51st THE INTERNATIONAL LIVER CONGRESS 2016
European Association for the Study of the Liver (EASL)
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1. Oral Presentations #GS02

General session 1 and opening ceremony - Hall 6.0
Date & Time: Thursday, 14 April 2016 - 14:05-14:20

FIVE-YEAR ON-TREATMENT SYSTEMATICALLY MONITORING OF DYNAMIC CHANGES OF LIVER STIFFNESS MEASUREMENT WITH TRANSIENT ELASTOGRAPHY COMPARED WITH PAIRED LIVER BIOPSIES IN A RANDOMIZED CONTROLLED TRIAL IN CHRONIC HEPATITIS B PATIENTS


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Background and Aims: Transient elastography is a rapid, noninvasive and reproducible method to measure liver stiffness. Liver stiffness measurement (LSM) has been shown to be a reliable tool to diagnose advanced fibrosis or liver cirrhosis in chronic hepatitis B (CHB). However, the use of LSM to monitor liver fibrosis dynamics has not been thoroughly evaluated during antiviral therapy.

Methods: Six hundred and six patients with HBV DNA ≥5 Log10 copies/mL, ALT 2–10 × ULN and compensated adult naive HBeAgpositive CHB were enrolled in a multicenter, randomized controlled trial (EFFORT Study; Sun J, et al. Hepatology. 2014; Fan R, et al. Gut. 2015), receiving telbivudine (LDT) alone or combined with adefovir (ADV) for up to 260 weeks (5 years). LSM was performed using transient elastography (FibroScan®, EchoSens, France) at the interval of 24 weeks during the 5-year antiviral treatment. Percutaneous liver biopsy was performed at baseline and week 104.

Results: Five hundred and ninety-nine of intent-to-treat population were enrolled in the analysis, among which 347 patients with qualified paired biopsies. During 5-year antiviral treatment, LSM decreased rapidly from 8.5 (2.6–49.5) kPa at baseline to 6.1 (2.2–37.4) kPa at week 24, and then decreased slowly from 6.1 (2.2–37.4) kPa at week 24–4.9 (2.3–19.6) kPa at week 260. From baseline to week 104, liver biopsy evaluation showed that the proportion of patients with no or mild necroinflammation (Knodell range 0–3) increased from 29.7% (103/347) to 77.2% (268/347), and the proportion of patients with no or mild fibrosis (Ishak range 0–2) increased from 29.1% (101/347) to 66.0% (229/347). At baseline, the AUCROC of LSM for patients with advanced fibrosis (Ishak ≥2) was 0.816. Multivariate logistic regression analysis showed that values of 24-week and 52-week LSM were independently associated with 104-week liver necroinflammation (Knodell ≤2; OR, 1.889; p = 0.014) and fibrosis (Ishak ≤2; OR, 3.002; p = 0.023), respectively.

Conclusions: The kinetics of LSM decreased during long-term antiviral therapy with bi-phase pattern, which may mainly reflect the resolution of inflammation during the first phase, and the regression of fibrosis during the second phase. Transient elastography is a useful tool for the evaluation of the change of liver inflammation and fibrosis during antiviral therapy.

2. Oral Presentations #GS13

General session 3 and awards 2 - Hall 6.0
Date & Time: Saturday, 16 April 2016 - 08:30-08:45

LEDIPASVIR/SOFOSBUVIR FOR 12 OR 24 WEEKS IS SAFE AND EFFECTIVE IN KIDNEY TRANSPLANT RECIPIENTS WITH CHRONIC GENOTYPE 1 OR 4 HCV INFECTION


1. Fondazione IRCCS Ca Granda Ospedale Maggiore Policlinico, Milan, Italy; 2. Gilead Sciences Inc., Foster City, United States; 3. Hôpital Saint Joseph, Marseille, France; 4. Medical University of Vienna, Vienna, Austria; 5. Hannover Medical School, Hannover, Germany; 6. Hôpital Cochin, Paris, France.

Background and Aims: Interferon (IFN) and ribavirin (RBV) for the treatment of chronic hepatitis C (HCV) in kidney transplant recipients is complicated by the risk of the allograft rejection and poor tolerability. We evaluated the safety and efficacy of the IFN-free, RBV-free regimen of ledipasvir/sofosbuvir (LDV/SOF) in chronic genotype (GT) 1 or 4 HCV infected kidney transplant recipients.

Methods: Kidney transplant recipients with chronic GT1 or GT4 HCV infection, treatment-naive and treatment-experienced, with or without compensated cirrhosis were randomized 1:1 at 5 sites in Europe to receive LDV/SOF (90 mg/400 mg) for 12 or 24 weeks. Randomization was stratified by HCV genotype, treatment history and presence or absence of cirrhosis. Cirrhosis was determined by liver biopsy (Metavir score = 4 or Ishak score ≥5), Fibroscan® >12.5 kPa, or Fibrotest® >0.75 and APRI >2. A pretreatment creatinine clearance <40 mL/min was an exclusionary criterion. The primary endpoint was SVR12.

Results: 114 patients were randomized and treated; median age was 53, 58% were male, 94% were white, 72% carried the non-C non-G IL28B allele, 91% had genotype 1 infection, 69% were treatment-naive, and 15% had compensated cirrhosis. The median eGFR was 56 mL/min (range 35–135 mL/min). All 92 patients with SVR4 data available achieved SVR4 including a patient discontinuing treatment at Week 4 due to an AE. SAEs were reported in 12 (11%) patients; 3 were assessed as treatment related: syncope, pulmonary embolism, and blood creatinine increased. The most frequent AEs were headache (19%), asthenia (13%), and fatigue (10%).

Conclusions: Administration of LDV/SOF for 12 or 24 weeks in patients with chronic HCV genotype 1 or 4 patients who have undergone kidney transplant was safe and highly effective with an SVR4 rate of 100%. Treatment was well-tolerated. SVR12 data for all patients will be presented.

3. Oral Presentations #GS15

General session 3 and awards 2 - Hall 6.0
Date & Time: Saturday, 16 April 2016 - 09:00-09:15

A MULTICENTRE, PHASE II, OPEN-LABEL, RANDOMISED CONTROLLED TRIAL OF REPEATED AUTOLOGOUS INFUSIONS OF GRANULOCYTE COLONY STIMULATING FACTOR MOBILISED CD133 + BONE MARROW STEM CELLS IN PATIENTS WITH CIRRHOSIS

Background and Aims: Liver disease mortality and morbidity are rising and liver transplantation is limited by organ availability. Small scale human studies showed that autologous stem cell therapy whilst safe and readily available needed a well conducted randomized controlled trial.

Methods: Patients with liver cirrhosis and MELD score 11.5–15.5 were randomised to Arm 1 – Conservative management; Arm 2 – Treatment with granulocyte colony stimulating factor (G-CSF) (Lenograstim) 15 mcg/kg od for 5 days or Arm 3 – Treatment with G-CSF 15 mcg/kg od for 5 days followed by leukapheresis, CD133+ cell isolation and infusion of freshly isolated CD133+ cells immediately and frozen doses at days 30/60 via peripheral vein (0.2 ± 106 cells/kg). Co-primary objectives were to determine if the severity of liver disease (change in MELD) at 3 months, and its trend over time, across Arms. To detect a 0.8 point reduction in MELD with a 2–sided α = 5% (α = 0.1 split equally) and 80% power required 27 participants per Arm (81 in total). Analyses were performed on a modified intention-to-treat basis.

Results: Mean (SD) age was 55 (8.8) years, 53 were male, 37 had alcohol related liver disease and 10 had HCV. One patient withdrew from Arm 1 (day 30) and two from Arm 3 (day 8 and 98). 19 (68%) Arm 3 and 27 (96%) Arm 1 withdrew fully from alcohol related treatment. 27 (96%) Arm 3 and 19 (68%) Arm 1 withdrew from alcohol related treatment. There was no evidence of a difference in change in MELD for the control, GCSF, and GCSF + LS treatments (F(2, 69) = 0.197; p = 0.826). Similarly, liver stiffness decreased similarly in patients with and without CSPH at BL (ρ = 0.529; p < 0.001), and without (BL: 14.4 ± 1.13 kPa vs. FU: 10.4 ± 0.857 kPa; p = 0.004). There was a statistically significant correlation between the relative changes in LS and HVPG (p = 0.448; p = 0.002). Importantly, subgroup analysis revealed a strong correlation among patients without CSPH at BL (p = 0.728; p = 0.003), while there was only a weak correlation in the subgroup of patients with BL CSPH (p = 0.398; p = 0.024).

Conclusions: Viral suppression by IFN-free therapies ameliorates portal hypertension, both in patients with CSPH, and without. In patients with BL CSPH, the observed improvements in liver stiffness do not adequately mirror the evolution of portal pressure, which drives the development of complications. Thus, in this subgroup of patients, the prognostic value of improvements in liver stiffness is questionable. The results will be updated to include more than 60 patients.

4. Oral Presentations #PS005

Parallel session: Viral hepatitis C (1) - Hall 6.0

THE EVOLUTION OF PORTAL PRESSURE AFTER VIRAL SUPPRESSION WITH INTERFERON-FREE THERAPIES AND ITS CORRELATION WITH THE CHANGE IN LIVER STIFFNESS

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Background and Aims: Monitoring the regression of liver disease after HCV eradication will be one of the main challenges in the post-HCV era, as it is fundamental for risk stratification and personalized treatment. We aimed to investigate the effect of viral suppression with interferon (IFN)-free therapies on portal hypertension, assessed by hepatic venous pressure gradient measurement (HVPG). Moreover, we investigated whether the change in liver stiffness (LS) mirrors the evolution of portal pressure.

Methods: Forty-nine patients with portal hypertension (HVPG ≥ 6 mmHg) who achieved a sustained virologic response to IFN-free therapies underwent simultaneous HVPG and LS measurement before (baseline [BL]) and after (follow-up [FU]) viral suppression. Clinically significant portal hypertension (CSPH) was defined by a HVPG ≥ 10 mmHg.

