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

Yunqiang Bai, Yanli Tong, Yi Liu, Yubin Luo. *Department of Rheumatology and Immunology, West China Hospital, Sichuan University, chengdu, China*

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.

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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

Hans Gühring¹, Jeffrey Kraines², Flavie Moreau², Benjamin Daelken¹, Christoph Ladel¹, Wolfgang Wirth^{3,4}, Philip G. Conaghan⁵, Felix Eckstein^{3,4}, Marc Hochberg⁶. ¹Merck KGaA, Darmstadt, Germany; ²EMD Serono (a business of Merck KGaA, Darmstadt, Germany), Billerica, United States of America; ³Paracelsus Medical University, Salzburg, Austria; ⁴Chondrometrics GmbH, Ainning, Germany; ⁵University of Leeds, Leeds, United Kingdom; ⁶University of Maryland, Baltimore, United States of America

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–

3.5 mm AND pain score ≥ 40 at BL led to greater differentiation in WOMAC total and pain scores for sprifermin 100 μ g q6mo vs PBO than having either BL characteristic alone. At Year 3 (18 mos after last injection), the exploratory dose-effect trend test had a nominal p-value of <0.05 (Fig 1; Table 1).

Conclusion: Despite substantial structural and symptomatic progression in the "at risk" subgroup, structural improvement with sprifermin was maintained, and WOMAC score improvements vs PBO increased over time and were significant at Year 3. This supports further investigation of sprifermin as a potential disease-modifying osteoarthritis drug in a targeted population where structural improvement may translate into symptomatic benefit vs PBO within a reasonable timeframe.

Table 1. Observed and adjusted mean difference [95% CI] in WOMAC pain scores for sprifermin vs PBO in the "at risk" subgroup

	Sprifermin 100 μ g q6mo (N=33) vs PBO (N=34)		
	Obs mean diff [95% CI]	Adj mean diff [95% CI]	Trend test* (nominal p value)
Y1	-5.81 [-15.96, 4.35]	-3.65 [-15.73, 8.43]	>0.05
Y2	-10.45 [-22.76, 1.85]	-5.82 [-18.87, 7.23]	>0.05
Y3	-14.51 [-26.16, -2.85]	-8.75 [-22.42, 4.92]	<0.05

*Across 4 sprifermin groups and PBO

Figure 1. Observed mean differences [95% CI] in WOMAC pain scores for sprifermin 100 μ g q6mo vs PBO across different risk subgroups at 2 and 3 years

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OP0011

EFFECT OF LIRAGLUTIDE ON BODY WEIGHT AND PAIN IN THE TREATMENT OF OVERWEIGHT AND KNEE OSTEOARTHRITIS: A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

Henrik Gudbergson¹, Anders Overgaard¹, Marius Henriksen^{1,2}, Eva Ejlersen Wæhrens^{1,3}, Henning Bliddal^{1,4}, Robin Christensen^{1,4}, Sabrina Mai Nielsen¹, Mikael Boesen^{1,5}, Filip Krag Knop^{6,7}, Arne Astrup⁸, Marianne Uggen Rasmussen¹, Cecilie Rødgard Bartholdy¹, Cecilie Dagaard¹, Else Marie Bartels¹, Karen Ellegaard¹, Berit Lilienthal Heitmann^{1,9}, Lars Erik Kristensen¹. ¹Bispebjerg-Frederiksberg Hospital, University of Copenhagen, The Parker Institute, Frederiksberg, Denmark; ²Bispebjerg-Frederiksberg Hospital, University of Copenhagen, Department of Physio- and Occupational Therapy, Frederiksberg, Denmark; ³Research Unit for General Practice, Institute of Public Health, University of Southern Denmark, Research Initiative for Activity Studies and Occupational Therapy, Odense, Denmark; ⁴Odense University Hospital, Department of Rheumatology, Odense, Denmark; ⁵Bispebjerg-Frederiksberg Hospital, University of Copenhagen, Department of Radiology, Frederiksberg, Denmark; ⁶Steno Diabetes Center Copenhagen, Gentofte Hospital, Clinical Metabolic Physiology, Hellerup, Denmark; ⁷Faculty of Health and Medical Sciences, University of Copenhagen, Department of Clinical Medicine, Copenhagen, Denmark; ⁸Faculty of Science, University of Copenhagen, Department of Nutrition, Exercise and Sports, Copenhagen, Denmark; ⁹Section for General Medicine, University of Copenhagen, Department of Public Health, Copenhagen, Denmark

Background: Weight loss is recommended as treatment of concomitant knee osteoarthritis (OA) and overweight. The GLP-1 receptor agonist liraglutide has

been shown effective in maintaining or even further reducing weight loss, but the compound has not been tested in a population of patients with overweight and knee OA.

Objectives: The objective of this trial was to investigate if liraglutide in a 3 mg/day dosage was effective in maintaining weight loss and symptomatic effects 52 weeks after an initial 8-week dietary-based weight loss intervention dosing in patients with overweight and knee OA.

Methods: Patients with overweight or obesity and knee OA participated in a randomised, double blind, placebo-controlled, parallel group, single-centre trial. Patients were provided an initial 8-week run-in diet intervention (week -8 to 0) including a low-calorie diet from Cambridge Weight Plan and dietetic counselling. At week 0 patients who had lost at least 5% of their initial body weight were randomised to liraglutide 3 mg/day or placebo for 52 weeks. The co-primary outcomes were changes in body weight and the KOOS pain subscale from week 0 to 52. Trial registration: NCT02905864. Analyses were based on the intention-to-treat population.

Figure 1. Flow diagram

Figure 2. Least square means during the 52-week study period (after achieving at least 5% weight loss initially), according to randomised treatment group: A, body weight, and B, KOOS pain subscale.

Results: 168 patients (Kellgren-Lawrence grade 1-3) were enrolled in the initial 8-week diet intervention and 156 patients were randomised (Figure 1). Before randomisation the 156 patients had lost 12.46 kg (SD:3.82) ($\approx 12\%$) and improved in KOOS pain corresponding to 11.86 points (SD:15.13) ($\approx 19\%$). Baseline characteristics were similar in the intervention and control groups. From baseline to 52 weeks there was a statistically and clinically significant difference in the weight loss between the liraglutide and the placebo groups (mean -2.76 and 1.17 kg, respectively; group difference, 3.93 kg; 95%CI -6.85 to -1.02; $p=0.008$), there was no difference between groups in change in KOOS pain (mean changes: 0.35 and