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.

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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–