Results: Viral suppression by IFN-free therapies significantly decreased HVPG (BL: 13.2 ± 0.794 vs. FU: 10.6 ± 0.834 mmHg [see figure panel A]; −2.57 ± 0.394 mmHg [see figure panel B]; p < 0.001), both in patients with BL CSPH (n = 34; BL: 15.8 ± 0.791 vs. FU: 13.0 ± 0.922 mmHg; −2.76 ± 0.529 mmHg; p < 0.001), and without (n = 15; BL: 7.27 ± 0.33 vs. FU: 5.13 ± 0.413 mmHg; −2.13 ± 0.477 mmHg; p < 0.001). HVPG normalized (<6 mmHg) in 60% (9/15) of patients with a BL HVPG of 6–9 mmHg and none progressed to CSPH. Among patients with CSPH at BL, a HVPG decrease ≥10% was observed in 62% (21/34). A decrease ≥20% or to ≤12 mmHg was observed in 54% (14/26) of patients with a BL HVPG ≥12 mmHg. Similarly, liver stiffness decreased both in patients with CSPH (BL: 34.4 ± 3.14 vs. FU: 28.6 ± 3.35 kPa; −5.82 ± 1.68 kPa; p = 0.002) and without (BL: 14.4 ± 1.13 kPa vs. FU: 10.4 ± 0.857 kPa; −3.99 ± 1.16 kPa; p = 0.004). There was a statistically significant correlation between the relative changes in LS and HVPG (p = 0.448; p = 0.002). Importantly, subgroup analysis revealed a strong correlation among patients without CSPH at BL (p = 0.728; p = 0.003), while there was only a weak correlation in the subgroup of patients with BL CSPH (p = 0.398; p = 0.024).

Conclusions: Viral suppression by IFN-free therapies ameliorates portal hypertension, both in patients with CSPH, and without. In patients with BL CSPH, the observed improvements in liver stiffness do not adequately mirror the evolution of portal pressure, which drives the development of complications. Thus, in this subgroup of patients, the prognostic value of improvements in liver stiffness is questionable. The results will be updated to include more than 60 patients.

5. Oral Presentations #PS0075

Parallel Session: Alcoholic liver disease and drug induced liver disease - Hall 8.0-D2

Date & Time: Friday, 15 April 2016 - 16:30-16:45

DRAMATIC ALTERATIONS OF ANTI-BACTERIAL MAIT-CELL NETWORK IN ALCOHOLIC LIVER DISEASE


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6. National Institute for Health Research (NIHR) Birmingham Liver Biomedical Research Unit and Centre for Liver Research;
7. University of Birmingham, Birmingham;
Background and Aims: Dysbiosis, impaired gut barrier and systemic distribution of bacterial products are key in the immunopathogenesis of ALD, yet the links with intestinal immunity remain elusive. Mucosal associated invariant T cells (MAIT) are innate-like T cells that respond to bacterial metabolites and recirculate between blood, intestinal mucosa and liver. They control gut flora homeostasis and play key roles in antibacterial defences. We previously described a dramatic depletion of MAIT in ALD patients and here we aimed to elucidate the mechanisms that drive this.

Methods: We investigated if peripheral MAIT depletion was due to bacterial antigen overload, alcohol, gut microbiota or MAIT relocation to the liver or intestine in acute alcoholic hepatitis patients — AAH, alcohol cirrhosis — AC, long-term alcohol abusers undergoing alcohol withdrawal, non-alcohol cirrhosis — nAC, and healthy controls. We measured (a) frequency, activation (CD69/HLA-DR) and inhibitory status (PD1/TIM3/LAG3) of MAIT (CD161+/Vα7.2+ CD8 T cells); (b) frequency and inhibitory status (PD1/PDL1/TIM3/ Gal9) of MAIT-presenting cells — MPC; (c) E.coli-induced cytokine and cytotoxicity profiles (IFNy/TNFa/IL17; GranzymeB/Perforin/CD107a). We also examined direct impact of ethanol (EtoH, 50–100–250 mM), fixed crude stool bacteria and antigenic hyperstimulation. MAIT in colon mucosa were detected by Vα7.2-specific RT-PCR and intrahepatic MAIT by immunohistochemistry.

Results: In ALD patients, peripheral MAIT were dramatically depleted, activated and hyperexpressed immunoinhibitory markers. They had weak cytokine responses to E.coli, notably different between AAH and AC. MAIT/MPC alterations correlated with severity of liver damage, measured by FibroScan E and CAP scores. Peripheral MAIT were not depleted by antigen-induced apoptosis nor by direct EtoH effects, as neither in-vitro exposure to increasing amounts of EtoH nor EtoH withdrawal in-vivo induced changes; moreover, similar alterations were also observed in a small group of nAC. ALD stool bacteria induced MAIT alterations, and we observed accumulation of intrahepatic MAIT in ALD patients.

Conclusions: ALD is accompanied by dramatic alterations of the peripheral MAIT network, in correlation with severity of liver damage. MAIT relocation from the periphery to the liver occurs during ALD, and gut flora composition seems to drive functional changes. MAIT reactivation via modulation of the gut flora may be a promising immunotherapeutic target for ALD to restore a competent host immunity.

6. Oral Presentations #PS081
Parallel Session: Non-invasive tests for evaluation of liver disease severity and prognosis - Hall 8.0-B3
Date & Time: Friday, 15 April 2016 - 16:00-16:15
EASL-ALEH GUIDELINES FOR THE NON-INVASIVE EVALUATION OF LIVER DISEASE SEVERITY IN CHRONIC HEPATITIS B: AN INDEPENDENT VALIDATION

Background and Aims: Various non-invasive methods (elastography and serum biomarkers) have been evaluated in chronic hepatitis B, but none of them have been fully validated for the assessment of liver fibrosis. The recently issued EASL-ALEH 2015 guidelines provide detailed algorithms based on liver stiffness (LS) values and ALT serum levels. The aim of our study was to validate the diagnostic accuracy of these algorithms.

Methods: Four hundred and thirteen (413) patients from 3 centers were prospectively included. All were HBsAg carriers, had available liver biopsy, LS, HBV DNA and ALT serum levels within the 3 months of the liver biopsy. Fibrosis stage was assessed using the METAVIR scoring system (F0–F4). The overall diagnostic value was expressed with AUROCs given with 95% confidence intervals (95% CI) for the diagnostic targets: F ≥ 2 and F ≥ 3. For each diagnostic target optimal cut-offs were determined according to the Youden method. The study was performed cross-sectionally on 142 patients with NAFLD (identified by liver biopsy, mean body mass index, 28.1 kg/m2) and ten control subjects. All study subjects were evaluated by 5 different clinical scoring systems including the FIB4 index, NAFLD fibrosis score (NFS), aspartate aminotransferase (AST) to platelet ratio index (APRI), AST-to-alanine transaminase (ALT) ratio (AAR), and BARD score, TE with the M probe and MRI using the MRE (Figure 1) and PDDF techniques.
Results: Among these clinical scoring systems, the FIB4 index had the highest diagnostic performance to assess liver fibrosis. FIB4 index or TE identified patients with fibrosis stage ≥1, ≥2, ≥3 and ≥4 with an area under the receiver operating characteristic (AUROC) curve value of 0.80 or 0.78, 0.83 or 0.82, 0.86 or 0.88 and 0.88 or 0.92, respectively, whereas MRE identified these patients with an AUROC curve value of 0.80, 0.89, 0.89 and 0.97, respectively. TE-based CAP measurements identified patients with hepatic steatosis grade ≥1, ≥2 and ≥3 with an AUROC curve value of 0.88, 0.73 and 0.70, respectively, whereas PDFF methods identified them with an AUROC curve value of 0.99, 0.90 and 0.79, respectively.

Conclusions: MRE had high diagnostic accuracy in the assessment of each liver fibrosis stage relative to all clinical scoring systems and TE, and was significantly superior to the clinical scoring systems and TE in the diagnosis of the fibrosis stage. In addition, PDFF was significantly superior to CAP in the diagnosis of each steatosis grade. MRI-based noninvasive assessment of liver fibrosis and steatosis is a promising alternative to liver biopsy in clinical practice.

8. Oral Presentations #PS083
Parallel Session: Non-invasive tests for evaluation of liver disease severity and prognosis - Hall 8.0-B3
Date & Time: Friday, 15 April 2016 - 16:30-16:45

COMPARISON OF CLASSICAL AND NOVEL RELIABILITY CRITERIA FOR ACCURACY OF TRANSIENT ELASTOGRAPHY IN A MULTICENTER PROSPECTIVE COHORT OF PATIENTS WITH VIRAL HEPATITIS AND GOOD QUALITY LIVER BIOPSIES
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Background and Aims: Reliability of liver stiffness evaluation (LSE) results is a critical issue as transient elastography (TE) is now the first line tool for liver fibrosis assessment and prioritization of antiviral treatment. Recently, it has been suggested that the classical reliability criteria (≥10 valid measurements, success rate >60%, and interquartile range/median (IQR/M) ≤ 0.30) were not optimal and novel criteria (“poorly reliable” IQR/M > 0.30 with LSE median >7.1 kPa, “reliable” 0.10 < IQR/M ≤ 0.30 or IQR/M > 0.30 with LSE median ≤7.1 kPa and “very reliable” IQR ≤ 0.10) have been proposed but not validated independently. The aim of this study was to compare both reliability criteria for accuracy of liver fibrosis staging.

Methods: 1170 patients (mean age 48 ± 4 yrs; male 65%) with chronic viral hepatitis (HCV 75% HBV 25%) enrolled in a multicenter prospective study (FIBROSTIC) who underwent TE and liver biopsy (≥15 mm) within <3 months (94% same day) were studied. Accuracy of LSE results was evaluated as the percentage of well classified patients (FFS ≥ 3: ≥7.5 kPa) and cirrhosis (FFS4: ≥12.5 kPa), taking liver biopsy for significant fibrosis (FFS ≥ 2: ≥7.1 kPa), severe fibrosis (FFS ≥ 3: ≥9.5 kPa) and cirrhosis (FFS4: ≥12.5 kPa), taking liver biopsy as reference.

