Comparative Effectiveness Studies

P094
A COMPARISON OF EXERCISE MEASURES AMONG ADULTS WITH INFLAMMATORY BOWEL DISEASE
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Background: Individuals with IBD, comprised of Crohn's disease (CD) and Ulcerative Colitis (UC), often have ongoing gastrointestinal symptoms that limit their ability to exercise. Importantly, exercise can help to maintain remission in individuals with IBD. Other positive health outcomes of exercise include improvement in quality of life, social and psychological well-being, weight maintenance, bone health, fatigue management and maintaining muscle mass and function. Unfortunately, many of the tools used to measure exercise are burdensome for clinical utility or are not applicable to the IBD population. The purpose of this secondary analysis was to determine if one question related to physical activity would capture exercise in adults with either UC or CD and those with active or inactive disease.

Methods: This study is a cross-sectional study using the data obtained from IBDD Partners, an internet-based longitudinal cohort of adults ≥ 18 year of age living with IBD. This secondary analysis includes only those participants without a current ostomy or pouch, who completed demographic information, disease activity and exercise characteristics. Disease activity was measured via the simple clinical colitis activity index (SCCAI) for UC and the short Crohn's disease activity index (sCDAI) for CD. Exercise was measured via the Godin Leisure-Time Activity Index (GLTA) questionnaire that assessed type of exercise and intensity for the past seven days. A separate measurement of physical activity included a single question: “How often did you participate in 1 or more physical activities of 20–30 minutes’ duration per session during your leisure time within the past 6 months?” measured via a 6-point ordered category item.

Results: A total of 8327 patients with IBD were included. Most (63%) of the participants had CD, and 54% were in remission. Majority of the participants were physically active based on GLTA scores (49.7%), and one question physical activity scores (62%; combined scores of 5 & 6). Polychoric correlation coefficient was computed, with a strong correlation between GLTA and the one question (r = 0.74, p < 0.001). Ordinal regression analysis between the one physical activity question and IBD type (UC vs CD) yielded higher odds of physical activity with UC (Odds ratio (OR)=1.2, 95% CI [1.11 -1.31], p < 0.0001). Similar results were noted with ordinal regression analysis between GLTA scores and UC/OR=1.2, 95% CI [1.09 -1.31], p < 0.0001).

Conclusions: Both GLTA and the single question of physical activity were highly correlated. The ordinal regression results were comparable for both measures. Adoption of the single physical activity question may adequately reflect exercise status in IBD patients and reduce burden for clinical use. Further longitudinal studies are need to support the use of one question in measuring exercise in those with IBD.

Controlled Clinical Trials in Humans

P063
A COMPREHENSIVE, MULTOMIC DIET INTERVENTION STUDY COMPARING A LOW FAT, HIGH FIBER DIET TO AN IDEALIZED STANDARD AMERICAN DIET IN ULCERATIVE COLITIS PATIENTS
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Background and Aims: There is a lack of evidence-based dietary interventions in ulcerative colitis (UC) management. A diet high in fat and animal meat has been linked to an increased risk of UC. The aim of our study was to use a multilayered, multi-omic approach to comprehensively characterize the effect of a low fat, high fiber diet or a high fat diet in UC patients.

Methods: We enrolled patients with UC who were in remission or had mild disease with a flare within the last 18 months. We used a cross-over design in which patients received two dietary interventions: a low fat diet (LFD), containing 10% total calories from fat with an omega 6 to 3 ratio of below 3:1, and an idealized standard American diet (SAD), containing 35–40% total calories from fat with an omega 6 to 3 ratio of 20–30:1. Each diet was four weeks long with a two-week wash-out in between. The diet was catered and delivered to patients' homes. Clinical symptoms, quality of life, and biochemical data were collected. Stool was collected for microbiome and metabolomic analyses. The primary endpoint was to determine adherence to a specified diet using catered meals; the secondary endpoint was to determine the clinical and subclinical effects of a low fat, high fiber diet or high fat diet in UC patients.

Results: Baseline diets varied widely but were generally lower in fiber as well as fruits and vegetables and higher in saturated fat than either of the study diets. There was a high rate of adherence to catered meals (SAD=86.68%, LFD=84.8%) with a 96.8% and 94.33% adherence to fat for SAD and LFD respectively. Patients that started in remission remained in remission (partial Mayo and sIBDQ). Following a LFD, patients saw a 20% improvement in their quality of life as measured by sIBDQ compared to their baseline. The effect of diet intervention on microbial diversity was reflected in the beta diversity with a significant increase in Faecalibacterium prausnitzii after LFD. CRP, sIBDQ, IL-6, and IL1β had a significant effect on overall gut microbiota composition as measured by Bray Curtis beta diversity (PERMANOVA)(P<0.007, P<0.001, P<0.021, P<0.048 respectively). The top taxa that contributes the most to this microbial variation from these clinical parameters was Faecalibacterium prausnitzii. Patients following a SAD had an increase in lauric acid, myristic acid, and N-oleoyl-L-phenylalanine with an increase in omega-6 metabolism pathways. Patients following a LFD had higher glycolic, alanine, and phenyllactic acid with omega 3 metabolism pathways increased after LFD.

