linear models were conducted between dietary intake and microbial species and pathways, adding age, sex, caloric intake and sequencing read depth as covariates. Analyses were conducted per cohort, followed by a meta-analysis and heterogeneity estimation. Multiple testing correction was performed on the obtained p-values and a FDR <0.05 was defined as significance cut-off.

Results: We identified 38 associations between dietary patterns and microbial clusters. Moreover, 61 individual foods and nutrients were associated with 61 species and 249 metabolic pathways in the meta-analysis across healthy individuals and patients with IBS, Crohn's disease and UC (FDR<0.05, heterogeneity p-value>0.05). Processed foods and animal-derived foods were consistently associated with higher abundances of Firmicutes, *Ruminococcus* species of the *Blautia* genus and endotoxin synthesis pathways. The opposite associations were found for clusters comprising fish, nuts, bread and legumes. Moreover, while total plant protein intake was associated with a higher *Bifidobacterium* abundance (FDR=0.048, coef=4.98), animal-derived protein showed a negative association (FDR=$1.^{30}x10^{-05}$, coef= -4.1). Lastly, we observed positive associations of fecal calprotectin with a fast food cluster (FDR=$4.^{14}x10^{-4}$, coef=0.24) and a cluster comprised of high-fat meat, potatoes and gravy (FDR=0.003, coef =0.22), while the opposite was seen for clusters of fish and nuts (FDR=0.038, coef= -0.1) and bread and legumes (FDR=0.005, coef= -2.48).

Conclusion: We identified dietary patterns that consistently correlate with groups of bacteria with shared functional roles in both, health and disease. Moreover, specific foods and nutrients were associated with species known to infer mucosal protection and anti-inflammatory effects. A decrease in these bacteria has already been associated with both IBS and IBD. We propose microbial mechanisms through which the diet affects inflammatory responses in the gut as a rationale for future intervention studies.

OP30

Lyophilised orally administered faecal microbiota transplantation for Active Ulcerative Colitis (LOTUS study)

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Background: Faecal microbiota transplantation (FMT) administered via the lower GI tract effectively induces remission in ulcerative colitis (UC). Orally administered FMT capsules may improve patient tolerability and facilitate maintenance therapy while it is unclear if pre-FMT antibiotics enhance therapeutic efficacy.

Methods: We performed a dual-centre randomised, double blind, placebo-controlled trial of oral lyophilised FMT in adults with mild-moderately active UC (total Mayo 4–10). All subjects received 2-weeks of pre-FMT antibiotics (amoxycillin, metronidazole and doxycycline) before 1:1 randomisation to either oral FMT (0.^{35}g stool content per capsule from 1 of 2 healthy donors) or identical placebo for 8 weeks. Enforced tapering and cessation of corticosteroids was mandated. The primary endpoint was week 8 steroid-free clinical remission with endoscopic remission or response (total Mayo score ≤2 with subscores ≤ 1 for rectal bleeding, stool frequency and endoscopic appearance, and ≥1-point reduction from baseline in endoscopy subscore). Responders to FMT induction were re-randomised to either continue maintenance FMT or withdrawal of FMT with final outcomes assessed at week 56.

Results: Recruitment was paused due to the COVID-19 pandemic. 37 patients were randomised. Baseline patient and disease characteristics were balanced between the randomised groups. The primary outcome was achieved in 8/16 (50%) receiving FMT versus 3/19 (16%) receiving placebo (OR: 4.63; 95%CI: 1.74–12.30; *P*=0.002). Steroid-free clinical remission rates and endoscopic remission rates were 69% vs 26% (*P*=0.012) and 44% vs 16% (*P*=0.074) in the FMT and placebo arms, respectively. Reported SAE were worsening colitis (2 FMT, 1 placebo) and PR bleeding relating to previous anal surgery (placebo). Ten patients entered the maintenance withdrawal study. Steroid-free clinical, endoscopic and histologic remission was achieved in 4/4 patients who continued daily oral FMT, with all 6 patients randomised to FMT withdrawal having a flare of disease with a median time to relapse of 6 months.

Conclusion: Oral lyophilised FMT following antibiotic pre-treatment for mild-moderately active ulcerative colitis was associated with a significant increased rate of clinical remission with endoscopic remission or response versus antibiotic treatment alone at week 8. Pre-treatment antibiotics had an additive impact upon treatment efficacy compared with previous studies utilising FMT. Maintenance FMT therapy was associated with sustained clinical, endoscopic and histologic remission at week 56. Treatment was well tolerated and there were no new safety signals related to FMT therapy.

OP31

RESTORE: Interim analysis of a Phase 2 study of QBECO SSI for the induction and maintenance of clinical and endoscopic remission in subjects with Moderate to Severe Crohn's Disease

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Background: Innate immune defects play a role in the pathogenesis of CD. Enhancing innate immune competency and restoring mucosal barrier function provide a novel approach to treat CD. QBECO SSI is a first-in-class immunotherapy designed to correct innate immune dysfunction underlying CD. This analysis is from subjects in the open label portion of a planned controlled trial. Objectives were to assess endoscopic response at Wks 16 and 26, and select the optimal induction timepoint for the RCT. Safety and treatment compliance were also evaluated.