Results: Distribution of histological stages (METAIVIR) on liver biopsy was Fibrosis FM ≥ 2 55%, FM ≥ 3 26%, FM4 11%, and median liver stiffness was 6.9 kPa (5.3–10.1). LSE were considered unreliable in 21% (classical criteria), and poorly reliable, reliable, and very reliable in 8%, 72% and 20%, respectively (novel criteria). The rates of well classified patients according to the different reliability criteria are given in the table. The accuracy for FFS ≥ 3 and FFS4 ≥ 12.5 kPa was significantly increased.

Conclusions: Our results suggest that IQR/M ≤ 0.30 is the most important reliability criteria increasing accuracy of transient elastography for diagnosing severe fibrosis and cirrhosis in patients with viral hepatitis. IQR/M ≤ 0.30 is simpler than previously proposed criteria and could be used in clinical practice to prioritize these patients for antiviral treatment.

9. Oral Presentations #PS084
Parallel Session: Non-invasive tests for evaluation of liver disease severity and prognosis - Hall 8.0-B3
Date & Time: Friday, 15 April 2016 - 16:45-17:00

LIVER FIBROSIS EVALUATION USING REAL-TIME SHEARWAVE ELASTOGRAPHY: APPLICATION, ASSOCIATION WITH ACTIVITY AND STEATOSIS, AND DIAGNOSTIC PERFORMANCE. DIRECT COMPARISONS WITH TRANSIENT ELASTOGRAPHY USING BIOMARKERS AS REFERENCES
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Background and Aims: Real-time shear wave elastography (2D-SWE) is a two-dimensional transient elastography and a competitor as a biomarker of liver fibrosis in comparison with the standard reference transient elastography (TE). Unmet needs were the definition of applicability criteria (failure and reliability) for results’ interpretation and assessments of the impact of inflammation [necroinflammatory activity (A) and steatosis (S)] on elasticity. The aims were in a large population to compare several criteria of applicability recently published, and to assess A and S impact on elasticity values.

Methods: We took FibroTest as a reference to compare the strength of concordance (Lin concordance coefficient [LCC]) with fibrosis severity, between 2D-SWE, TE by M probe (TE-M) and by XL probe (TE-XL) after standardization of the different estimates. Validated ActiTest and SteatoTest were used as quantitative estimates of A and S severity, in order to assess their impact on elasticity independently of fibrosis severity presumed by FibroTest.

Results: A total of 2251 patients (pts) were included (37% CHC, 22% CHB, 27% NAFLD, 4% ALD, 9% Others). We validated the predetermined 0.2 kPa cut-off as too low minimal elasticity value identifying not-reliable 2D-SWE results (LCC with FibroTest = 0.0281 [-0.119; 0.175]). We were not able to identify discriminating cutoffs using variation-coefficient, BMI and depth of measures. The applicability of 2D-SWE (89.6%; 95%CI (88.2–90.8)) was significantly higher than that of TE-M (85.6%; 84.0–87.0) and not different than that of TE-XL (88.2%; 86.8–89). In pts with nonadvanced fibrosis (METAIVIR F0/F1/F2), elasticity estimated by 2D-SWE was less impacted (LCC) by A and S than elasticity estimated by TEM: 0.039 (0.021; 0.058) vs. 0.090 (0.068; 0.112; p < 0.01) and 0.105 (0.068; 0.143) vs. 0.192 (0.153; 0.230; p < 0.01) respectively. The curve fitting, the univariate and the multivariate analyses clearly demonstrated that A and S increased elasticity, but A increased more elasticity value than S, whatever the elastography method or the S measure evaluated for the first time by two non-invasive tests (SteatoTest or CAP), (A vs p-values <0.01).

Conclusions: 2D-SWE had a higher applicability than TE-M the reference elastography, with less impact of necro-inflammatory activity and steatosis especially in pts with non-advanced fibrosis, as presumed by blood tests. Elasticity results including very low minimal signal in the region of interest should be considered as not reliable.
FIBROSCAN IMPROVES THE ABILITY OF THE NEW PROGNOSTIC SCORING SYSTEMS TO PREDICT OUTCOMES OF PBC

Background and Aims: Despite ursodeoxycholic acid (UDCA) therapy, the course of primary biliary cholangitis (PBC) remains variable and a significant proportion of patients still experiences unfavorable outcomes. Several prognostic markers, including biochemical response to UDCA and liver stiffness measurement (LSM), have shown significant ability to recognize patients in need for second-line therapies. Recently, two high-performance scoring systems, namely the Globe and UK-PBC risk scores, were shown to improve risk stratification. The additive value of LSM relative to these new prognostic scores remains unknown.

Methods: All PBC patients from a single referral center with at least one valid LSM and a subsequent follow-up ≥6 months were included in a longitudinal retrospective study. LSM was obtained using transient elastography (Fibroscan, Paris). The Globe, UK-PBC risk score, and biochemical response to UDCA (Paris-I) were determined at the time of LSM. The endpoint was death, liver transplantation or occurrence of a cirrhotic complication. Risk factors were assessed using Cox proportional hazards models. The predictive performances of the models were compared using the Harrell’s C statistic and net reclassification improvement (NRI).

Results: 200 patients (179 women; median age: 57 years) treated with UDCA (13–15 mg/kg/d) and followed-up for up to 11 years (median: 5.5 years) were included. Median LSM at entry was 7.2 kPa (range, 3.1–69.1 kPa). Twenty nine percent of patients had severe fibrosis or cirrhosis and 24% had a suboptimal response to UDCA. The endpoint was reached in 25 (12.5%) patients. LSM, Globe score, UK-PBC risk score, and Paris-I response were all associated with outcomes in univariate models. C-statistics for those models were 0.90, 0.90, 0.86, and 0.82, respectively. LSM provided an additive independent prognostic value to all scoring systems. A model derived from the Globe score and a log transformation of LSM (called LSM Globe score) showed a significantly higher predictive performance than the Globe score alone, mainly due to a better concordance for non-event patients (C-statistic = 0.93; NRI = 1 1%; p = 0.008). The optimal predictive cutoff for this score was associated with a 124-fold increased risk of events (95% CI: 28.4–542.0; p < 0.1e-6; Figure).

Conclusions: LSM significantly improves the risk stratification of PBC independently of the newly established prognostic scores. LSM should be added to the decision algorithm for second-line therapy in PBC.

REAL-WORLD VALIDATION OF BAVENO VI RECOMMENDATIONS FOR SCREENING ENDOSCOPY IN PATIENTS WITH COMPENSATED ADVANCED CHRONIC LIVER DISEASE

Background and Aims: The recent Baveno VI consensus recommends that patients with a liver stiffness measurement (LSM) <20 kPa and a platelet count>150,000 have a very low risk of large varices and can safely avoid screening endoscopy. We sought to validate these recommendations in a real-world cohort of patients with compensated advanced chronic liver disease (cACLd) to determine the accuracy of these recommendations for exclusion of large varices.

Methods: We performed a retrospective analysis to identify cACLd patients (defined by LSM >12 kPa) who underwent screening gastroscopy for assessment of varices within one year of LSM. The primary outcome was the specificity and positive predictive value (PPV) of the Baveno VI recommendations for exclusion of large varices in a real-world setting.

Results: Of a total of 2748 patients who underwent LSM from 2006 to 2012 in our center, we identified 579 with LSM >12 kPa. Mean age was 56 ± 12 years, 62% were males, 55% had viral etiology of cACLd and mean LSM was 23.5 ± 13.9 kPa. Of these, 173 (30%) had screening gastroscopy performed within one year of LSM. Varices were present in 54 (31.2%) of which 14 (26%) had large varices that
required treatment. Application of the Baveno VI recommendations to this real-world cohort identified 34 patients for which screening endoscopy could be avoided. Of these, large varices would be missed in three (1.7%). Of the remaining 139 who would have undergone screening endoscopy, large varices would be identified in 11 (7.9%). In comparison, performing screening endoscopy on all patients with LSM >12 kPa would have detected large varices in 14/173 (8.1%). Baveno VI criteria had a specificity of 78.6% to predict absence of large varices with a PPV of 91.2%.

**Conclusions:** Application of Baveno VI recommendations in a real-world setting can lead to avoidance of screening endoscopy in 20% of cAHLD patients with a <2% risk of missing large varices, without any significant reduction in detection rate of large varices.

12. Oral Presentations #PS088

**Parallel Session: Non-invasive tests for evaluation of liver disease severity and prognosis - Hall 8.0-B3**

**Date & Time:** Friday, 15 April 2016 - 17:45-18:00

**NEW RECOMMENDATIONS OF BAVENO VI CONFERENCE FOR THE SCREENING OF PORTAL HYPERTENSION: AN INDEPENDENT SEQUENTIAL VALIDATION IN PATIENTS WITH COMPENSATED VIRAL CIRRHOSIS TAKING INTO ACCOUNT VIROLOGICAL STATUS (ANRS CO12 CIRVIR COHORT)**


1. APHP, Paris;
2. CHU Toulouse, Toulouse;
3. APHP, Bondy;
4. ANRS, Paris;
5. APHP, Clichy;
6. CHU Nantes, Nantes;
7. CHU Montpellier, Montpellier;
8. CHU Lyon, Lyon;
9. APHP, Bobigny;
10. CHU Bordeaux, Bordeaux;
11. CH St Laurent du Var, St laurent du Var;
12. CHU Nice, Nice;
13. CH Nancy, Nancy;
14. CHU Rouen, Rouen;
15. CHU Angers, Angers;
16. CH Marseille, Marseille;
17. CHU Lille, Lille;
18. CHU Grenoble, Grenoble;
19. APHP, Créteil, France;

**Background and Aims:** The early detection of cirrhosis by noninvasive methods, and the cure of viral cirrhosis by new antiviral drugs, lead to a decrease of portal hypertension (PHT)-related events in patients with compensated cirrhosis. Hence, recommendations for the screening of esophageal varices (EV) have been revised recently (Baveno VI conference). Patients with liver stiffness (LS) <20 kPa and EV or a PHT followed in inclusion, and (4) endoscopic procedure at inclusion and at least once during follow-up, (3) LS <20 kPa and plt >150,000 at follow-up, which occurred in 4/6 (66.7%) of patients with progression of PHT vs 49/150 (32.7%) of patients without progression.

