Table 1. Comparison of body composition parameters in PsA, MDF controls, and type 2 diabetes

Variable	PsA	MDF controls	p-value*	Adj. p value**	Type 2 diabetes	p-value†	Adj. p value‡
Age (years)	56.0 (9.0)	57.4 (6.5)	0.766	-	65.4 (6.9)	< 0.001	-
BMI (kg/m^2)	31.2 (6.4)	30.5 (5.3)	0.799	-	29.9 (5.2)	0.397	-
VAT (L)	5.89 (2.10)	4.34 (1.83)	<0.001	<0.001	5.93 (2.56)	0.662	0.301
Visceral fat index (L/m^2)	2.06 (0.73)	1.52 (0.64)	<0.001	<0.001	2.03 (0.84)	0.337	0.175
Abdominal subcutaneous adipose tissue (L)	10.48 (4.90)	9.42 (4.86)	0.288	0.071	8.58 (3.93)	0.109	0.339
Abdominal fat index (L/m^2)	5.87 (2.39)	4.93 (2.29)	0.084	<0.001	5.04 (1.92)	0.052	0.024
Liver fat (%)	8.88 (4.42-13.18)	3.29 (1.98-7.25)	0.002	0.002	6.13 (2.77-11.63)	0.392	0.656
MFI (%)	7.74 (2.57)	7.43 (1.95)	0.748	0.292	8.61 (2.29)	0.736	0.191

Values are mean (SD) (liver fat, median (IQR)). *PsA vs. MDF controls. **PsA vs. MDF controls adjusted for age, sex, and BMI. †PsA vs. Type 2 diabetes. ‡ PsA vs. Type 2 diabetes adjusted for age, sex, and BMI.

Conclusion: This is the first study to report that individuals with PsA have a body composition profile associated with an adverse metabolic phenotype, with greater VAT and ectopic liver fat than the general population and more similar to that of type 2 diabetes, in line with their greater cardiometabolic risk. These data mandate a revision of the management approach to PsA that includes attention to weight loss interventions.

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Dendritic cells as therapeutics

OP0193

BIIB059, A HUMANIZED MONOCLONAL ANTIBODY TARGETING BDCA2 ON PLASMACYTOID DENDRITIC CELLS (PDC), SHOWS DOSE-RELATED EFFICACY IN THE PHASE 2 LILAC STUDY IN PATIENTS (PTS) WITH ACTIVE CUTANEOUS LUPUS ERYTHEMATOSUS (CLE)

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Background: CLE represents an unmet medical need with no approved therapy. BIIB059, a humanized monoclonal antibody, binds to BDCA2 and inhibits pro-inflammatory mediators production, including type I interferons. BIIB059 was evaluated in Phase 1 studies NCT02106897 and NCT03224793. LILAC is a 2-part Phase 2 study: Part A enrolled SLE pts; Part B enrolled pts with active CLE (NCT02847598).

Objectives: Evaluate efficacy and safety of BIIB059 in pts enrolled in Part B at Week 16, end of treatment (EOT) period.

Methods: Pts with active CLE, SCLE and/or CCLE and adjudicated Cutaneous Lupus Disease Area and Severity Index – Activity (CLASI-A) ≥8 were enrolled and randomized to receive either BIIB059 (50, 150 or 450 mg) or placebo (PBO) s.c. Q4W. Primary endpoint was dose response defined by % change in CLASI-A score from baseline (BL) to Week 16. Secondary endpoints included CLASI-50 response rate and ≥ 7-point reduction in CLASI-A score from baseline to EOT. Adverse events and serious adverse events were recorded throughout the study.

Results: 132 pts with active CLE were randomized. The study met its primary endpoint, demonstrating a dose response (p= 0.0005) and a statistically significant difference in % change from BL in CLASI-A score in BIIB059-treated pts vs PBO. Table 1 and Table 2 summarize efficacy and safety results, respectively.

