAG-2004, British Isles Lupus Assessment Group 2004 index; CI, confidence interval; LS, least squares; OR, odds ratio; Pts, patients; SE, standard error; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000

greater with BIIB059 than placebo, as were the proportions with improvements in the BILAG-2004 musculoskeletal and mucocutaneous domains (Table 1). Mean changes in total joint count and CLASI-A score from baseline were numerically greater with BIIB059 than placebo in the respective subpopulations.

Conclusions Among patients with active SLE in both joints and skin, those receiving BIIB059 had greater improvements versus placebo in both manifestations. These data support the potential benefit of BIIB059 treatment for joint and skin manifestations in SLE.

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PO.4.77 AGREEMENT BETWEEN LLDAS AND EXPERT ASSESSMENT IN IDENTIFYING SLE PATIENTS WITH LDA: STUDY ON A REAL-WORLD COHORT OF CAUCASIAN PATIENTS

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Purpose Both lupus low disease activity state (LLDAS) and remission have been proven to be good and achievable targets in the management of SLE. Nevertheless, considerable overlap between LLDAS and remission exists: an average of 80% of patients in LLDAS also meet the definition of remission in different cohorts worldwide, raising the question whether LLDAS definition is too close to definition of remission. Our aim was to evaluate the performance of LLDAS in identifying patients in LDA, defined according to gold standard, which is physician judgement.

Methods We prospectively collected data of SLE patients attending our outpatient clinic from October 2021 to January

Abstract PO.4.77 Table 1

	Expert LDA (%)	LLDAS/no rem (%)	Expert LDA/rem (%)	LLDAS* (%)
N° of patients	45 (21.7)	29 (14)	173 (84)	154 (74)
Articular manifestations	19 (40.4)	17 (58.6)	19 (10.3)	17 (11)
Cutaneous manifestations	9 (19.1)	5 (17.2)	9 (5.1)	5 (3.2)
Renal manifestations	7 (14.9)	-	7 (4)	-
Hematological manifestations **low WBC** **low PLT**	8 (17): • 6 (12.7) • 2 (4.2)	7 (24.1) • 5 (17.2) • 2 (6.9)	8 (4.5) • 6 (3.4) • 2 (1.1)	7 (4.5) • 5 (3.2) • 2 (1.3)
Serositis	2 (4.2)	-	2 (1.1)	-
No clinical activity (cSLEDAI=0)	-	-	128 (73.2)	125 (80.6)
Serological activity	27 (61.7) positive serology: • 11 (23.4) dsDNA only • 6 (12.7) C3/C4 only • 10 (25.5) both 18 (38.3) none	17 (58.6) positive serology • 10 (34.5) dsDNA only • 3 (10.3) C3/C4 only • 4 (13.7) both 12 (41.4) none	94 (54.9) positive serology: • 29 (16.6) dsDNA only • 30 (17.1) C3/C4 only • 35 (21.1) both 79 (45.1) none	85 (54.8) positive serology 28 (18) dsDNA only 27 (17.4) C3/C4 only 30 (19.3) both 69 (45.1) none
PDN daily dose	3.48±5.1 (median 2.5, IQR 0-5) • **PDN=0:** 5 (10.6) • **PDN≤5:** 41 (87.2) • **PDN 5-7.5:** 1 (2.1) • **PDN ≥7.5:** 1 (2.1)	3.56±1.91 (median 3.75, IQR 2.5-5.0) • **PDN=0:** 2 (6.9) • **PDN≤5:** 26 (89.6) • **PDN 5-7.5:** 1 (3.5) • **PDN ≥7.5:** 0	2.1±2.6 (median 0, IQR 0-5) • **PDN=0:** 90 (51.4) • **PDN≤5:** 83 (47.4) • **PDN 5-7.5:** 1 (0.56) • **PDN ≥7.5:** 1 (6.6)	1.7±2.3 (median 0, IQR 0-3.75) • **PDN=0:** 88 (57.1) • **PDN≤5:** 65 (42.2) • **PDN 5-7.5:** 1 (0.7) • **PDN ≥7.5:** 0
PGA>1	0	0	0	0

cSLEDAI: clinical Systemic Lupus Erythematosus Disease Activity Index, LDA: Low Disease Activity, LLDAS: Lupus Low Disease Activity State, PDN: prednisone or prednisone equivalent dose, PGA: Physician Global Assessment, PLT: platelets, Rem: DORIS Remission, WBC: white blood cells