OP0007

HIGH BODY MASS INDEX (BMI) IN PSORIATIC ARTHRITIS (PSA) IS ASSOCIATED WITH HIGHER DISEASE ACTIVITY IN JOINTS AND SKIN, IMPAIRED QUALITY OF LIFE AND MORE DISABILITY: RESULTS FROM THE PSABO STUDY

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Background: The link between obesity and disease activity in PSA is unclear. Obesity has been associated with a poorer therapeutic response and higher treatment discontinuation rates in patients with PSA being treated with tumour necrosis factor inhibitors (TNFi). Recent data confirm the favourable effect of weight reduction on these factors. There are no data available for other biologics.

Objectives: To investigate the relationship between baseline overweight/obesity and disease activity, patient-reported outcomes and disability, in a large real-world cohort of patients with PsA starting biologic treatment with either ustekinumab (UST) or TNFi.

Methods: The PsABIO study (ClinicalTrials.gov: NCT02627768) is an ongoing observational study evaluating efficacy, tolerability and persistence of 1st, 2nd, and 3rd-line UST or TNFi in PsA in 8 European countries¹ when introduced as part of standard clinical care. Baseline data of the study population were collected and analysed for BMI, disease activity (cDAPSA, psoriasis BSA), patient-perceived impact (PsAID-12), disability (HAQ-DI) and presence or history of CVD/MET. Descriptive statistics on available data and 3 exploratory multiple regression models are shown, to investigate the relationship of cDAPSA, PsAID-12 and HAQ-DI (dependent variables) with BMI, adjusted for age, sex, smoking, BSA, CRP, disease duration and biologic treatment.

Results: In all, 917 patients were included, starting either UST (n=450) or TNFi (n=467): mean (SD) age 49.7 (12.5) years, 55.5% female. The mean (SD) baseline BMI (N=827) was 28.1 (5.8) kg/m², with 40.0% and 30.4% in BMI categories overweight (>25–30) and obese (>30), respectively. In univariate analyses, obesity was linked to worse outcomes (Table 1). More severe disease was associated with higher BMI (Table 2). In multiple regression modelling, higher BMI was independently linked to higher cDAPSA (BMI: $\beta=0.09$ $p=0.026$); to higher patient-perceived disease impact measured by PsAID-12 (BMI: $\beta=0.16$, $p<0.0001$) and to higher disability measured by HAQ-DI (BMI: $\beta=0.21$, $p<0.0001$).

Conclusion: This multi-country routine-care PsA cohort of patients in need of biologic treatment confirms the high prevalence of overweight/obesity and indicates an independent association between high BMI and disease activity as well as patient-reported impact of disease and disability. These results emphasize the need for lifestyle-directed approaches in PsA, such as overweight management in parallel with joint- and skin-focused treatment.

Table 1. PSA outcomes in the PSAbio population according to presence of obesity

	Obese patients (n=231)	Non-obese patients (n=576)
cDAPSA, mean (SD)	33.4 (18.8)	27.7 (18.6)
BSA, %		
<35	41.6	46.3
35-50%	33.1	35.7
>50%	25.3	18.0
Twelve joint count, mean (SD)	6.8 (7.8)	5.1 (7.2)
CRP, mg/L, mean (SD)	3.75 (3.73)	3.2 (3.2)
HAQ-DI (0-1), mean (SD)	0.63 (0.28)	0.51 (0.21)
HAQ-DI (0-3), mean (SD)	1.06 (0.67)	1.01 (0.64)
CRP/HAQ-DI, %	138 (50.5)	189 (32.8)

Table 2. BMI by disease severity/disease characteristics

		N	Mean BMI (SD), 95% CI
CVD/MIT*	No CVD/MIT	500	26.0 (5.3), 26.4-27.4
	CVD/MIT	327	30.0 (5.1), 29.3-30.6
Skin parasites	None	377	27.0 (6.0), 26.3-27.6
	Bite or tick infest	262	28.1 (5.3), 27.5-28.8
Eye treatment	Blepharitis	152	29.4 (6.0), 28.7-30.2
	Blepharospasm*	251	27.5 (5.5), 26.9-28.2
Joint pattern	Normal	277	28.0 (6.0), 27.3-28.7
	Pain/articular	151	28.1 (5.5), 27.5-28.6
	Pure alopecia	53	28.1 (5.5), 27.5-28.6
	Polycystic	334	28.5 (5.6), 28.0-29.0
CRP	Normal	500	27.1 (5.6), 26.5-27.7
	Abnormal	347	28.8 (5.2), 28.2-29.5
Genetic activity by cDNA*	None	313	26.1 (5.1), 25.6-26.6
	LDA	82	26.9 (4.7), 25.7-27.9
	MAA	32	26.4 (5.6), 25.8-27.1
	PMO	29	29.1 (6.3), 28.1-30.1
QoI/Impact of disease	Pain ID, HESD	177	26.4 (5.5), 25.9-26.9

PSaID: 12, non-PASS 602 28.7 [6.1], 28.2; 29.2

REFERENCE:

[1] Gossec L. et al. Ann Rheum Dis. 2018;77(Suppl):A1033.