**Conclusions:** In patients with compensated viral cirrhosis, endoscopic screening can be avoided when plt >150,000 and LS <20 kPa (20% of patients). A decrease in plt or increase in LS during follow-up should prompt endoscopic screening even when virosuppression is obtained.

13. Oral Presentations #PS107

**Parallel session: Fatty liver disease: Clinical Hall 8.0-A1**

**Date & Time:** Friday, 15 April 2016 - 12:00-12:15

**ENDOTOXAEMIA IS ASSOCIATED WITH HISTOLOGICAL SEVERITY OF NON-ALCOHOLIC FATTY LIVER DISEASE AND MAY BE INCREASED IN PATIENTS WITH THE TM6SF2 GENE VARIANTS**


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3. Department of Anatomical and Cellular Pathology, The Chinese University of Hong Kong, Hong Kong, Hong Kong, China

**Background and Aims:** Patients with non-alcoholic steatohepatitis (NASH) have gut dysbiosis and intestinal bacterial overgrowth. We aimed to test the hypothesis that endotoxaemia was associated with the histological severity of non-alcoholic fatty liver disease (NAFLD) and to determine factors associated with endotoxaemia.

**Methods:** The endotoxaemia markers lipopolysaccharide-binding protein (LBP; Hycult Biotech, Uden, the Netherlands) and endotoxin levels (QCL-1000 Limulus Amebocyte Lysate Endpoint Assay; Lonza, NJ) were measured in 237 NAFLD patients within 1 day before liver biopsy (age 51 ± 11, 129 [54%] males, body mass index 28.0 ± 4.2 kg/m2). Serum cytokerin-18 fragments, aspartate aminotransferase-to-alanine aminotransferase (AST/ALT) ratio and liver stiffness measurement by transient elastography were additional markers of disease severity.

**Results:** 114 (48%) patients had NASH and 80 (34%) had F2-F4 fibrosis. LBP correlated with the degree of lobular inflammation (p = 0.001), while both LBP (p = 0.0004) and endotoxin levels (p = 0.008) correlated with fibrosis. LBP also correlated with cytokerin-18 fragments (p = 0.002) and AST/ALT ratio (p = 0.006), and both LBP (p = 0.019) and endotoxin (p = 0.006) correlated with liver stiffness. LBP was increased in patients with NASH (15.3 ± 4.6 vs. 13.8 ± 3.3 μg/mL; p = 0.005) and F2-F4 fibrosis (15.4 ± 4.4 vs.14.0 ± 3.7 μg/mL; p = 0.008).

**Conclusions:** Endotoxaemia is associated with NASH and significant fibrosis. The association between TM6SF2 variants and high LBP level warrants further investigations. The findings may shed light
on the pathogenesis of NASH and inform a novel treatment target. (This project was supported by a grant from the Food and Health Bureau of the Hong Kong SAR Government [Ref 11120621]).

**14. Oral Presentations #PS127**

**Parallel session: Autoimmune and hepato biliary disease Hall 8.0-D2**

**Date & Time:** Saturday, 16 April 2016 - 13:00-13:15

**FIBROSCAN AND MRI HAVE COMPLEMENTARY PROGNOSTIC VALUES IN PRIMARY SCLEROSING CHOLANGITIS**

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2. Inserm UMR_S938, Université Pierre et Marie Curie;
3. Service d’Imagerie Médicale, Hôpital Saint-Antoine, APHP, Paris, France

**Background and Aims:** was significantly associated with clinical outcomes. The aim of the present study was to assess the complementary values of MRI and LSM in assessing prognosis of PSC.

**Methods:** All PSC patients from a single center with a valid LSM by Fibroscan (Echosens, Paris) and a MRI within a 6-month interval or less were included in a longitudinal retrospective study. Exclusion criteria consisted of decompensated cirrhosis, primary liver cancer, severe stricture of common bile duct, acute cholangitis, autoimmune hepatitis overlap syndrome, and small-duct PSC. MRI risk score without gadolinium administration included the following features: dilatation of intrahepatic bile ducts, hepatic dysmorphy, and portal hypertension. Death, liver transplantation, cirrhotic complications, acute cholangitis, and primary liver cancer were used as a composite endpoint. Individual and combined prognostic values of LSM and MRI risk score were assessed qualitatively and quantitatively using Cox proportional hazards models. Optimal cutoffs were defined by the Youden’s index. Survival rates were assessed using the Kaplan-Meier method.

**Results:** 80 patients (68% men; mean age: 39 years; 82% IBD) followed-up for up to 8.4 years (mean: 3.9 years) were included. All were treated with ursodeoxycholic acid. The mean LSM at entry was 13.2 kPa (range: 3.9–73.5 kPa). The mean MRI risk score at entry was 2.3 (range: 0–5). LSM and MRI risk score were significantly correlated (p < .0001) and individually associated with clinical outcomes (p < .001 and p < .05, respectively). Optimal prognostic thresholds were 8.1 kPa for LSM and 3 for MRI risk score (Hazard Ratios: 2.8 and 3.5, respectively; p < .05). Qualitative and quantitative (LSM-MRI risk score) combinations of the 2 parameters increased the performance of the models (HR for LSM-MRI risk score ≥ 1.1: 4.8; p = .004; Figure). The incidence of adverse outcomes according to LSM and MRI risk score at entry was 7% (LSM < 8.1 kPa and MRI risk score <3), 29%

**Conclusions:** Combination of Fibroscan and MRI improves the stratification of PSC patients into low and high-risk groups for adverse outcomes.
1. Poster (#LBP502)

**Late breakers: Posters - Hall 6.0**

**Date & Time:** Thursday, 14 - Saturday 16 April 2016 - 16:00 - 18:00

**APPLICABILITY, RELIABILITY AND DIAGNOSTIC PERFORMANCE OF FIBROSCAN FOR LIVER EVALUATION IN SEVERE OBESE PATIENTS CANDIDATE TO BARIATRIC SURGERY**

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**Introduction:** The XL probe of FibroScan was recently developed to render liver stiffness measurements (LSM) in overweight patients. This study aims to assess the FibroScan applicability, reliability and diagnostic performances in severe obese patients’ candidates for bariatric surgery.

**Material and Methods:** 132 severe obese patients candidates for bariatric surgery having a FibroScan examination before the surgery were prospectively recruited. Per-operative liver biopsy samples were collected during surgery. CAP values were computed retrospectively on the raw data stored in the examination files. For patients with a skin-to-capsula distance (SCD) ≥ 35 mm, LSM was reprocessed deeper (45 ~ 80 mm) to adapt the LSM to the patient’s morphology. FibroScan applicability (feasible with at least 10 valid measurements) and reliability according to Boursier’s criteria (IQR/LSM ≤ 30% if LSM > 7.1 kPa) was evaluated. Diagnostic performance was assessed using area under the ROC curve (AUC).

**Results:** Patients were for 77% female with a median [IQR] age of 41 [17] years and a BMI of 43.0 [8.2] kg/m². 73% of patients had at least minimal fibrosis, 8% at least severe fibrosis and 2% advanced fibrosis or cirrhosis. 70% had steatosis, 5% NASH, 12% no liver lesions. 130 patients had a FibroScan feasible, giving to the examination a 98% applicability in severe obese patients in our center. 10 patients (8%) were measured using the MProbe.120 (92%) using the XL probe. LSM was reliable 92% of the patients. Patients with unreliable LSM had a significantly higher BMI than patients with reliable examination (48.0 [7.7] vs 42.7 [9.9] kg/m², p = 0.02). AUROC for LSM for the detection of F ≥ 2 was 0.78 [0.67;0.90]. When reprocessing the data for patients with a SCD > 35 mm, AUROC for F ≥ 2 was 0.80 [0.68;0.92] which was significantly higher than with regular depth LSM (p = 0.04). The 3 patients with F ≥ 3 had a LSM significantly higher than in patients with F ≤ 2 (27.0 [11.3] versus 5.8 [4.1] kPa, p < 0.01). AUROC for CAP for the detection of steatosis was 0.80 [0.70;0.89].

**Conclusion:** Severe obese patients candidate to bariatric surgery with no history of liver disease have a large prevalence of liver lesions. FibroScan applicability and reliability in this type of patients is high. Its performance for the diagnosis of significant fibrosis and steatosis are good. FibroScan appears as a reliable and noninvasive tool for screening chronic liver disease severity in severe obese patients. Further studies are needed to confirm these results.

2. Poster (#LBP515)

**Late breakers: Posters - Hall 6.0**

**Date & Time:** Thursday, 14 - Saturday 16 April 2016 - 16:00 - 18:00

**PROSPECTIVE COMPARISON TO LIVER BIOPSY OF CONTROLLED ATTENUATION PARAMETER AND PROTON DENSITY FAT FRACTION FOR PREDICTING DEGREE OF STEATOSIS IN NON-ALCOHOLIC FATTY LIVER DISEASE**

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**Introduction:** Nonalcoholic fatty liver disease (NAFLD) is a global health concern that is increasing in prevalence due to the rise in obesity and diabetes mellitus. The ability to distinguish between simple steatosis and non-alcoholic steatohepatitis (NASH) is limited to histopathology. However, new imaging advances may begin to allow for non-invasive assessment of NAFLD and NASH in the near future. The purpose of this ongoing study is to assess the current prevalence and severity of NAFLD in adult subjects. Secondary endpoints include assessing the ability of novel imaging techniques to predict the degree of steatosis, inflammation and fibrosis on biopsy.

