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 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, anergy 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 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.