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OP0008

SUSTAINED LOW DISEASE ACTIVITY AFTER WEIGHT LOSS TREATMENT IN PATIENTS WITH PSORIATIC ARTHRITIS AND OBESITY: A 12-MONTHS FOLLOW-UP

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Background: Obesity is over-represented in patients with psoriatic arthritis (PsA) and associated with increased disease activity. We have previously shown in 41 patients with PsA (Caspar criteria) and obesity (body mass index BMI ≥ 33 kg/m²) that weight loss treatment with Very Low Energy Liquid Diet (VLED), 640 kcal/day during 12-16 weeks, followed by a structured reintroduction of an energy restricted diet resulted in a median weight loss of 18.6% and concomitantly a significant improvement of the disease activity in joints, entheses and skin. At 6-months follow-up Psoriatic Arthritis Response Criteria (PsARC) was reached by 46.3% and American College of Rheumatology (ACR) 20, 50, 70 criteria for treatment response by 51.2%, 34.1% and 7.3% of the patients.

Objectives: To study the effects of the weight loss treatment on disease activity in longer term (12 months) in patients with PsA and obesity, when the patients are on a weight loss maintenance diet.

Methods: The patients were assessed with 66/68 joints count, Leeds enthesitis index, body surface area (BSA), questionnaires, CRP and BMI at the 12-months follow-up.

Results: Totally 39 PsA patients, median age 56 (IQR 49-63) years, 64% women were examined at the 12-month follow-up. The median weight reduction since baseline was 16.1 kg (IQR 10.5–22.8) or 16.0% (10.5–22.4). A majority of the disease activity parameters remained significantly improved (Table). At the 12-month follow-up PsARC was still fulfilled by 35.9% (n=14) and ACR 20, 50, 70 response criteria by 53.8% (n=21), 35.9% (n=14) and 15.5% (n=6) respectively.

Conclusion: Weight loss treatment with VLED in patients with PsA and obesity was associated with sustained weight reduction and lowered disease activity at 12-months follow-up.

N=39	Baseline Median (IQR)	12-months Median (IQR)	p-value
Weight, kg	106 (93.5–112.5)	87.5 (80.6–95.5)	<0.001
Body Mass Index kg/m ²	35.2 (33.9–37.9)	30.5 (28.1–32.9)	<0.001
Tender joints 68, count	4 (1–14)	3 (0–6)	0.001
Swollen joints 66, count	0 (0–1)	0 (0–0)	0.015
Leeds enthesitis index	1 (0–4)	0 (0–2)	<0.001
Psoriasis Body Surface Area, %	0.75 (0–2)	0.25 (0–1)	0.018
CRP, mg/L	5 (3–9)	2 (1–5)	0.009
VAS Pain, mm	30 (17–62)	29 (10–55)	0.251
VAS Global health, mm	34 (18–58)	23 (9.5–38)	0.009
VAS Fatigue, mm	57 (21–67)	32.5 (16–62)	0.007
HAQ, score	0.63 (0.13–1.00)	0.25 (0–0.63)	0.002
DAS-28CRP, score	2.9 (2.2–3.5)	2.2 (1.7–3.0)	<0.001
DAPSA, score	15.3 (6.5–28.2)	10.2 (4.2–16.6)	0.001

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Environmental influences on disease development

OP0009

RESISTANT STARCH INTAKE ALLEVIATES COLLAGEN-INDUCED ARTHRITIS IN MICE BY MODULATING GUT MICROBIOTA AND PROMOTING SCFA PRODUCTION

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Background: Dietary intervention has been an auxiliary therapy in many diseases treatment¹. Increasing evidences indicate that dietary compositions vary in their impacts on gut microbial constitution and function capable of affecting the systemic immune status of the host^{2, 3}. Recently, a high fiber diet (HFD) receives close attention due to its effective improvement in symptoms in metabolic diseases and inflammatory diseases. It is also reported that intake of fruits and vegetables can improve the clinical symptoms of rheumatoid arthritis (RA) to a moderate extent. However, it remains unclear how a high fiber diet cross-talks with gut flora and RA initiation or remission.

Objectives: To systemically evaluate the effect of a high fiber diet mainly composed of resistant starch, a new resource of soluble fiber, on collagen-induced arthritis (CIA) mice and gut microbial composition. Meanwhile, the relative mechanisms was explored in this study.

