

**Conclusion** Sequential OAV therapy following treatment failure with PEG-IFN $\alpha$  is associated with greater reductions of HBsAg than PEG-IFN $\alpha$  alone or OAV monotherapy. This suggests PEG-IFN $\alpha$  may prime the immune response, even in the context of treatment failure, leading to better responses with sequential OAV therapy. Further studies are needed to confirm this finding and determine whether a similar priming effect is observed with shorter courses of PEG-IFN $\alpha$  in line with current PEG-IFN $\alpha$  stopping rules.

**Disclosure of Interest** None Declared.

#### PWE-144 FRAX SCORE IN THE ASSESSMENT OF BONE MINERAL DENSITY CHANGES IN TENOFOVIR TREATED CHRONIC HEPATITIS B PATIENTS

doi:10.1136/gutjnl-2013-304907.432

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**Introduction** Tenofovir Disoproxil Fumarate (TDF) is an established oral antiviral (OAV) in the treatment of Chronic Hepatitis B (CHB). Bone Mineral Density (BMD) loss has been described in TDF treated HIV patients, but limited data exist in CHB. We have used DEXA scanning to determine BMD changes in TDF treated patients and have reported the possibility of BMD loss. DEXA scanning, however, is costly and requires longitudinal follow-up. We assessed the value of the FRAX<sup>®</sup> score and of bone biochemistry to evaluate their utility in TDF treated patients.

**Methods** The FRAX score is a WHO web-based tool, used to calculate 10-year fracture risk and the need for lifestyle modification, DEXA scanning or preventative treatment. CHB patients treated with TDF for a minimum of 12-months and a control group not exposed to TDF were studied. 122 TDF exposed patients (male = 89), median age 45 (range = 26–64) and 48 patients (male = 31), median age 36 (range = 20–62) not exposed to TDF were DEXA scanned and included in the study. We calculated FRAX scores and recorded bone biochemical markers, comprising serum Alkaline Phosphatase (sALP), Calcium (sCa) and Phosphate (sPO).

**Results** TDF treated patients had lower hip T-scores compared to controls ( $p = 0.02$ ). On univariate analysis factors associated with a hip T-score  $< 1$  included older age, lower BMI, smoking and TDF exposure ( $p = < 0.05$ ). On multivariate analysis the same factors were associated with a hip T-score  $< 1$ , but TDF lost significance. For the development of a major osteoporotic fracture the pre-DEXA FRAX score was 4.77% compared to 4.33% (post-DEXA FRAX) ( $p = 0.9$ ) and for a hip fracture this was 0.54% (pre-DEXA FRAX) and 0.77% (post-DEXA FRAX) ( $p = 0.5$ ). The pre-DEXA FRAX score was a significant predictor of the post-DEXA FRAX treatment recommendation ( $p = < 0.001$ ). TDF therapy was associated with increased sALP after 12-months, but this was not significant. No change was observed in pre-treatment sCa and sPO levels compared to those after 12-months exposure ( $p = 0.5$  &  $0.09$  respectively).

**Conclusion** Our results demonstrate the FRAX score alone can accurately predict the risk of developing an osteoporotic fracture in TDF treated CHB patients. This potentially obviates the need for DEXA scanning and the associated costs. The relationship between sALP and TDF is noteworthy, but bone parameters are of limited use in predicting BMD changes. Although BMD loss in TDF treated CHB patients remains unproven, we demonstrate the use of the FRAX score may determine those at risk of osteoporotic fractures in CHB.

**Disclosure of Interest** None Declared.

#### PWE-145 RESTROSPECTIVE REVIEW OF HEPATITIS B DATABASE

doi:10.1136/gutjnl-2013-304907.433

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**Introduction** Chronic Hepatitis B Virus (HBV) affects 350 million people worldwide with potential serious consequences. The aim of this study was to measure adherence at Sandwell and West Birmingham Hospitals (SWBH) NHS Trust to recent guidance regarding HBV assessment and treatment.

**Methods** A retrospective review of the SWBH HBV database (2003–2012) was undertaken. On the basis of European Association for the Study of the Liver (EASL) guidance, attainment of the following outcomes (standard 100%) was calculated: ALT measurement, liver ultrasound (US) examination, HBV DNA measurement, HIV testing, further liver assessment where indicated (using biopsy or Fibroscan) and use of antiviral therapy where indicated.

**Results** 322 patients with HBV were identified. Attainment of the EASL standards were as follows: ALT measurement 92%, liver US examination 80%, HBV DNA measurement 95%, HIV testing 72%, further liver assessment where indicated 82% and use of antiviral therapy where indicated 100%.

