Abstract OWE-010 Figure 4 NMDS weighted UniFrac (bacteria-biopsies – disease distribution) R²=0.17 p=0.001

The mucosal bacterial community was dysbiotic and influenced by subject, disease distribution (figure 4) and diagnosis (figure 5). In terms of mycobiome, fewer viable reads were experienced by subject, disease distribution (figure 4) and diagnosis

Abstract OWE-010 Figure 5 NMDS weighted UniFrac (bacteria-all biopsies – diagnosis) R²=0.11 p=0.001

The mucosal bacterial community was dysbiotic and influenced by subject, disease distribution (figure 4) and diagnosis (figure 5). In terms of mycobiome, fewer viable reads were obtained, due to limited template. Saccharomyces was the most abundant fungi, but it was absent in some samples, other relevant genera were Malassezia, Cladosporium, Aspergillus and Candida. The last was found more often in controls.

Conclusions CD patients’ bacterial community is dysbiotic but fungi are not. Saccharomyces dominated most of faecal samples, but not biopsies. This implies it may not be a permanent resident of the mucosae. Fungi may arise from food: it is hard to discriminate what comes from food and what is active in the gut. The concept of a resident, symbiotic mycobiome needs further exploration.

Introduction PANTS (Personalised Anti-TNF Therapy in Crohn’s disease [CD]) is a 3 year prospective observational UK-wide study investigating primary non-response (PNR), loss of response and adverse drug reactions to infliximab (IFX: Remicade [REM], CT-P13) and adalimumab (ADL: Humira). We now report the wk 54 clinical effectiveness and safety outcomes, and immunogenicity data to date.

Methods Inclusion criteria included: CD patients aged ≥6 years, active inflammatory disease (raised CRP ≥3 mg/L or calprotectin [≥50 μg/g]) and no prior anti-TNF therapy. PNR was defined at wk 12–14 as a requirement for ongoing steroids, or both HBI failed to fall by ≥3 points or to ≤4 and CRP failed to fall by ≥50% or to ≤3 mg/L. Remission was defined at wks 14 and 54 as HBI ≤3 points and CRP ≤3 mg/L and no concomitant steroids. Patients who stopped drug other than for elective withdrawal, pregnancy or loss to follow-up were regarded as treatment failures for subsequent endpoints. Drug (DL) and anti-drug antibody (ADA) levels were measured using the IDKmonitor drug tolerant assays. Immunogenicity was defined as ADA titre ≥10 AU/ml +undetectable DL.

Results 1601 (49% male, median age 33 years [IQR 23–47]) eligible patients were recruited from 118 sites. Patients were treated with IFX (751 [47%]: REM, 200 [12%] CT-P13) or ADL (650 [41%]). Baseline characteristics included: median disease duration 3 years (IQR 1–10); steroids 27%, azathioprine 44%, mercaptopurine 8%, methotrexate 5%; median CRP in IFX 9 mg/L (IQR CI 3–24) and 6 mg/L (IQR CI 2–14) in ADL. PNR at week 12–14 was 21%, 21% and 26% in the REM, CT-P13 and ADL treated patients respectively. PNR was associated with older age (p=0.0004), higher BMI (p=0.03) and low DL (p<0.0001 for IFX and ADL). Week 54 remission rate was 40%, 40% and 34% of the REM, CT-P13 and ADL treated patients. At wk 54, the immunogenicity rate for REM, CT-P13 and ADL was 26%, 28% and 11% rising to 42%, 38% and 23% by 3 years respectively (IFX vs. ADL p<0.0001, REM vs. CT-P13 p=0.25). Immunogenicity was associated with non-remission at wk 54 (p<0.0001 for both IFX and ADL). Immunomodulator use reduced the risk of immunogenicity for both IFX (HR=0.37, p<0.0001) and ADL (HR=0.34, p<0.0001). 140 patients (9%) withdrew drug for SAEs including 5 who died, 3 from CD and 2 from possibly drug-related acute respiratory illness.

Conclusions This is the largest prospective real-life study of anti-TNF therapy in IBD. We report the clinical effectiveness, safety and immunogenicity of REM, CT-P13, and ADL. This cohort provides a unique bioresource for multi-omic studies investigating personalised approaches to anti-TNF therapy.