Methods: CIA was established by immunization mice with collagen on day 0 and 21. Arthritis severity was evaluated by clinical score, histological staining and micro CT. Fresh stool was collected and gut microbiota analyses were performed by 16s RNA sequencing. Gut barrier dysfunction was evaluated by detecting the genes expression of intestine epithelial tight junction protein Zonulin-1 (ZO-1), Claudin-1 and Occludin. Flow cytometry was applied to measure the proportions of T cell subsets in various immune organs. Short chain fatty acids (SCFA) levels in the circulation and their receptor GPR41, 43 and 109A gene expressions were examined via GC-TOFMS and real-time PCR, respectively.

Results: High fiber feeding accelerated the arthritis remission in CIA mice, evidenced by the inflammatory cell infiltration reduction in the joints and bone erosion improvement. Th1, 2 and 17 cell population were not affected by HFD. While, regulatory T cell (Treg) percentages in the intestinal lamina propria and spleen were significantly higher in HFD-treated CIA mice, accompanied with an increase of interleukin-10 (IL-10) in the blood. Importantly, HFD modified gut dysbiosis in CIA mice, in particular, promoted the ratio of *Bacteroidetes* to *Firmicutes* and the prevalence of *Bacteroides acidifaciens*. Claudin-1 gene expression in the intestine was significantly increased with the gut flora alteration. Meanwhile, HFD-treated CIA mice had much higher levels of SCFAs in the blood and GPR43 gene expression in the intestine. Blocking SCFAs production by adding hops extract β-acids

into drinking water completely eliminated the beneficial effect of HFD on joint swelling, bone erosion and Treg cell expansion in CIA mice.

Conclusion: Intake of resistant starch drives the significant modifications of the gut microbial composition and SCFAs production capable of triggering Treg cells differentiation and IL-10 production, which favorable to the alleviation of RA.

REFERENCES:

- [1] Complex Relationships Between Food, Diet, and the Microbiome. Pace LA, Crowe SE. Gastroenterol Clin North Am. 2016 45:253-65.
- [2] The Gut Microbiota, Food Science, and Human Nutrition: A Timely Marriage. Barratt MJ, Lebrilla C, Shapiro HY, Gordon JI. Cell Host Microbe. 2017 22:134-141.
- [3] Food and microbiota in the FDA regulatory framework. Green JM, Barratt MJ, Kinch M, Gordon JI. Science. 2017 357:39-40.

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Pharmaceutical pipeline in OA

OP0010

CARTILAGE THICKNESS MODIFICATION WITH SPRIFERMIN IN KNEE OSTEOARTHRITIS PATIENTS TRANSLATES INTO SYMPTOMATIC IMPROVEMENT OVER PLACEBO IN PATIENTS AT RISK OF FURTHER STRUCTURAL AND SYMPTOMATIC PROGRESSION: POST-HOC ANALYSIS OF THE PHASE II FORWARD TRIAL

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Background: Results from the 5-year Phase II FORWARD study showed significant dose-dependent modification of total femorotibial joint (TFTJ) cartilage thickness change with sprifermin at 2 and 3 years, by quantitative MRI. Total Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores improved by ~50% in all treatment groups, including placebo (PBO). Selection of a patient (pt) subgroup with higher pain scores and lower joint space width (JSW) at baseline (BL), to identify pts who are at risk of further structural and symptomatic progression, may facilitate better WOMAC discrimination.

Objectives: Post-hoc analysis to evaluate cartilage thickness changes and symptomatic outcomes in an “at risk” subgroup of pts (BL medial or lateral minimum [m]JSW 1.5–3.5 mm and BL WOMAC pain score of 40–90).

Methods: Pts in FORWARD were randomized 1:1:1:1 to: sprifermin 100 µg every 6 months (q6mo); 100 µg q12mo; 30 µg q6mo; 30 µg q12mo; and PBO. The treatment period was 2 years, with an extended follow up at 3 years. Post-hoc analysis was conducted in the “at risk” subgroup.

Treatment effects were estimated using a repeated measures model, controlling for BL, treatment, time, country and treatment by time interaction. Linear dose-effect trend tests were performed exploratively at each timepoint. Confidence intervals (CIs) were adjusted for multiplicity of treatments using Dunnett adjustment.

Results: 161/549 (29%) pts met criteria for the “at risk” subgroup. In this subgroup, BL characteristics were balanced between treatment arms. Pts in the PBO arm had more cartilage loss at 2 and 3 years vs the modified intent-to-treat (mITT) PBO arm (mean change from BL in mm [SD]: Year 2 -0.05 [0.10] vs -0.02 [0.07]; Year 3 -0.07 [0.09] vs -0.05 [0.07]), but TFTJ net cartilage modification with sprifermin 100 µg q6mo vs PBO was similar (adjusted mean difference from PBO [95% CI] in the at risk subgroup vs the mITT group: Year 2 0.06 [0.01, 0.11] vs 0.05 [0.02, 0.08]; Year 3 0.05 [-0.01, 0.12] vs 0.05 [0.02, 0.09]). Having both medial or lateral mJSW 1.5–