**Conclusion** In general patients were managed according to EASL guidance. Liver US examination was not 100% mainly because patients failed to attend their appointment. HIV testing was not 100% as routine testing in HBV patients was introduced only in 2008. Further liver assessment with biopsy was deferred in a number of cases after discussion between patient and physician; recent acquisition of a Fibroscan at SWBH should increase the proportion of appropriate patients undergoing further liver assessment. It is encouraging that all patients received antiviral therapy where indicated. It is hoped that data from this review and recent acquisition of a Fibroscan at SWBH Trust will promote improved adherence to guidelines.

**Disclosure of Interest** None Declared.

#### REFERENCES

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#### PWE-146 RELAXIN IS A RENAL VASODILATOR IN EXPERIMENTAL MODELS OF CIRRHOSIS AND A POTENTIAL NOVEL THERAPY FOR HEPATORENAL SYNDROME IN HUMANS

doi:10.1136/gutjnl-2013-304907.434

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**Introduction** Hepatorenal syndrome (HRS) is a feared complication of cirrhosis with a high mortality rate and limited treatment options. The hallmark features of HRS are profound renal vasoconstriction, resulting in a functional renal failure but with normal kidney histology. The peptide hormone relaxin (RLN) mediates maternal haemodynamic adaptations to pregnancy, including increased renal blood flow (RBF) and glomerular filtration rate (GFR). We hypothesised that RLN could beneficially modulate RBF in cirrhosis and HRS.

**Methods** Cirrhosis, with reduced RBF, was induced in rats by 16 weeks of intraperitoneal (i.p.) carbon tetrachloride (CCl<sub>4</sub>) and decompensated biliary cirrhosis by 3 weeks bile duct ligation (BDL). We measured the effect of acute intravenous (i.v.) and extended (72 hr) subcutaneous (s.c.) RLN on systemic haemodynamics, RBF, GFR and organ histology. Subgroups of rats were co-treated with the nitric oxide (NO) synthase inhibitor L-NAME. Blood oxygen

dependent-magnetic resonance imaging (BOLD-MRI) was used to quantify changes in renal oxygenation. Tissue expression and distribution of RLN receptor (RXFP1) was determined by qPCR and immunofluorescence. Expression of vasoconstrictor genes was quantified by qPCR array.

**Results** RXFP1 was detected on glomerular podocytes, renal pericytes, and endothelial cells of the renal, segmental and interlobar arteries of cirrhotic rats. In CCl<sub>4</sub> cirrhosis, acute i.v. RLN (4µg) induced a 50% increase in RBF after 60 minutes ( $p < 0.01$  vs. placebo,  $n = 6$ ). BOLD-MRI showed increased tissue oxygenation at the same timepoint in renal cortex and medulla. Extended s.c. RLN increased RBF by 54% in CCl<sub>4</sub> ( $p < 0.01$  vs. placebo,  $n = 8$ ) and 57% in BDL ( $p < 0.001$  vs. placebo,  $n = 5$ ) and increased GFR by 138% in CCl<sub>4</sub> ( $p < 0.01$  vs. placebo,  $n = 8$ ) and 103% in BDL ( $p < 0.05$  vs. placebo,  $n = 5$ ). Mean arterial pressure was unaffected by RLN. L-NAME (250mg/L) orally (p.o.) abrogated the effect of RLN on RBF and GFR. The relative expression of vasoconstrictor genes in the kidney was markedly reduced by RLN treatment.

**Conclusion** RLN increases RBF in experimental cirrhosis. Crucially, RLN also improves renal function and oxygenation but does not induce systemic hypotension even in decompensated disease. The effects of RLN are mediated via augmentation of NO and downregulation of vasoconstrictor genes known to be important in the pathogenesis of HRS. RLN has potential as a treatment for HRS and further translational studies are warranted.

**Disclosure of Interest** None Declared.

#### PWE-147 HUMAN HERPESVIRUS AND ADENOVIRUS UNIQUE GENETIC SEQUENCES DETECTED IN HEPATOCELLULAR CANCER GENOMES

doi:10.1136/gutjnl-2013-304907.435

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**Introduction** Hepatitis C virus (HCV) is the most common cause of hepatocellular cancer (HCC) in the western world. HCV is an RNA virus that does not integrate with human DNA and so the oncogenic mechanisms of HCV remain unclear. Next generation sequencing (NGS) provides a flexible platform and generates large amounts of data at a relatively small time and constantly reducing costs. The role of viral infection is well established in the aetiology of a wide range of tumours. In this study we investigate DNA of HCV driven HCC for the possibility of integration of all known viral genomes.