Conclusion: BIIB059 administration to pts with active CLE resulted in statistically significant dose-related improvement in disease activity vs PBO with no untoward safety signals. Further development of BIIB059 in CLE is warranted.

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Table 1. Efficacy Endpoints

	PBO	BIIB059							
		50 mg			150 mg			450 mg	
	LS Mean (SE)	LS Mean (SE)	LSMD* from PBO (95% CI)	P val.	LS Mean(SE)	LSMD* from PBO (95% CI)	P val.	LS Mean (SE)	LSMD* from PBO (95% CI)	P val.
Primary Endpoint CLASI-A % change from BL	-14.5 (6.4)	-40.8 (7.5)	-26.3 (-45.7; -7.0)	0.008	-47.9 (7.4)	-33.5 (-52.7; -14.3)	0.001	-43.5 (5.5)	-28.0 (-44.5; -11.5)	0.001
Secondary Endpoints	n(%)	n(%)	LSMD* from PBO (95% CI)	P val.	n(%)	LSMD* from PBO (95% CI)	P val.	n(%)	LSMD* from PBO (95% CI)	P val.
Prop. of participants achieving CLASI 50	7/32 (21.9%)	10/26 (38.5%)	15.8% (-7; 39)	0.133	11/25 (44.0%)	21 (-2.8; 45)	0.059	20/43 (46.5%)	23 (3; 44)	0.024
Prop. of participants achieving a ≥7-point CLASI-A reduction from BL	7/32 (21.9%)	9/26 (34.6%)	12.3 (-11.3; 35.8)	0.228	12/25 (48.0%)	22.2 (-2.0; 46.3)	0.055	18/43 (41.8%)	16.8 (-6.7; 40.4)	0.048

*LSMD=LS Mean Difference

Table 2. Safety Profile: Number of participants (%) experiencing any event

	PBO	BIIB059				OVERALL
	N=33	50 mg N=26	150 mg N=25	450 mg N=48	Pooled N=99	N=132
Any Event, n(%)	18 (54.5)	17 (65.4)	12 (48)	33 (68.8)	62 (62.6)	80 (60.6)
Severity						
Mild	11 (33.3)	11 (42.3)	8 (32.0)	19 (39.6)	38 (38.4)	49 (37.1)
Moderate	4 (12.1)	6 (23.1)	3 (12.0)	12 (25.0)	21 (21.2)	25 (18.9)
Severe	3 (9.1)	0	1 (4.0)	2 (4.2)	3 (3.0)	6 (4.5)
Related events	6 (18.2)	9 (34.6)	4 (16.0)	16 (33.3)	29 (29.3)	35 (26.5)
Serious events	2 (6.1)	0	3 (12.0)	2 (4.2)	5 (5.1)	7 (5.3)
Related serious events	1 (3.0)	0	1 (4.0)	1 (2.1)	2 (2.0)	3 (2.3)
Events leading to drug withdrawal	0	1 (3.8)	1 (4.0)	1 (2.1)	3 (3.0)	3 (2.3)
Events leading to study withdrawal	0	0	0	1 (2.1)	1 (1.0)	1 (0.8)
Fatal events	0	0	0	0	0	0

