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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Acknowledgments: Celgene; BHF (RE/13/5/30177)

Disclosure of Interests: Lyn D. Ferguson: None declared, Jennifer Linge Shareholder of: AMRA Medical AB, Employee of: AMRA Medical AB, Olof D. Leinhardt Shareholder of: AMRA Medical AB, Employee of: AMRA Medical AB, Iain McInnes Grant/research support from: Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Janssen, and UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, Janssen, Novartis, Pfizer, and UCB, Stefan Siebert Grant/research support from: BMS, Boehringer Ingelheim, Celgene, GlaxoSmithKline, Janssen, Novartis, Pfizer, UCB, Consultant of: AbbVie, Boehringer Ingelheim, Janssen, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, Celgene, Janssen, Novartis, Naveed Sattar Grant/research support from: Boehringer Ingelheim, Consultant of: Amgen, Boehringer Ingelheim, AstraZeneca, Eli Lilly, Novo Nordisk, Sanofi, and Janssen, Speakers bureau: Amgen, Boehringer Ingelheim, AstraZeneca, Eli Lilly, Novo Nordisk, Sanofi, and Janssen
DOI: 10.1136/annrheumdis-2020-eular.1074

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.

Disclosure of Interests: Victoria Werth Grant/research support from: Biogen, Celgene, Gilead, Janssen, Viela, Consultant of: Biogen, Gilead, Janssen, Abbvie, GSK, Resolve, AstraZeneca, Amgen, Eli Lilly, EMD Serono, BMS, Viela, Kyowa Kirin, Richard Furie Grant/research support from: AstraZeneca, Biogen, Consultant of: AstraZeneca, Biogen, Juanita Romero-Diaz Consultant of: Biogen, Sandra Navarra Speakers bureau: Astellas, Novartis, Pfizer, Johnson & Johnson, Abbvie, Kenneth Kalunian Grant/research support from: Pfizer, Lupus Research

Table 1. Efficacy Endpoints

	BIIB059									
	PBO	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

Alliance, Sanford Consortium, Consultant of: Genentech, Nektar, BMS, Janssen, AstraZeneca, Biogen, Vielabio, Equillium, Eli Lilly, ILTOO, Abbvie, Amgen, Roche, Gilead, Ronald van Vollenhoven Grant/research support from: AbbVie, Arthrogen, Bristol-Myers Squibb, GlaxoSmithKline, Lilly, Pfizer, and UCB, Consultant of: AbbVie, AstraZeneca, Biotest, Bristol-Myers Squibb, Celgene, GSK, Janssen, Lilly, Medac, Merck, Novartis, Pfizer, Roche, and UCB, Filippa Nyberg Consultant of: Biogen, Benjamin Kaffenberger Grant/research support from: Amgen, Biogen, InflaRx, Veloce Biopharmaceuticals, Dermatology Foundation, Saira Sheikh: None declared, Goran Radunovic: None declared, XIAOBI HUANG Shareholder of: Biogen, Employee of: Biogen, HUA CARROLL Shareholder of: Biogen, Employee of: Biogen, Francois Gaudreault Shareholder of: Biogen, Employee of: Biogen, Adam Meyers Shareholder of: Biogen, Employee of: Biogen, Catherine Barbey Shareholder of: Biogen, Employee of: Biogen, Cristina Musselli Shareholder of: Biogen, Employee of: Biogen, NATHALIE FRANCHI-MONT Shareholder of: Biogen, Employee of: Biogen
DOI: 10.1136/annrheumdis-2020-eular.5743

OP0194

IMMUNOSUPPRESSIVE EFFECT OF TOLEROGENTIC 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 fulfilled 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

DOI: 10.1136/annrheumdis-2020-eular.1291

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 TGF β 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 TGF β led to the fibrotic transformation of the skin equivalents, with activated TGF β downstream pathways, increased fibroblast-to-myofibroblast transition and excessive deposition of extracellular matrix. Treatment of models exposed to TGF β with nintedanib (a drug with proven antifibrotic effects) ameliorated the fibrotic transformation of skin equivalents with reduced TGF β signaling, fibroblast-to-myofibroblast transition and decreased extracellular matrix deposition.