**Methods** Bar-coded DNA libraries from 41 samples of various stages of development of HCC from 6 different patients were sequenced in parallel using NGS. One to two million 74bp reads per genome were generated. The reads were aligned to all known viral genomes downloaded from the National Center for Biotechnology Information using Burrows-Wheeler Aligner (BWA). Reads with mapping scores of  $< 37$  were discarded. Basic Local Alignment Search Tool (BLAST) was used to test if the sequences that aligned to viral genomes belonged to the human genome or any other viruses apart from the identified virus. Only those reads were the BWA alignment matched the leading BLAST hit were considered

**Results** Six test samples mapped to unique sequences from Human herpesvirus 6. The test samples included a single HCC and 5 premalignant nodules from 2 different patients. Six test samples mapped to unique sequences of Human Adenovirus (6/41). The test samples in this case included 4 HCCs and a 2 premalignant nodules from 2 different patients. A single dysplastic nodule mapped to Human papillomavirus.

**Conclusion** DNA from HCV driven HCC was searched for all viral genome sequences only Human Herpes 6, Human Adenovirus and Human papillomavirus were found in a small number of cases.

Further studies are needed to understand their relation to HCV hepatocarcinogenesis.

**Disclosure of Interest** None Declared.

#### PWE-148 HEPATOTOXICITY FROM ANABOLIC ANDROGENIC STEROIDS MARKETING AS DIETARY SUPPLEMENTS: CONTRIBUTION FROM ATP8B1/ABCB11 MUTATIONS?

doi:10.1136/gutjnl-2013-304907.436

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**Introduction** In the United Kingdom (UK) it is illegal to produce, supply, or possess androgenic anabolic steroids (AAS) with intent. Despite this, non-prescription use of AAS, often marketed as dietary supplements, persists. We encountered drug-induced liver injury (DILI) associated with use of AAS and attempted to elucidate underlying mechanisms.

**Methods** We describe two patients with cholestatic DILI following ingestion of the dietary supplement massdrol ("Celtic Dragon") containing the AAS 2a-17a-dimethyl-etiocholan-3-one,17b-ol.

**Results** Two Western European males (aged 25 and 45 years) presented to our institute between July, 2011, and March, 2012, with jaundice and intractable pruritus following use of massdrol acquired from fellow gym users. Screening found no other causes of hepatobiliary disease. Despite significant hyperbilirubinaemia (respective peaks: 614 and 229 µmol/L), peak gamma glutamyl transferase activities were within "normal range". Besides "bland" intralobular cholestasis, consistent with DILI, liver biopsy in both found deficiency of canalicular expression of the ectoenzymes neutral endopeptidase (CD10), alanyl aminopeptidase (CD13), GGT, and carcinoembryonic antigen (CD66). This suggested generalised abnormality in ectoenzyme trafficking to, or retention within, canalicular membranes, as seen in *ATP8B1* disease (familial intrahepatic cholestasis 1 [FIC1]). The younger patient showed normal expression of bile salt export pump (BSEP, encoded by *ABCB11*) and of multidrug resistance protein 3 (MDR3; encoded by *ABCB4*); in the older BSEP but not MDR3 marking was focally diminished. While this may have been due to AAS-induced inhibition of expression of normal *ATP8B1/ABCB11*, it also raised the intriguing possibility of mutation in either of these genes – in effect, that AAS exposure had triggered initial episodes of benign recurrent intrahepatic cholestasis type 1/2. On sequencing, *ATP8B1* was normal in both patients; the younger was heterozygous for the mutation c.2093G > A mutation in *ABCB11*, a known polymorphism previously encountered in association with intrahepatic cholestasis following antibiotic exposure (personal communication, R Thompson). Morbidity from cholestasis and pruritus was substantial, necessitating use of multiple antipruritic agents and consideration for extracorporeal albumin dialysis (MARS). At last follow-up, however, jaundice was resolved in both.

**Conclusion** AAS marketed as dietary supplements remain a cause of serious DILI in the UK; underlying mechanisms remain speculative but may include unmasking of genetic cholestatic syndromes.

**Disclosure of Interest** None Declared.

#### PWE-149 THE EFFICACY AND SAFETY OF TREATING HEPATITIS C IN PATIENTS WITH A DIAGNOSIS OF SCHIZOPHRENIA

doi:10.1136/gutjnl-2013-304907.437

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