



Abstract PWE-108 Figure 1

### PWE-109 MEASUREMENT OF INFlixIMAB AND ANTI-INFlixIMAB ANTIBODIES - ANALYTICAL ASPECTS AND CLINICAL IMPLICATIONS

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<sup>1</sup>N Unsworth, <sup>2</sup>Z Arkir, <sup>2</sup>P Irving, <sup>2</sup>M G Ward, <sup>1</sup>G Richards. <sup>1</sup>Reference Chemistry, GSTS Pathology, Guy's and St. Thomas' NHS Trust; <sup>2</sup>Department of Gastroenterology, Guy's and St. Thomas' NHS Trust, London, UK

**Introduction** Commercial assays for monitoring Infliximab (IFX) and anti-drug antibodies (ADAb) are currently available. The heterogeneity of these assays and lack of standardisation of ADAb may cause difficulties in interpretation, in particular comparing bridging ELISA and radioimmunoassay (RIA). Bridging ELISAs have high specificity but are more prone to inhibition by drug hence may underestimate ADAb, whereas false positive results can be seen with RIA.

**Aims** Evaluation of (i) the effect of common interferents in the LISA-Tracker Premium ELISA assay (Theradiag). (ii) the inhibitory effect of IFX on the detection of ADAb.

**Methods** The LISA-Tracker kit was used for the quantitative determination of free drug and ADAb by indirect and bridging assay principles respectively. The measurement range was 0.1 to 5 µg/mL for IFX and 10 to 200 ng/mL for ADAb (> 10 ng/mL considered positive).

Interference studies were carried out using samples with known levels of haemolysis, icterus, rheumatoid factor (RF) and paraprotein (IgG kappa = 17 g/L). All patients had no history of exposure to biologics. Samples were run neat and diluted with samples of known IFX and ADAb concentration to assess recovery.

Samples with known levels of ADAb were spiked with aqueous solutions of IFX (2.4, 1.2 and 0.3 µg/mL) at a ratio of 1:2. Predicted ADAb concentrations were calculated by sample dilution in drug-free diluent.

**Results** No interference was observed from haemolysis (up to 0.6 g/dL haemoglobin equivalent), icterus (up to 349 µmol/L bilirubin), RF (up to 885 U/mL) and paraprotein as confirmed by recoveries of 93–113% for drug and ADAb.

#### Spiking experiments

The inhibitory effect of IFX on ADAb detection was observed in both low and high level ADAb samples with ADAb only detectable in sample 2 i.e. as free, not complex form. Comparing expected with measured concentrations of IFX in the spiked samples indicated a difference in recovery between the low and high ADAb positive samples suggesting decreased availability of free IFX in the presence of ADAb.

**Conclusion** This study shows that the LISA-Tracker kit is not affected by tested interferents. Results from spiking experiments highlight the importance of measuring trough levels and also indicate that the presence of ADAb (detectable or undetectable) can limit the availability of free IFX, leading to sub-therapeutic levels.

LISA-Tracker is a simple, robust assay which has been implemented in our hospital and is routinely used as a personalised approach to prescribing and optimising anti-TNFα therapies in IBD.

**Disclosure of Interest** None Declared.

### PWE-110 ACCEPTANCE AND ADJUSTMENT IN A DISTRICT GENERAL COHORT OF INFLAMMATORY BOWEL DISEASE PATIENTS: FINDINGS AND IMPLICATIONS

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<sup>1</sup>N Swart, <sup>1</sup>D Wellsted, <sup>2</sup>K Lithgo, <sup>2</sup>T Price, <sup>2</sup>M W Johnson. <sup>1</sup>Centre for Lifespan and Chronic Illness Research, University of Hertfordshire, Hatfield; <sup>2</sup>Gastroenterology, Luton & Dunstable University Hospital, Luton, UK

**Introduction** 'Acceptance' refers to the patient's willingness to engage with their illness. Poor acceptance implies the avoidance or denial of an illness and the accompanying somatic experiences. A lack of acceptance highlights an unwillingness to make the necessary behavioural changes that are required to manage a disease effectively (e.g. missing clinical appointments, medication adherence, bad diet, poor coping strategies). This can have serious ramifications for long-term conditions such as inflammatory bowel disease (IBD).

**Objective** To assess the prevalence of poor acceptance within our IBD patients.

**Methods** 2400 patients with IBD in the Luton & Dunstable catchment area were invited to participate in a web-based quality of life assessment, with the option to request a paper copy. Eligibility required patients to be between 18 and 90 years of age, with no serious learning difficulties or pre-existing mental disorders. The 7-item self-report "Acceptance and Adjustment Questionnaire" (AAQ-II; Bond *et al* 2011) was used. AAQ-II scoring ranges from 7 to 49. A bimodal distribution suggested two groups of patients (Good and Poor Acceptance) separated by a cut-off score of 18. Logistic regression was used to identify predictors of acceptance and adjustment.