**Material and Methods:** Adult patients were prospectively enrolled predominantly at the time of referral for routine colon cancer screening. They were screened for evidence of NAFLD with FibroScan®, LiverMultiScan (LMS), and MR elastography (MRE). A prior history of liver disease or alcohol ingestion greater than the accepted range for NAFLD was considered exclusionary. Patients exceeding pre-specified cutoff values on any imaging test were offered liver biopsy. Liver biopsies were read by an expert pathologist using the Brunt criteria. The presence of and the histological grade of steatosis on biopsy was compared to controlled attenuation parameter (CAP) on FibroScan® and proton density fat fraction (PDDF) using LMS. Similarly, fibrosis stage was compared with FibroScan® elastography measurements vs that from MRE.

**Results:** To date, 293 participants have been enrolled, of which 222 had results available for interim analysis, and 43 have completed biopsy. There was a mean PDDF of 4.12%, 9.22%, and 16.9% for grade 0, 1, and 2 respectively. Those who did not qualify for biopsy had an average PDDF of 2.29%. All four groups were found to be significantly different in PDDF % (all p values were significant; Fig. 1). PDDF was found to be sensitive to identification of steatosis (≥5%) with an AUC of 0.932. Similarly, there was a mean CAP of 264.5 dB/m, 315.7 dB/m, 369.3 dB/m for grade 0, 1, and 2 steatosis. The comparisons between grades were significant (p < 0.05; AUC 0.85). CAP values of <240 dB/m excluded steatosis with a sensitivity of 97.3% and a CAP of >350 dB/m confirmed a diagnosis of NAFLD with a specificity of 100% as measured by PDDF.

**Conclusion:** Both CAP and PDDF are valid methods for predicting the grade of hepatic steatosis in NAFLD patients.
STRATIFYING THE RISK OF HEPATOCELLULAR CARCINOMA IN CIRRHOTIC PATIENTS USING LIVER STIFFNESS MEASUREMENT BY FIBROSCAN – A MULTICENTRE STUDY

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Background and Aims: Liver stiffness measurements (LSM) by transient elastography (FibroScan™) are well validated and integrated into clinical practice. Manufacturer guidelines are clear with respect to cut-off values for different stages of fibrosis, but there are limited data on the significance of LSM in the upper extreme end of the measurable spectrum. The aim of this study was to evaluate the risk of HCC in patients with liver stiffness ≥20 kPa.

Methods: Four hundred thirty-two patients (n = 432) with LSM ≥20 kPa were identified for follow-up in London, UK (n = 261) and Catania, Italy (n = 171) between June 2007 and October 2015. Patients were retrospectively followed-up using electronic medical records.

Results: A minimum of one year follow up was available for 278 patients (177 men, 101 women; average age 56.6, range 18–84). Baseline FibroScan™ readings ranged from 20.0–75.0 kPa (mean 34.6 kPa). HCC developed in 41 patients over a maximum follow-up period of 3 years, with cumulative HCC rates of 19, 30, and 41 at 1, 2 and 3 years respectively. These patients had higher mean age (p = 0.003), higher mean LSM (p = 0.005) and were associated with viral aetiology (p = 0.007). Patients were divided into 4 groups based on their LSM at entry: 20–25 kPa (n = 74); 25–30 kPa (n = 62); 30–40 kPa (n = 75); >40 kPa (n = 67). Multivariate hazards analysis showed that HCC risk rose with LSM. Compared to the 20–25 kPa group, already at significant risk of HCC, the 30–40 kPa group had a HR of 3.0 (95% CI, 1.1–8.3; p = 0.037), and the >40 kPa group had a HR of 4.8 (95% CI, 1.7–13.4; p = 0.003). Differences between the 20–25 kPa group and 25–30 kPa group were not significant.

Conclusions: This multicentre retrospective observational study shows an association between LSM at the upper extreme and HCC risk. LSM by FibroScan™allows simple, non-invasive stratification of HCC risk in cirrhotic patients. Physicians may find this beneficial as a dynamic approach to monitor HCC risk.

4. Poster (#THU-116)
Viral hepatitis: Hepatitis A, B, D, E – clinical (except therapy) - Hall 8.1
Date & Time: Thursday, April 14, 2016 - 08:00 - 18:00

HEPATITIS B DNA AND NOT QUANTITATIVE SURFACE ANTIGEN AS A PREDICTOR OF SEVERITY OF LIVER DISEASE IN UNTREATED GENOTYPE A E-ANTIGEN NEGATIVE DISEASE

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Background and Aims: Chronic hepatitis B (HBV) is a heterogenous phenotypic disease with genotypic variation in disease severity, outcome and response to treatment. Genotypes C and D have been associated with more severe disease and genotypes B and C associated with higher risk of hepatocellular carcinoma. Quantitative surface antigen level measurement (qHBsAg) is now routinely used in clinical practice.

Aim: In this cross-sectional study, we explored association between qHBsAg, ethnicity, hepatic function and fibrosis in genotype A HBV e-antigen negative (eAg-neg) patients.

Methods: We retrospectively reviewed patients at King’s College Hospital with untreated HBV genotype A eAg-neg disease and qHBsAg. Patients with liver fibrosis assessment (APRI score, King’s score, FibroScan or liver biopsy) around the time of qHBsAg testing were included. Statistical analysis was performed using SPSS v21.

Results: Since 2004, 132 (median age 36.6yrs IQR 14.3 55% female) genotype A eAg-neg patients had qHBsAg levels and liver fibrosis assessment. Majority (65%, 86/132) were African/Caribbean. Liver fibrosis was mild, moderate and severe in 97 (73%), 26 (20%) and 9 (7%) patients respectively. Age was similar across the groups (p = 0.887). HBV DNA (p = 0.001) and ratio of qHBsAg/HBV DNA (p = 0.001)were significantly different between the 3 groups, however qHBsAg was not (p = 0.177). qHBsAg/ HBV DNA ratio <1.0 was a marker of moderate/severe fibrosis (p = 0.000, OR 0.212 95% CI 0.48–0.93). Ratio cut off of 1.0 gave an AUROC of 0.7 (95%CI 0.59–0.81). No difference in fibrosis was seen between ethnicities (p = 0.352). There was a difference in quantitative surface antigen levels between
Conclusions: Genotype A HBV eAg-neg patients had low level of fibrosis, in contrast to genotype E patients at the same centre (EASL 2014). Although qHBsAg levels did not differ between fibrosis groups, qHBsAg/HBV DNA ratio <1.0 predicted patients with moderate/severe fibrosis. Caucasian patients had significantly higher qHBsAg without an increased fibrosis risk or low qHBsAg/HBV DNA ratio, suggesting true hepatitis B e-antigen seroconversion with low viral load. In this cohort qHBsAg/HBV DNA provided insight into disease trajectory and fibrosis.

5. Poster (#THU-122)

Viral hepatitis: Hepatitis A, B, D, E – clinical (except therapy) - Hall 8.1

Date & Time: Thursday, April 14, 2016 - 08:00 - 18:00

EARLY EXPERIENCES FROM THE FIRST TREATMENT PROGRAMS FOR CHRONIC HEPATITIS B IN SUB-SAHARAN AFRICA

H. Aberra1, on behalf of Centre for Imported and Tropical Disease, Oslo University Hospital, Norway; Aklilu Lemma Institute of Pathobiology, Addis Ababa, Ethiopia; St. Paul’s Hospital Millenium Medical College, Addis Ababa, Ethiopia, H. Desalegn2, N. Berhe3, G. Medhin4, S. Gundersen5, A. Johannessen6

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Background and Aims: Prevalence of HB in Ethiopia is estimated to be between 5.7-10.8%. However treatment for chronic hepatitis B (CHB) is virtually absent in sub-Saharan Africa. To better understand the epidemiology of CHB, and to study the efficacy, safety & feasibility of antiviral treatment, a pilot treatment program was started in February 2015.

Methods: The current Cohort Study was based in St.Paul’s Hospital Millennium Medical College located in the capital city, Ethiopia. All consenting adults above the age of 18 years with CHB were eligible for inclusion in the absence of hepatocellular carcinoma. Patients were subjected to a thorough baseline evaluation including hematological, serological, biochemical, viral markers & transient elastography (Fibroscan 402, Echosens, France). Treatment eligibility was based on the EASL criteria with some modification.

Results: Among the initial 300 patients, 138 (45.0%) were females, of whom 19(14.2%) were pregnant & 16(13.7%) were breastfeeding. Most patients (254 /84.7%) were between the age of 18-45 years. Five (1.5%) patients had HIV and 4(1.4%) had hepatitis C co-infection. Among 289 patients tested for hepatitis delta virus (HDV) antibody, 13 (4.5%) were positive. Eighteen (8.7%) of 207 patients were positive for hepatitis B e-antigen (HBeAg). The majority of patients had viral load <2000 IU/mL (166 ;57.6%) & ALT <40 IU/mL (246 ;83.4%). A total of 102 (34.0%) of patients had viral load <2000 IU/mL, ALT <40 IU/mL & Fibroscan <7.9 KPa which are possible inactive carriers at inclusion. Among 79 patients tested only A & D genotypes were identified. Harmful alcohol use was reported in 5 patients & Khat use in 18 (6.0%). The result of Fibroscan at inclusion showed that 70(26.4%) had significant liver Fibrosis (>7.9 KPa), of whom 47(17.7%) had cirrhosis (Fibroscan > 9.9 KPa). Twenty-six (9.5%) patients had a previous history of intake of antiviral treatment through different means. In total 54 (18.0%) patients met the EASL treatment eligibility criteria and started treatment.

Conclusions: Parallel to early HIV treatment program, we observed that many patients enrolled with advanced liver disease. This underscores the need for nationwide treatment programs for patients with CHB.

6. Poster (#THU-137)

Viral hepatitis: Hepatitis A, B, D, E – clinical (except therapy) - Hall 8.1

Date & Time: Thursday, April 14, 2016 - 08:00 - 18:00

CHRONIC HEPATITIS B IS ASSOCIATED WITH INCREASED CARDIOVASCULAR RISK ASSESSED BY INTIMA-MEDIA THICKNESS

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Background and Aims: The association between hepatitis C virus and insulin resistance, steatosis and dyslipemia is well established. However, there is scarce data concerning the potential role of hepatitis B virus as a cardiovascular risk factor. The aim of the study was to assess the association between atherosclerosis and chronic hepatitis B infection in patients with mild fibrosis.