Conclusions: A low fat, high fiber diet is well tolerated and did not increase biochemical markers of inflammation. Catered meals and collection of microbiome, metabolome and biochemical data may allow early stratification of diet responders.
**P064**

CHARACTERIZATION OF EARLY CLINICAL AND PHARMACOKINETIC RESPONSE PROFILES OF VEDOLIZUMAB: AN INTERIM ANALYSIS OF ENTERPRET, A PHASE 4 CLINICAL STUDY

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Introduction: Vedolizumab (VDZ), a gut-selective antibody that binds specifically to integrin α4β7, is approved for treatment of adults with moderate-to-severe ulcerative colitis (UC). An association between VDZ levels and clinical remission during induction therapy at Week (Wk) 6 was observed in pivotal trial data; the majority of nonresponders at Wk 6 had VDZ levels <40 μg/mL, and those with VDZ clearance >0.14 L/d had reduced efficacy outcomes (Osterman MT, et al. Aliment Pharmacol Ther. 2019). In the ongoing randomized controlled trial (ENTERPRET), we are evaluating whether dose escalation starting at Wk 6 in clinical nonresponders with high VDZ clearance (level <50 μg/mL at Wk 5) leads to improved outcomes at Wk 30. This is an interim analysis of ENTERPRET in which baseline predictors of response at Wk 6 were investigated.

Methods: Adults with moderately to severely active UC received VDZ 300 mg IV on Day 1 and Wk 2. At Wk 5, VDZ concentration in serum was measured; clinical response was assessed at Wk 6 based on partial Mayo score (reduction in partial Mayo score ≥2 points and ≥25% from baseline [Day 1] with an accompanying decrease in rectal bleeding subscore ≤1 point or absolute rectal bleeding score ≤1 point). Descriptive analysis was used for these interim data, including baseline characteristics in responder and nonresponder groups.

Results: A total of 117 patients (mean age 41.2 years, 40.2% female) were analyzed; 112 were classified as a responder (n=57) or nonresponder (n=55) based on Wk 6 response. At baseline, mean disease duration was higher in nonresponders than responders (9.5 vs 7.1 years), with 47.4% of nonresponders having disease duration ≥7 years compared with 38.2% of responders. Endoscopic activity score was higher in nonresponders vs responders (49.1% vs 36.4% had severely active disease [Mayo endoscopic subscore≥3]). 63.2% of nonresponders had a high stool frequency at baseline (Mayo subscore=3) compared with 49.1% of responders. 63.6% of responders had more severe rectal bleeding scores (Mayo subscore of ≥3) compared with 45.6% of nonresponders. More responders (67.3%) were anti-TNF-α naive at baseline than nonresponders (52.6%). At Wk 6, change in mean (SD) partial Mayo score from baseline was -4.2 (1.65) for responders and -0.2 (0.96) for nonresponders. Wk 5 mean VDZ serum concentrations were numerically lower in nonresponders (31.2 [SD=12.8] vs 40.3 [SD=15.3] μg/mL in responders). There were no unexpected treatment-emergent adverse events in either group.

Conclusion: Interim data from ENTERPRET show Wk 6 responders had higher VDZ serum concentrations at Wk 5 than nonresponders. Although current results are consistent with the hypothesis that lower response to VDZ at Wk 6 correlates with lower drug exposure, we await the final results of ENTERPRET to better understand the exposure-response relationship of VDZ.

**P065**

GB004, A NOVEL GUT-TARGETED PROLYL HYDROXYLASE INHIBITOR FOR INFLAMMATORY BOWEL DISEASE: FIRST-IN-HUMAN, MULTIPLE-DOSE STUDY IN HEALTHY SUBJECTS WITH GUT BIOPSYs

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Background: GB004 is a small molecule prolyl hydroxylase inhibitor (PHDi) that stabilizes hypoxia inducible factors (HIF1-α), key transcription factors involved in the protective cellular responses at the intersection of hypoxia and inflammation. GB004 was selected based on its gut-targeted profile to limit systemic on-target effects associated with HIF-1α stabilization. Consistent with this, orally administered GB004 in a healthy non-human primate model engaged HIF-related genes in the gut, and, in animal models of colitis, demonstrated a significant reduction in disease activity, improvements in histologic measures, and greater exposure in GI tissue relative to plasma. GB004 is in clinical development for treatment of inflammatory bowel disease (IBD) and was shown to be safe in a single ascending dose study. The study described here evaluates the safety, tolerability, and pharmacokinetic (PK) profiles of multiple daily doses of GB004 in plasma and colon biopsies.

Methods: This was a randomized, double-blind, placebo-controlled, multiple dose, Phase 1a study conducted in healthy subjects at a single site in Canada. Three dose levels of GB004 formulated as a solution or placebo solution were administered orally once a day for 8 days; safety and PK were evaluated. Plasma levels of HIF-targeted genes EPO and VEGF were determined by immunoassays from samples collected at pre-dose, 4, 8, and 12 hours post dose on Day 1 and Day 7. Colon biopsies were obtained one day prior to first dose and at Day 8.

Results: 42 subjects (20 male and 22 female) were dosed. No serious adverse events or deaths were recorded. The most commonly observed and adverse event in GB004-treated subjects was dizziness (31%;10/32); all events were mild and did not result in study drug discontinuation. There were no identified risks of GB004. Following oral dosing, GB004 was rapidly absorbed and eliminated from the systemic