**Results** 245 patients completed the assessment (43% male; mean age = 53, SD = 17). Approximately 37% of patients fell in the Poor Acceptance group. Significant predictors of Poor Acceptance were found in Anxiety, Depression, Emotional Illness Perception and Socio-Economic Deprivation. Anxiety levels were scored on a scale from 0 to 21 using the GAD-7. Depression levels were scored on a scale from 0 to 27 using the PHQ-9. Emotional Illness Perception on

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Expected IFX µg/mL	Sample 1		Sample 2			
	Measured IFX µg/mL	Expected ADAb ng/mL	Measured ADAb ng/mL	Measured IFX µg/mL	Expected ADAb ng/mL	Measured ADAb ng/mL
1.6	1.9	53	< 10	1.3	176	< 10
0.8	0.7	53	< 10	0.5	176	< 10
0.2	< 0.1	53	< 10	< 0.1	176	12

a scale from 3 to 21 using the Brief Illness Perception Questionnaire. Deprivation based on postcode area was expressed as percentile ranks. For each one point increase in Anxiety, Depression and Emotional Illness Perception scores the likelihood of Poor Acceptance increased by 22%, 21% and 27% respectively. Greater deprivation increased the likelihood of Poor Acceptance by 2% per percentile rank.

**Conclusion** Predictors of Poor Acceptance may be grouped into Mood and Deprivation. Education through self-management programmes may tackle some of the problems caused by deprivation. To optimise treatment success in IBD, we would advocate further research into a mood-orientated approach using screening tools, coupled with clinical judgement and targeted psychological interventions such as Acceptance and Commitment Therapy (ACT), which is based upon Acceptance and Adjustment Theory.

**Disclosure of Interest** None Declared.

#### PWE-111 ASSESSMENT AND IMPLICATIONS OF HEALTH-RELATED QUALITY OF LIFE IN A DISTRICT GENERAL COHORT OF INFLAMMATORY BOWEL DISEASE PATIENTS

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<sup>1</sup>N Swart, <sup>1</sup>D Wellsted, <sup>2</sup>K Lithgo, <sup>2</sup>T Price, <sup>2</sup>M W Johnson. <sup>1</sup>Centre for Lifespan and Chronic Illness Research, University of Hertfordshire, Hatfield; <sup>2</sup>Gastroenterology, Luton & Dunstable University Hospital, Luton, UK

**Introduction** Health-Related Quality of Life (HRQOL) has been shown to have far-reaching implications for patient self-management, treatment efficiency and engagement with their own illness.

**Objectives** To assess the levels of HRQOL experienced by inflammatory bowel disease (IBD) patients within the district general setting.

**Methods** 2400 patients with IBD in the Luton & Dunstable catchment were invited to participate in a web-based quality of life assessment, with the option to request a paper copy. All patients were deemed eligible provided they were between 18 and 90 years of age, with no major learning difficulties or pre-existing serious mental disorders. HRQOL was measured using the 10-item "short Inflammatory Bowel Disease Questionnaire" (sIBDQ; Irvine *et al* 1996). The sIBDQ is divided into four subscales: Systemic, Emotion, Social and Bowel. Possible scores for the sIBDQ ranged from 7 to 70, with lower scores indicating poorer quality of life.

**Results** 245 patients completed the assessment (43% male; mean age = 53, SD = 17). 45% had Ulcerative Colitis, 45% had Crohn's Disease and 10% had an alternative form of IBD (eg. Proctitis, Lymphocytic Colitis or Collagenous Colitis). The HRQOL of patients in this study was low, and similar to that reported by Irvine *et al* The mean score of the sample was 48 (CI = 46.6 – 49.4).

There are no published validated cut-off values for the sIBDQ indicating a "normal" QoL. Using Huaman *et al*'s (2010) estimated value for the IBDQ-36 (209 in the range 36–252) we assumed a cut-off of 56 in the range 7–70 to estimate a cut-off for the sIBDQ. This would mean that approximately 70% of the sample had an 'abnormally' low Quality of Life. For comparison, subscale scores were divided by the number of items they contained. Mean subscale scores were: Systemic – 4.3 (CI = 4.1–4.5); Emotion – 4.8 (CI = 4.7–4.9); Social – 5.4 (CI = 5.2–5.6); Bowel – 4.8 (CI = 4.6–5.0). A 'tail-off' effect was also noted, representing a small group of patients who reported having a significantly reduced health-related quality of life.