Methods: Prospective study including 128 naïve chronic HBsAg negative patients with mild fibrosis (FibroScan <9.2 kPa or liver biopsy <F2) and HBV DNA <20.000 IU/mL. 56% male with mean age 48 years. The cardiovascular risk was evaluated according to the presence of risk factors, metabolic syndrome and carotid Doppler. This last test assesses: 1) the intima-media thickness (that is associated with increased incidence of cardiovascular events); 2) the presence of atheroma plaques. The results were compared with a Spanish cohort of healthy subjects, stratified by sex and age.

Results: risk factors were: 32% former or active smokers, 20% dyslipemia, 19% arterial hypertension, 5% diabetes. Overall, 9% meet criteria of metabolic syndrome. Carotid plaques were observed in 19% of chronic hepatitis B, similar rate to healthy subjects (p NS). However in CHB patients >55 years, carotid plaques were presented in 46% compared to 5% of patients <55 years. Factors associated with atheroma plaques in the univariated analysis were age, tobacco use, abdominal diameter, GGT levels, insulin resistance, dyslipemia and hypertension. In the multivariate analysis only age was associated with plaques. Greater intima-media thickness was observed in HBV infected patients in comparison with healthy controls (Figure). This difference reached statistical significance for all age groups except for patients over 65 years. Increased intima-media thickness was associated with age, presence of metabolic syndrome, male sex,
7. Poster (#THU-138)

Viral hepatitis: Hepatitis A, B, D, E – clinical (except therapy) - Hall 8.1

Date & Time: Thursday, April 14, 2016 - 08:00 - 18:00

HBSAG LEVELS NEED HBV GENOTYPING TO DIFFERENTIATE INACTIVE CARRIERS HBSAG CARRIERS FROM HBEAG NEGATIVE CHRONIC HEPATITIS B

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**Background and Aims:** At least 3 determinations of ALT and HBV DNA levels throughout a year are needed for proper diagnosis of hepatitis B inactive carriers. HBsAg levels <1,000 IU/mL allows identification of inactive carriers in a single analysis, but this criterion has only been assessed in patients infected by genotype D and HBV DNA <2,000 IU/mL. The aim was to assess the usefulness of HBsAg levels in patients with normal ALT levels and HBV DNA <20,000 IU/mL, infected by different HBV genotypes.

**Methods:** 177 consecutive patients with the following criteria were included: naïve, HBeAg negative, normal ALT and HBV DNA <20,000 IU/mL. HBV was genotyped by direct sequencing, HBsAg was quantified by electrochemiluminescence Elecsys HBsAg II, and the degree of liver fibrosis was assessed by FibroScan.

**Results:** Majority of patients were male (57%), Caucasian (68%), mean age 46 ± 13 years old and mean value of transient elastography was 5.5 ± 2 kPa. HBV Genotypes were: A = 38%, B = 2%, D = 27%, E = 20%, F or H = 11%, Mixed = 2%. HBV DNA was statistically similar among different HBV genotypes (p > 0.23). HBsAg levels were statistically different among HBV genotypes (p < 0.001): A = 6,356 ± 7,736 IU/mL; D = 2,923 ± 5,067 IU/mL; E = 8,574 ± 10,061 IU/mL; H or F = 22,506 ± 20,047 IU/mL. The criteria for inactive carrier (HBsAg <1,000 IU/mL plus HBV DNA <2,000 IU/mL) was presented in 72% patients infected by genotype D but only in <30% of patients infected by genotype A, E, H or F (Table). Overall, in all patients with HBV DNA <20,000 IU/mL, 62% of genotype D-infected patients presented HBsAg <1,000 IU/mL, percentage ≤25% for genotype A, E, H or F (Table).

Conclusions: HBsAg <1,000 IU/mL is not useful for classification of inactive carriers infected by non-D genotypes. HBsAg levels were higher in patients infected by genotype A, E, H or F than D. HBsAg cutoff for identification of HBV inactive carriers require HBV genotyping.

Table HBSAg and HBV DNA levels and percentage of patients with HBsAg <1,000 IU/mL according to HBV genotype

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>ALT ≥ 20 IU/mL</th>
<th>ALT &lt; 20 IU/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>N = 67</td>
<td>N = 47</td>
</tr>
<tr>
<td>B</td>
<td>N = 35</td>
<td>N = 20</td>
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<td>C</td>
<td>N = 17</td>
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<td>N = 19</td>
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| p | 0.001 | 0.001 | 0.001 | 0.001 | 0.001 | 0.001 |

8. Poster (#THU-141)

Viral hepatitis: Hepatitis A, B, D, E – clinical (except therapy) - Hall 8.1

Date & Time: Thursday, April 14, 2016 - 08:00 - 18:00

NATURAL HISTORY OF CHRONIC HEPATITIS B VIRUS INFECTION IN INACTIVE CARRIERS AND IN “GRAY ZONE” PATIENTS

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**Background and Aims:** EASL guidelines defined the inactive HBV carrier state (IC) by persistently low HBV-DNA (<2,000 IU/mL) and normal ALT, while the gray zone (GZ) state was defined by HBV-DNA <20,000 IU/mL and ALT ≤ 2 ULN. These patients may present HBV-DNA peaks or ‘reactivations’ during follow-up. We aimed to assess the incidence and impact of these reactivations on the natural history of patients classified as IC and GZ.

**Methods:** Patients who fulfilled the EASL criteria of IC and GZ seen in our Unit between 1988–2010 were retrospectively analyzed. We assessed: 1) transition between states: IC, GZ and HBeAg- chronic B hepatitis (CHB); 2) transient reactivations (TR) defined by increase of HBV-DNA >2,000 IU/mL in IC or >20,000 IU/mL in GZ; 3) persistent reactivations (PR) or HBV-DNA >20,000 IU/mL for at least 6 months; 4) HBsAg loss and 5) liver-related events. Patients were censored at the time of CHB, clinical events or last FU.

**Results:** 194 patients were included, 144 (74%) IC and 50 (26%) GZ. All patients were treated naïve and cirrhosis was excluded. No differences in demographic variables between IC/GZ were found: 59% and 56% were male, median age was 38 and 36 years, and 85% and 86% were Caucasians. After a median FU of 12 years (6–19), 57% of IC presented TR and 10% PR. On last assessment, 79% remained IC although 43% had presented TR episodes; 19% changed to GZ and 8% to CHB. Among patients classified as GZ 24% and 18% presented TR and 10% PR. On last assessment, 73% remained IC and 86% were Caucasian. After a median FU of 12 years (6–19), 57% of IC presented TR and 10% PR. On last assessment, 74% remained IC although 43% had presented TR episodes; 19% changed to GZ and 8% to CHB. Among patients classified as GZ 24% and 18% presented TR and 10% PR. On last assessment, 73% remained IC and 86% were Caucasian. Among patients classified as GZ 24% and 18% presented TR and 10% PR. On last assessment, 73% remained IC and 86% were Caucasian. Among patients classified as GZ 24% and 18% presented TR and 10% PR. On last assessment, 73% remained IC and 86% were Caucasian. Among patients classified as GZ 24% and 18% presented TR and 10% PR. On last assessment, 73% remained IC and 86% were Caucasian.
who developed cirrhosis following CHB. No patient developed hepatocellular carcinoma.

Conclusions: During the natural history of IC and ZG patients, transient HBV-DNA peaks or RE are frequent. The number of reactivations was associated with transition to CHB and inversely correlated with HBsAg loss. After a long FU, RE did not generally lead to liver disease progression.

9. Poster (#THU-163)

Viral hepatitis: Hepatitis A, B, D, E — clinical (except therapy) - Hall 8.1

Date & Time: Thursday, April 14, 2016 - 08:00 - 18:00

THE ROLE OF CELLULAR IMMUNITY AND CYTOKINES IN THE PATHOGENESIS OF CHRONIC HEPATITIS B IN CHILDREN

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2. Mother and Child Institute, Chisinau, Republic of Moldova

Background and Aims: The purpose of this work was to study the role helper T lymphocytes, cytotoxic T lymphocytes, B lymphocytes and significance of cytokines IL-1β, INF-γ, TNF-α in the pathogenesis of chronic hepatitis B in children with chronic hepatitis B in Republic of Moldova.

Methods: There were examined 55 children aged 3–17 years with chronic viral hepatitis B that cellular immunity were assessed by determining CD3, CD4, CD8 and their immunophenotyping by enzyme immunoassay monolonal and IFN-γ serum levels of TNF-α IL-1β by ELISA (6 children). The diagnosis was confirmed clinical, epidemiological, biochemical, immunologic modification, including degree of viremia HBV DNA (PCR Real Time Rotor Gene6000 Corbett Research) and transient elastometry (Fibroscan) and histological activity by liver biopsy needle Menghini (5 children). Statistical analysis was performed with the Student’s test determining average values, standard error of the mean. The cases with p ≤ 0.05 were considered statistically significant.

Results: In 82% of cases of children aged between 6 and 15 years were with predominance of males. HBV infection in children was 43.8% in the usual horizontal horses from family members with chronic HBsAg porting average duration of chronic HVB infection was 2.7 ± 0.47 years. 69.5% of patients had HBV viremia phase with the presence of HBeAg and DNA VHB. In 52.7% (29) cases it has been found significant in reducing the immunosuppression condition of total T lymphocytes (CD3), helper T lymphocytes (CD4) cytotoxic T lymphocytes (CD8) and B lymphocytes (p < 0.01). 6 children serum values determined TNF-α reduction found in 5, IFN-γ of - 4, IL-1β- 4 children.

Conclusions: Presence of disorders a system T-lymphocytes (CD3, CD4, CD8), B lymphocytes 52.7% (29) in cases and the lower the proinflammatory cytokines IFN-γ, TNF-α, IL-1β determined in our study explains the installation secondary immunodeficiency (p < 0.01) and the inability to eliminate HBeAg thus favoring chronic HBV infection in children.