OBT-003 PAEDIATRIC CROHN’S DISEASE PATIENTS IN REMISSION HAVE A REDUCED SKELETAL MUSCLE PROTEIN BALANCE AFTER FEEDING

1Gordon Moran, 1Amanda Walker, 3Alene Nixon, 3David Devadason, 4Rafeeq Muhammed, 3Kostas Tsintzas, 1Sian Kirkham, 5Francis Stephens. 1Nottingham University Hospitals NHS Trust; 2NHR Nottingham Biomedical Research Centre; 3School of Life Sciences, University of Nottingham; 4Birmingham Children’s Hospitals; 5Sports and Health Sciences, University of Exeter

OBT-003 PAEDIATRIC CROHN’S DISEASE PATIENTS IN REMISSION HAVE A REDUCED SKELETAL MUSCLE PROTEIN BALANCE AFTER FEEDING

1Gordon Moran, 1Amanda Walker, 3Alene Nixon, 3David Devadason, 4Rafeeq Muhammed, 3Kostas Tsintzas, 1Sian Kirkham, 5Francis Stephens. 1Nottingham University Hospitals NHS Trust; 2NHR Nottingham Biomedical Research Centre; 3School of Life Sciences, University of Nottingham; 4Birmingham Children’s Hospitals; 5Sports and Health Sciences, University of Exeter

Introduction Sarcopenia is common in active Crohn’s disease (CD) and still prevalent in remission. This can lead to fatigue, physical inactivity and poor quality of life but the aetiology is
unclear. We aimed to investigate the association between sarcopenia and anabolic resistance (AR) and insulin resistance (IR), and the role of physical activity in age, gender matched children with CD.

Methods 18 fasted, male and female CD (on thiopurines ± anti-TNFα) in deep remission (16 γ, BMI=21) and 9 matched controls (Con) (16 γ, BMI=21) drank a liquid meal (Ensure plus, 44 g CHO, 14 g PRO, 11 g fat) at t=0. Arterialised hand and venous forearm blood samples were collected concurrently and brachial artery blood flow measured at baseline and every 20 mins for 2 hours. Net balance of branched chain amino acids (BCAA) and glucose were derived, giving indices of skeletal muscle protein balance and IR. Subjects had a DEXA scan and handgrip dynamometer test on the day, and wore a pedometer and completed a food diary (for 3 days) to assess physical activity and food intake. Patient questionnaires (incl. IBD-fatigue) were completed.

Results Net BCAA balance across the whole 2 hours was lower in CD vs Con (p=0.05). Yet an initial response to feeding (t=0 to t=20) was exhibited by both CD (+1μmol/min) and Con (+0.8μmol/min) but was only sustained post 40 mins in Con. IBD-fatigue scores indicated CD had moderate fatigue (6), which had a moderate effect on daily activities (17). Handgrip dynamometer testing showed a trend towards greater fatigue in CD vs Con (+8%) in the dominant arm (p=0.061). A trend towards lower total body lean mass in CD (−15%, p=0.084) was found. No differences were detected in strength, physical activity, diet or IR. Thus despite not exhibiting AR (initial response to the meal) CD could not maintain a positive protein balance post feeding. This was associated with reduced muscle mass and function.

Conclusions The inability to sustain a positive protein balance postprandially could provide an explanation for the reduced muscle mass seen in CD patients in remission and be contributing to fatigue and poor muscle function. Pharmacological interventions to reduce protein breakdown and a high protein diet and/or exercise to improve anabolic response could be investigated as potential treatments.

ADTU-02 V565, A NOVEL ORAL ANTI-TNF DOMAIN ANTIBODY, REDUCES COLONIC MUCOSAL INFLAMMATION IN PATIENTS WITH UC

Gareth Parkes*, Shail Nurbhai, Mike West, Ray, Tom MacDonald, Anna Vossenkaemper, Crowe, Royal London Hospital, London, UK; VHSquared, Cambridge, UK

Introduction Monoclonal antibodies to TNF transformed treatment options for patients with Inflammatory Bowel Disease (IBD). V565 is a novel oral anti-TNF domain antibody (Vora- body) engineered to be resistant to intestinal proteases. It is in development as a potential oral treatment for IBD. In vitro it suppressed phosphorylation of tyrosine kinases and signalling proteins and inhibited the release of inflammatory cytokines following culture with biopsies taken from patients with CD (Crowe et al. 18th International Congress of Mucosal Immunology, July 19–22 2017, Washington DC, USA). It was safe and well tolerated after single and multiple doses in healthy volunteers and patient volunteers with CD and resulted in high concentrations of active drug in ileal fluid and faeces.