Methods: 20 pts with moderate-to-severe CD were enrolled and received QBECO SSI by sc injection every other day for up to 52 wks. Minimum eligibility: Simple Endoscopic Score for CD (SES-CD) ≥7 (ileitis ≥4), abdominal pain (AP) score >21 (11-point scale) or liquid/very soft stools (SF) (BFS Type 6 or 7) >10 for 7 consecutive days during screening. Pts were evaluated for clinical symptoms and endoscopy at Wks 16, 26, and 52. After evaluation at the induction period (Wk 26) pts could continue in maintenance up to Wk 52. Endoscopies were evaluated by central blinded read and pts reported

daily symptoms. Endoscopic response defined as ≥50% reduction in SES-CD from baseline. Clinical remission defined as AP and SF ≤21.
Results: Mean age was 43.6 (SD 13.6) yrs; 60% men and 60% previously treated with biologics. Mean yrs since CD diagnosis was 14.4 (10.1), AP score 30.4 (15.8), SF score 36.2 (19.1) and mean SES-CD at baseline was 12.5 (6.7) indicating a more difficult to treat population. Endoscopic response rate by central read during the induction period was 30% (6/20) overall, 38% (3/8) for biologic naïve and 25% (3/12) biologic experienced pts (ITT analysis). Similar number of pts achieved endoscopic response at Wk 16 (4 pts) as 26 (3 pts). Mean SES-CD improved through Wk 26 with a 0.6 point greater reduction at Wk 26 compared to 16. Change in SES-CD from baseline in biologic naïve pts was -2.9 (5.8) at Wk 16 and -4.1 (6.7) at 26. Clinical remission was achieved by 45% (9/20) of pts at Wk 16 and 40% (8/20) at Wk 26; 16 pts continued into the maintenance phase of the study. By central evaluation, 13% (2/16) were in endoscopic response at Wk 52. QBECO SSI was very well tolerated. 8/20 (40%) pts reported AEs related to treatment. Most frequency reported related AE was injection site erythema (2/20, 10% pts). Majority of AEs were mild and no other related AE was reported by more than 1 patient.
Conclusion: Week 26 was the optimal endoscopic evaluation timepoint for QBECO SSI treatment and will be utilized in the larger RCT. Both biologics naïve and experienced patients showed response to QBECO SSI treatment by Weeks 26 and 52, with higher response rates in biologics naïve patients. QBECO SSI was well tolerated.

OP32

Stool microbiome communities predict remission in treatment-naïve Pediatric Crohn's Disease patients

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Background: Early relapse in paediatric Crohn's Disease (CD) is associated with severe disease course that heavily impairs quality of life. Changes in gut microbiome composition have been linked to active CD and disease course. This has led to development of microbiome-based prediction models for diagnosis and response to treatment. Our aim was to identify community-level microbiome signatures of treatment-naïve children with mild-to-moderate CD who did not require anti-TNF or surgery at diagnosis, with the goal of predicting need for re-induction or treatment escalation within the first year after diagnosis.
Methods: We selected de novo, treatment-naïve paediatric CD patients from the RISK cohort(Gevers 2014). Taxonomic labels were assigned to the [16]s rRNA amplicon data using QIIME and closed OTU-picking. A hierarchical Bayesian model for microbial community structure was used to learn how baseline gut microbiomes differed according to treatment outcome. Model predictions were assessed using a leave-one-out analysis. We compared [16]S rRNA sequences of CD patients with non-IBD controls(Gevers 2014) and healthy siblings of CD patients(Turpin 2016).
Results: Metadata and [16]S rRNA amplicon data were available from 197 stool samples of de novo paediatric CD patients from the RISK cohort. We selected 44 out of 197 samples of patients that were treatment-naïve. Prior to treatment, PCDAI scores were similar between patients reaching remission and those that did not at 6 months. Bayesian analysis characterized 4 assemblages that accounted for 93% of the posterior probability distribution. The Bayesian model on pre-treatment stool microbiomes was able to predict 6-month outcome of patients that maintained remission and those that did not from the pre-treatment microbiome in 81% and 75% of samples (AUC=0.79). When comparing CD samples to 28 non-IBD controls (many with GI symptoms but negative for IBD during endoscopy, e.g. Irritable Bowel Syndrome), 6 assemblages were characterized with 44% of distributions shared between groups (AUC=0.61). In contrast, in CD samples compared to 728 healthy sibling samples (with increased genetic susceptibility), shared distribution within 4 characterized assemblages was less than 1% (AUC=1).
Conclusion: A Bayesian approach predicted clinical course in treatment-naïve children with CD in the first year after diagnosis with high accuracy, when ensuring only treatment-naïve faecal samples in the analysis. This classification level is comparable to previous findings using mucosal samples. Further study is needed to validate these pre-treatment microbiome signatures of newly diagnosed paediatric CD patients to allow identification of patients with mild-to-moderate disease who are most likely to require treatment escalation.

Scientific Session 10.1: CD and UC: Similar disease burden and treatment goals? Is it the organ or the disease process?

OP33

Oral ritlecitinib and brepocitinib in patients with Moderate to Severe Active Ulcerative Colitis: Data from the VIBRATO umbrella study

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