10. Poster (#THU-166)

Viral hepatitis: Hepatitis A, B, D, E — clinical (except therapy) - Hall 8.1

Date & Time: Thursday, April 14, 2016 - 08:00 - 18:00

IMPACT OF DYNAMIC VIRAL AND BIOCHEMICAL PARAMETERS ON PROGRESSION OF LIVER FIBROSIS IN A COHORT OF INACTIVE EUROPEAN HEPATITIS B (HBV)

CARRIERS: A PROSPECTIVE LONGITUDINAL STUDY (ALBATROS STUDY)


Background and Aims: Former studies from Asia demonstrated the impact of single point HBV-DNA levels at baseline for prediction of development of disease progression during natural course of HBV infection. Little is known about the relevance of dynamic viral and biochemical parameters for the outcome during long-time follow-up. The aim of the present study was to analyse the significance of HBV DNA levels and liver enzymes within the first three years of follow-up on fibrosis stage in a cohort of inactive HBsAg carriers from Europe.

Methods: 830 patients with HBeAg-negative HBV infection were prospectively followed. They were considered not to be candidates for antiviral therapy at study inclusion based on international guidelines. Biochemical, virological and non-invasive fibrosis parameters including FibroScan, ARFI (acoustic radiation force impulse) and APRI score were performed at baseline as well as during annual follow-up.

Results: Data of 1, 2, 3, 4 and 5 years follow-up (FU) were available in 352 (FU1), 208 (FU2), 150 (FU3), 76 (FU4) and 28 (FU5) patients. 12/150 (8%) never had detectable HBV DNA, 79/150 (53%) showed persistently low-level replication (<2000 IU/mL) and 13 out of 150 patients (9%) had at least once HBV DNA > 20 000 IU/mL. 122/150 (81%) and 117/150 (78%) had constantly normal AST and ALT, respectively. Results of FibroScan at FU3 were as follows: 116/150 (91%) were consistent with fibrosis stage 0 or 1(F0-F1), 7/150 (5 %) with F2 and 5/150 (4%) with F3. Univariate analysis detected no significant association between viral dynamics and fibrosis stage by FibroScan /ARFI. The subgroup of HBV carriers who were detected at least once >20,000 IU/mL for HBV DNA showed more frequently permanent normal liver transaminases were considered as being at lower risk of advanced fibrosis within 3 years prospective follow-up.

Conclusions: Patients with low-replicative chronic HBV infection and permanent normal liver transaminases were considered as being at lower risk of advanced fibrosis within 3 years prospective follow-up. Fluctuation of HBV DNA up to 20,000 IU/mL had no influence on fibrosis progression.

11. Poster (#THU-217)

Viral hepatitis: Hepatitis C – clinical (new compounds, resistance) - Hall 8.1

Date & Time: Thursday, April 14, 2016 - 08:00 - 18:00

RETREATMENT OF HCV DAA FAILURES: HCV INFECTION MAY BE INCURABLE

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Background and Aims: Current EASL recommendations suggest that patients who failed on a DAA-containing regimen should be retreated with an IFN-free combination including sofosbuvir (SOF), plus one or two other direct-acting antiviral (DAAs), ideally with no crossresistance with the DAAs already administered. The goal of this pilot experience was to evaluate the efficacy and safety of a triple combination of SOF + daclatasvir (DCV) + simeprevir (SMV) with ribavin RBV) for 24 weeks in patients who previously failed on a DAA combination administered 12 weeks without RBV.

Methods: Eight patients (mean age: 56.2 years, range: 48–64) infected with HCV genotype 1 (1a: n = 4; 1b: n = 2); 4 (n = 1) or 6 (n = 1) with compensated liver disease (fibroscan: 6.6–35.3 kPa) who failed to achieve SVR were included. They had received SOF + DCV (n = 3); SOF + SMV (n = 2); SOF + LDV (n = 1); GRZ + EBV (n = 1); Mericitabine + Danoprevir + ritonavir (n = 1); without RBV for 12 weeks. HCV RNA levels were measured with Abbott RealTime Assay (LLOQ/LOD: 12 IU/mL). HCV resistance was assessed at retreatment baseline by means of population sequencing of the NS3 protease, NSSA and NS5B polymerase coding regions. Antiviral efficacy was assessed monthly during treatment and at post treatment weeks 4 and 12.

Results: The table shows the outcomes. One patient relapsed post-treatment and one patient discontinued early (week 4) due to the occurrence of a SAE (pulmonary arterial hypertension). Two patients achieved SVR4. The remaining 4 patients are still on treatment.

Conclusions: The combination of SOF + DCV + SMV + RBV for 24 weeks was associated with on-treatment response in all patients. However, at least 2 patients failed to achieve an SVR, one due to SAE, the other one due to post-treatment relapse. Given the lack of other DAA class options, the latter patients should be considered incurable. SVR12 data from the full series of patients will be presented.
shows a high inter-individual variability in progression to liver fibrosis and cirrhosis. Whether these progressions are influenced by an altered CCM is unclear. Moreover, it is unknown to what extent the CCM is restored by interferon-free antiviral therapy. The aim of this study was to investigate to what extent the CCM is altered in chronic HCV infection, to identify potential cytokines/chemokines associated with viral infection vs. stage of liver disease and to analyze whether DAA treatment restores this milieu.

Methods: We performed multianalyte profiling of 50 cytokines and chemokines in the plasma of patients with persistent HCV infection using the BioPlex bead array method. A total of 27 patients were recruited, who were treated for 24 weeks with sofosbuvir and ribavirin. Samples were collected longitudinally during therapy and after treatment cessation. All patients had advanced stages of liver fibrosis or cirrhosis, roughly 40% of the patients experienced a viral relapse after end of therapy. Principle component analysis was performed to identify networks of interactions and associations.

Results: We found that (I) the CCM was markedly altered in HCV patients compared to healthy controls and individuals with nonalcoholic steatohepatitis; (II) CCM patterns and distinct cytokines and chemokines were associated with the level of fibrosis (fibroscan values) (e.g. HGF, IL-18) while others were driven by inflammation or viral replication (HGF, IFNγ, VCAM-1, or GRO-α, IP-10, TNF-β); (III) SVR and relapse patients could be differentiated by several baseline cytokine and chemokine levels, i.e. IL-12p40, IL-16, IFNα-2 and TGF-β; (IV) significant changes of the CCM could be observed during therapy, however the CCM pattern was not normalized even in SVR patients for the majority of parameters.

Conclusions: In conclusion, our results show that cHCV infection appears to disrupt the cytokine/chemokine compartment and that these alterations persist even after viral clearance. Thus, HCV cure does not lead to immunological restitution. Further, CCM patterns may be used to individualize treatment duration with novel DAAs as some cytokines and chemokines were associated with treatment outcome.

14. Poster (#THU-309)
Alcoholic liver disease and drug-induced liver disease – Hall 8.1
Date & Time: Thursday, April 14, 2016 - 08:00 - 18:00
EXPRESSION OF PRO-INFLAMMATORY AND HEPATOPROTECTIVE FACTORS AT EARLY STAGES OF ALCOHOLIC LIVER DISEASE IN HUMANS AND THE IMPACT OF SHORT TERM ABSTINENCE
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Background and Aims: Animal models imperfectly mimic the spectrum of alcoholic liver disease (ALD) seen in humans. Some studies have investigated late stages and severe forms of human ALD, but little is known about the pathophysiological mechanisms occurring in the human liver at early stages of the disease. Here, we investigated inflammatory mechanisms in alcohol dependent patients undergoing a standardized inpatient alcohol withdrawal program.

Methods: Patients with suspicion of significant ALD (ALT, AST increase, fibroscan >7.8 kPa) were randomly assigned to undergo liver biopsy either in the active drinking phase or after 2 weeks of abstinence. Patients without significant fibrosis on histology were included in the study (n = 40). Liver tissue (n = 6) from size-reduced liver grafts was used as normal controls. Expression and cellular localization of various factors was assessed by Western-blotting, qPCR and immunohistochemistry and immunofluorescence.

Results: The active drinking phase, a strong activation of the Kuffer cell (KC) compartment was found with KCs forming clusters adjacent to ballooned, steatotic hepatocytes. KC showed a pro-inflammatory M1 phenotype with activation of NFκB and increased expression of TNFα, IL-1β and iNOS. After 2 weeks of abstinence, the staining pattern of KC returned to normal and NFκB, IL-1β and iNOS levels but not TNFα decreased to almost control levels. In addition, abstinence induced a partial shift to a M2 phenotype with increased production of the anti-inflammatory cytokine IL-10. Interestingly, we did not find activation of TLR4 since TLR4, CD14, and LPB levels remained at control values in active drinkers. By contrast, we found a strong and persistent upregulation of the intracellular TLR3 and TLR7 which correlated with high production of interferon beta and gamma principally located to hepatocytes and bile ducts. Moreover, the hepatoprotective factors IL-6, IL-22, MCP-1 and Stat3 DNA-binding were strongly down-regulated in active drinkers and did not recover after short term abstinence. Hepatocyte Ki67 proliferation index was low in active drinkers and increased modestly but significantly after 2 weeks of abstinence.

Conclusions: At early stages of ALD, a strong pro-inflammatory, KC-dependent response is observed which rapidly reverses upon abstinence. By contrast, down-regulation of hepatoprotective factors is more long lasting and might significantly impair liver repair mechanisms in sustained drinkers.

15. Poster (#THU-318)
Alcoholic liver disease and drug-induced liver disease – Hall 8.1
Date & Time: Thursday, April 14, 2016 - 08:00 - 18:00
ASSOCIATIVE ROLE OF GENETIC ALTERATION IN ALCOHOL METABOLIZING GENES WITH ALCOHOL MEDIATED LIVER DISEASE SUSCEPTIBILITY AND SEVERITY IN ETHNICALLY DISTINCT NORTHEAST INDIAN POPULATION
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Background and Aims: Limited data is available on the genetic aspects in the ethnically distinct Northeast Indian population (NEI), which has a very high incidence rate of ALD and mortality related to it, mainly because of customary tribal practices. Alteration (s) in alcohol metabolizing pathway genes influences ALD development and consumption, and have been evaluated in this present study.