Aims & Methods This open label study was designed to demonstrate that V565 enters GI mucosa and exerts a beneficial effect on inflammatory processes following oral dosing for 7 days to patients with Ulcerative Colitis. Patients with a Mayo score of ≥10 including an endoscopy score of ≥1 had up to 7 days of oral dosing with 555 mg tid V565. Sigmodoscopy with biopsies was performed before and after the dosing period. The primary outcomes of interest were presence of V565 in the mucosa and reduction from baseline in phosphorylation of tyrosine kinases and signalling proteins. Detection of V565 was determined by immunohistochemistry. Phosphorylation was determined using PathScan RTK signalling arrays (Voskenkaemper et al 2014. Gastroenterology 147:172–83).

Results Five patient volunteers were treated Due to visit scheduling, most received 6 days treatment. Presence of V565 was confirmed in the inflamed lamina propria and co-localised with CD14 + macrophages in post-treatment biopsies. Overall phosphorylation of tyrosine kinases and the role of physical activity in age, gender matched children with CD.

Methods 18 fasted, male and female CD (on thiopurines ± anti-TNFα) in deep remission (16 γ, BMI=21) and 9 matched controls (Con) (16 γ, BMI=21) drank a liquid meal (Ensure plus, 44 g CHO, 14 g PRO, 11 g fat) at t=0. Arterialised hand and venous forearm blood samples were collected concurrently and brachial artery blood flow measured at baseline and every 20 mins for 2 hours. Net balance of branched chain amino acids (BCAA) and glucose were derived, giving indices of skeletal muscle protein balance and IR. Subjects had a DEXA scan and handgrip dynamometer test on the day, and wore a pedometer and completed a food diary (for 3 days) to assess physical activity and food intake. Patient questionnaires (incl. IBD-fatigue) were completed.

Results Net BCAA balance across the whole 2 hours was lower in CD vs Con (−0.1±0.2μmol/min vs 0.6±0.3μmol/min, p=0.05). Yet an initial response to feeding (t=0 to t=20) was exhibited by both CD (+1μmol/min) and Con (+0.8μmol/min) but was only sustained post 40 mins in Con. IBD-fatigue scores indicated CD had moderate fatigue (6), which had a moderate effect on daily activities (17). Handgrip dynamometer testing showed a trend towards greater fatigue in CD vs Con (+8%) in the dominant arm (p=0.061). A trend towards lower total body lean mass in CD (−15%, p=0.084) was found. No differences were detected in strength, physical activity, diet or IR. Thus despite not exhibiting AR (initial response to the meal) CD could not maintain a positive protein balance post feeding. This was associated with reduced muscle mass and function.

Conclusions The inability to sustain a positive protein balance postprandially could provide an explanation for the reduced muscle mass seen in CD patients in remission and be contributing to fatigue and poor muscle function. Pharmacological interventions to reduce protein breakdown and a high protein diet and/or exercise to improve anabolic response could be investigated as potential treatments.

ADTU-03 IMPACT OF IMPROVED ACCESS TO BIOLOGIC THERAPIES AND PHYSICIAN ENGAGEMENT ON EXCESS STEROID EXPOSURE


Background Steroid free remission is an important goal of IBD therapy. The aim of this study was to evaluate temporal changes in steroid prescribing in UK IBD outpatient departments in the context of major changes in UK prescribing guidelines and physician participation in audit and tailored service changes.

Methods Steroid use over the previous 12 months was recorded for unselected outpatient attenders against a definition of excess from ECCO guidelines. Data were collected from 7 centres that had completed a steroid assessment audit cycle in 2015, as well as from 12 new matched centres.

Results Data was collected for 2385 patients May-July 2017 and compared with 2015 data from 1176 patients. Overall disease distribution was 47.1% CD, 49.6% UC and 3.3% IBD-U, whilst 77.7% of patients were in clinical remission at the time of assessment. There was only a modest increase in patient exposure to anti-TNF from 2015 to 2017: 30.6% to 37.2% in CD (p=0.009) and 9.9% to 12.0% in UC (p=NS). Anti-integrin usage increased from 0.8% to 3.3% in CD (p=0.002) and from 1.6% to 2.4% in UC (p=NS). For