**Conclusion** This study found that Social aspects of Quality of Life were less severely affected by IBD than Emotional or Bowel-related aspects, allowing patients to maintain a relatively high level of social activity. The medical (or Bowel) aspects of the condition were perceived to have the greatest negative impact on HRQOL. However, to make significant improvements in the patients' total QOL

one has to focus on improving their emotional engagement with the condition and their overall perception of the IBD and the symptoms they suffer.

**Disclosure of Interest** None Declared.

## Liver

#### PWE-112 MATERNAL OBESITY PROMOTES OFFSPRING NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) THROUGH DISRUPTION OF ENDOPLASMIC RETICULUM HOMEOSTASIS

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<sup>1</sup>J Soeda, <sup>1</sup>A Mouralidarane, <sup>1,2</sup>S Ray, <sup>1</sup>R Carter, <sup>3</sup>G Fusai, <sup>4</sup>M Novelli, <sup>5</sup>J Pombo, <sup>5</sup>A Socioanowska, <sup>5</sup>D Sugden, <sup>5</sup>L Poston, <sup>5</sup>P Taylor, <sup>1,2</sup>J Oben. <sup>1</sup>Institute of Liver & Digestive Health, University College London; <sup>2</sup>Gastroenterology, Guy's & St Thomas' Hospitals; <sup>3</sup>Hepatobiliary Surgery & Liver Transplantation, Royal Free Hospital; <sup>4</sup>Department of Pathology, University College London; <sup>5</sup>Division of Women's Health, King's College London, London, UK

**Introduction** We have previously shown that maternal obesity (MO) programmes offspring obesity and consequent liver disease (non-alcoholic fatty liver disease, NAFLD) but involved mechanisms are unclear. Accumulating evidence suggests endoplasmic reticulum (ER) stress induced unfolded protein response (UPR) plays a central role in the pathogenesis of steatosis and subsequent non-alcoholic steatohepatitis (NASH). However, little is known about the role of UPR in developmentally programmed NAFLD.

**Methods** C57BL6 mice were fed standard or obesogenic diet (OD) for 6 weeks prior to pregnancy and throughout pregnancy and lactation. Litters were weaned onto standard or OD to produce 4 groups. Animals were sacrificed at 6 months. Blood and tissue samples were collected to assess the liver phenotype and expression analysis of UPR related proteins and genes.

**Results** Offspring exposed to MO and a post-weaning OD (OffOb-OD) developed profound NAFLD compared to those exposed to post-partum (OffCon-OD) or the control group (OffCon-SC), as assessed by raised ALT ( $p < 0.001$ ) and NAFLD Activity Score ( $p < 0.01$ ). Among 3 proximal sensors of ER stress, PERK protein expression and phospho eIF-2alpha were specifically increased in OffOb-OD ( $p < 0.05$ ). ATF6 cleavage and spliced form of XBP-1 were observed in all groups except for OffCon-SC. Phospho SAPK/JNK, CHOP, and LC3BII protein expression were significantly increased in OffOb-OD. Furthermore, hepatocytes apoptosis as detected by TUNEL and active caspase-3 staining in OffOb-OD. These results indicate that unresolved UPR is significantly activated in OffCon-OD. However, GRP78, a major ER chaperone and central regulator for ER stress, was significantly downregulated in OffOb-OD. UPR induced chaperon (GRP94) and ER-associated protein degradation related gene (HERP and EDEM) were downregulated in OffCon-OB and OffOb-OD. Furthermore rhythmic expression of GRP78 and HERP were blunted in OffOb-OD.

**Conclusion** MO and a post-natal obesogenic diet profoundly disrupted ER homeostasis in offspring. Disrupted ER homeostasis may be involved in the propagation of NAFLD.

**Disclosure of Interest** None Declared.

#### PWE-113 LOW RISK FOR HEPATOCELLULAR CANCER (HCC) IN HEPATITIS B VIRUS (HBV) INFECTED ASIAN MIGRANTS: IMPLICATIONS FOR CANCER SURVEILLANCE

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<sup>1</sup>K-K Li, <sup>2</sup>S Von Heimendahl, <sup>1</sup>T Bruns, <sup>1</sup>S Ward, <sup>1</sup>P Trivedi, <sup>1,2</sup>Y Oo, <sup>1,2</sup>D Mutimer. <sup>1</sup>Centre for Liver Research & NIHR Biomedical Research Unit, University of Birmingham; <sup>2</sup>Liver Unit, Queen Elizabeth Hospital, Birmingham, UK