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OP0194 **IMMUNOSUPPRESSIVE EFFECT OF TOLEROGENIC DENDRITIC CELLS ON AUTOLOGOUS T-CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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Background: Dendritic cells (DCs) are known to contribute to the pathogenesis of rheumatoid arthritis (RA) through presentation of cartilage glycoprotein, production of proinflammatory cytokines and activation of Th1/Th17 responses. Along with stimulating activity, DCs may exhibit suppressive functions via capacity to induce T cell apoptosis/anergy and to generate regulatory T cells. Since these DCs have potential to control autoreactive T-lymphocytes, the enhancing of tolerogenic properties of DCs seems to be a new important strategy in treatment of RA. However, it remains unclear whether autoreactive T lymphocytes are sensitive to the immunosuppressive effects of DC.
Objectives: The aim of our study is to investigate the mechanisms of the inhibitory effect of dexamethasone-modified DCs (dexDCs) in patients with RA on autologous T cells.
Methods: Twenty patients with RA with high and moderate activity of disease were recruited in this study. All patients fullfield ACR/EULAR criteria (2010). All studies were performed after receiving informed consent. DCs were generated from blood monocytes culturing for 5 days with GM-CSF and IFN-α in the presence dexamethasone, applied on third day. LPS as maturation stimuli was added on fourth day. The study evaluated the ability of dexDCs to induce T cell apoptosis, inhibit the production of Th1 and Th17 cytokines in auto-mixed leukocytes culture (MLC), induce the activation of T-regulatory cells, and inhibit the purified protein derivative (PPD)-specific immune response.
Results: We revealed that dexDCs markedly suppressed the production of IFN-γ and IL-17, while the decreasing of IL-4 and IL-13 was less pronounced. Thus, in comparison with Th2 cells, Th1 and Th17 T lymphocytes were more sensitive to suppressor effects of dexDCs. We also revealed a significant increasing of cells in the stage of late apoptosis (An+Pi+) during the cultivation of autologous T cells with dexDCs. We have also proved the suppressive effect of dexDCs on culture T cells that are co-cultivated with mature DCs (reduction of proliferation from 2700 cpm to 1500 cpm, p=0.0015). In addition, we have shown the ability of dexDCs to induce T-regulatory cells with a phenotype CD4+IL10+Tr1. In conclusion, we have shown the ability of PPD-loaded dexDCs to inhibit the proliferative response of both mature DCS and mature dexDCs-loaded PPD, that indicates the ability of dexDCs to possess antigen-specific suppression.
Conclusion: The data obtained indicate that, dexDCs from RA patients have an immunosuppressive effect on autologous T cells through the induction of apoptosis, anergia and activation of T regulatory cells that authorise their application as a DCs-vaccine.
Disclosure of Interests: None declared
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Creating in vitro patients - how to best model disease

OP0195 **VASCULARIZED THREE-DIMENSIONAL MODELS OF HUMAN SKIN FIBROSIS**

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Background: The complex pathophysiological processes that result in fibrotic tissue remodeling in systemic sclerosis involve interplay between multiple cell types (1). Experimental models of fibrosis are essential to provide a conceptual understanding of the pathogenesis of these diseases and to test antifibrotic drugs. Current models of fibrosis have important limitations: the *in vivo* models rely on species that are phylogenetically distant, whereas the *in vitro* models are oversimplified cultures of a single cell type in an artificial two-dimensional environment of excessive stiffness, which imposes an unphysiological cell polarization (2).
Objectives: Here we evaluated the potential use of vascularized, three-dimensional *in vitro* human skin equivalents as a novel model of skin fibrosis and a platform for the evaluation of antifibrotic drugs.
Methods: Skin equivalents were generated by seeding human endothelial cells, fibroblasts and keratinocytes on a decellularized porcine extracellular matrix with perfusable vascular structure. The skin models were cultured for one month in a system that ensured perfusion of the vascular network at physiological pressure. Fibrotic transformation induced by TGFβ and response to nintedanib as an established antifibrotic drug was evaluated by capillary Western immunoassays, qPCR, histology and immunostaining.
Results: The vascularized human skin equivalents formed the major skin structures relevant for the pathogenesis of fibrosis: a polarized, fully matured epidermis, a stratified dermis and a perfused vessel system with small capillaries. Exposure to TGFβ led to the fibrotic transformation of the skin equivalents, with activated TGFβ downstream pathways, increased fibroblast-to-myofibroblast transition and excessive deposition of extracellular matrix. Treatment of models exposed to TGFβ with nintedanib (a drug with proven antifibrotic effects) ameliorated the fibrotic transformation of skin equivalents with reduced TGFβ signaling, fibroblast-to-myofibroblast transition and decreased extracellular matrix deposition.