Methods: Whole blood samples were collected from different hospital centers in NEI from ALD patients [n = 150 (CLD = 110, cirr = 40), alcoholic without liver disease [AWLD = 93] and healthy controls [n = 274] along with their fibroscan based LSM score, and informed consent. Genomic DNA was extracted by standard phenolchloroform method. Variation in allele frequencies of ADH2 and ALDH2 genotypes was determined by PCR-CTPP method; and ADH3 polymorphism studies was performed by PCR-RFLP method. Statistical analysis was performed using SPSSv13.0 software.

Results: Presence of predominant ADH2*2 genotype in NEI population was found to be associated with increased risk of cirrhosis compared to controls, AWLD and CLD cases; and CLD compared to AWLD cases. Variant ADH3 genotype was also predominant, and was found to be associated with disease severity as its presence significantly increased the risk of cirrhosis compared to controls, AWLD and CLD cases (p < 0.001). ADH3*2/3 genotype in alcoholic cases in the NEI population has relevance with both disease susceptibility as well as alcohol dependency since individuals with slow alcohol degradation capacity and are more likely to consume alcohol excessively and to develop alcoholism. Distribution of variant genotype ALDH2 was uncommon in our study cohort. Joint affects
analysis showed that the presence of higher variant genotype combination resulted in increased risk of CLD(1.577folds) and cirrhosis (2.036folds) compared to AWLD, and cirrhosis compared to CLD(1.291folds); thereby confirming the association of the polymorphisms in key alcohol metabolizing genes in the predisposition to alcohol related liver disease susceptibility and severity. The presence of variant ADH2, ADH3 and ALDH2 genotypes showed the higher LSM score in ALD.

Conclusions: Alterations in the alcohol metabolizing genes does play an important role in the susceptibility and severity of ALD. ADH2 genotype individually and combinatorially is the detrimental factor in ALD susceptibility and severity in NEI population, and has prognostic significance for stratification of ALD cases and early possible interventions.

16. Poster (#THU-322)

Alcoholic liver disease and drug-induced liver disease – Hall 8.1
Date & Time: Thursday, April 14, 2016 - 08:00 - 18:00

PRIMARY LIVER INJURY AND DELAYED RESOLUTION OF LIVER STIFFNESS AFTER ALCOHOL DETOXIFICATION IN HEAVY DRINKERS WITH THE PNPLA3 VARIANT I148M

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Background and Aims: PNPLA3 rs738409 (I148M) SNP has been identified as important progression factor in patients with ALD and NAFLD. However, its molecular function still remains poorly understood. Aim of our study is to investigate PNPLA3 genotype, histology and liver stiffness (LS) in heavy drinkers prior and after alcohol withdrawal.

Methods: We here studied LS, serum markers (both n = 521) and histology (n = 80) using the Kleiner score in Caucasian heavy drinkers prior and after alcohol detoxification.

Results: PNPLA3 rs738409 genotype distribution for CC, CG and GG was 39.2%, 52.6% and 8.2%. GG genotype primarily correlated with histological steatohepatitis (r = 0.404, p < 0.005), ballooning (0.319, p < 0.005) and least with steatosis (r = 0.264, p < 0.05). Mean LS was lowest in CC carriers (13.1 kPa) as compared to CG and GG carriers (both 17.6 kPa). LS primarily correlated with fibrosis stage (r = 0.826, p < 0.005), ballooning (r = 0.516, p < 0.005), steatohepatitis (r = 0.319, p < 0.005) but not with steatosis. After alcohol withdrawal, LS significantly decreased in CG carriers from 17.6 to 12.7 kPa but not in CC carriers. Notably, LS decreased to a lesser extent in GG carriers from 17.6 to 14.5 kPa due to prolonged resolution of inflammation. Non-invasive fibrosis assessment by LS in all patients showed 3.8% more CC carriers in the F0 group and 3.7% less in the F4 cirrhosis group. The OR to develop cirrhosis corrected for age, gender and BMI was 1.295 (95% CI 0.787-2.131) for CG + GG carriers.

Conclusions: In heavy drinkers, PNPLA3 GG primarily correlates with liver damage but not steatosis resulting in a reversible, inflammation associated increase of LS.

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Background and Aims: Upper gastrointestinal endoscopy (UGE) is the gold standard method to assess gastroesophageal varices (GOV) in patients with cirrhosis. Platelet count (PC) and liver stiffness measurement (LSM) using transient elastography (TE) have shown high correlation with portal hypertension (PHT) and development of GOV. A recent study performed by Ding et al., [Liver International 2015] has suggested a predictive model using PC and LSM to exclude the presence of high-risk GOV (diameter >5 mm and/or the presence of high-risk stigmata). However, further studies are needed to validate these findings. The aim of our study was to evaluate the prevalence of GOV in compensated cirrhotic patients and to identify variables related to the incidence/absence of GOV.

Methods: From January 2010 to June 2015, compensated HCVcirrhotic patients (LSM ≥ 14 kPa) were prospectively evaluated in 6 Spanish centers. All included patients were Child-Pugh A, without history of clinical decompensation or PHT-related bleeding. All patients performed an UGE to investigate the presence of GOV. Clinical and analytical data were collected.

Results: We included 368 Child-Pugh A HCV-cirrhotic patients, 55 (14.9%) showed high-risk GOV. Patients with high-risk GOV had higher BMI, LSM, bilirubin and INR values, and lower albumin, platelet and hemoglobin values (all p < 0.05). In a multivariate analysis (OR, 95% CI, p) only platelet count (0.99, 0.98–0.99, p = 0.022), bilirubin (2.09, 1.13–3.88, p = 0.019) and albumin levels (0.88, 0.81–0.95, p = 0.001) were predictors of high-risk GOV, but not LSM. Similarly, to Ding et al., 149 patients (40.5%) showed platelet count >100.000 and LSM <25 kPa. However, 10 of these patients (6.7%) presented high-risk GOV (NPV = 93.3%). These patients had a median PC of 143.000 and LSM of 19 kPa. Algorithms combining different levels of bilirubin, albumin or PC did not improve the combination of Ding et al., algorithm to identify high-risk GOV.

Conclusions: In this large multicentric cohort of compensated cirrhotic patients, the combination of PC and LSM excluded 93% of patients without high-risk GOV. Algorithms combining other variables did not improve this combination.

18. Poster (#THU-362)

Cirrhosis: Clinical aspects – Hall 8.1
Date & Time: Thursday, April 14, 2016 - 08:00 - 18:00

RAPID IMPROVEMENT IN LIVER AND SPLEEN STIFFNESS DURING TREATMENT WITH NEW ORAL ANTIVIRAL THERAPY FOR HCV

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Background and Aims: Sustained virological response (SVR) after HCV treatment improves liver fibrosis and decrease portal pressure. Liver stiffness (LS) measurement by transient elastography is useful to estimate liver fibrosis and spleen stiffness (SS) correlates with portal pressure. The aim of our study was to determine the effect of antiviral treatment in LS and SS.
METHODS: We included 40 patients with compensated advanced chronic liver disease (cACLD) due to HCV infection who started antiviral treatment (sofosbuvir + simeprevir + ribavirin 12 weeks for genotype 1/4 and sofosbuvir + daclatasvir + ribavirin 24 weeks for genotype 3). LS and SS (under ultrasound assistance) were performed at the beginning of treatment, at week 4, at the end of treatment and 24 weeks after, using a FibroScan Touch 502. M or XL probe were used as per device indication. Clinical and laboratory parameters were also collected.

RESULTS: All patients (87.5% genotype 1) have finished treatment and 31 out of 32 achieved SVR (96.9%). During treatment, patients presented a significant increase in platelets and albumin, and a decrease in LS, SS and ALT. A rapid decrease in LS (median baseline LS 20.8 kPa, range 11.1–75) was seen during the first 4 weeks (17.5 kPa, 7.8–48; p = 0.001) with minimal change at the end of treatment (17.1 kPa, 7.8–61.5). Changes in LS were correlated with ALT levels: patients with basal ALT ≥ 2 × ULN presented a higher and significant decrease in LS during treatment compared with patients with ALT < 2 × ULN (mean decrease 6.3 kPa vs 2.1 kPa; p = 0.049). Similarly, baseline SS (45.7 kPa, 17.3–75) rapidly decreased during first 4 weeks (34.6 kPa, 13.9–75; p = 0.05) without significant changes at the end of treatment (33.2 kPa, 12.3–75). Patients with decrease in SS during treatment presented a higher increase in platelets (mean increase 21 ± 30 × 109/L; p = 0.005) significant since week 4, and a higher decrease in LS (mean decrease 6.7 ± 10.8 kPa; p = 0.012). In patients who did not improve SS, change in platelets was not significant (mean increase 18.2 ± 24 × 109/L; p = 0.07) and no differences between basal and end of treatment LS were found (mean decrease 0.3 ± 12.6 kPa; p = 0.942). LS and SS at 24 weeks after finishing therapy were similar to values obtained at the end of treatment.

CONCLUSIONS: In patients with cACLD, the new antivirals rapidly decrease LS, because of improvement in liver inflammation, and SS due to a possible combination of portal pressure reduction and spleen inflammation.

RESULTS: Baseline characteristics: age: 53 ± 11 years, 73% male, main etiologies: 46.7% viral, 29.6% ALOD, 23.7% others. Median TE values were 26.6 kPa (12.2–75). 88 (65%) patients were found with varices. Of those 67% were found with small varices and 33% with large varices. 92 patients could be classified into the Baveno VI cut-off groups (43 patients just fulfilled either TE <20 kPa or PLT <150 G/L and could not be classified). 58/82 (71%) within the group >20 kPa and PLT <150 G/L were found with varices (AUC = 0.568). Most importantly, four out of ten patients (40%) within the group TE < 20 kPa and PLT > 150 G/L were found with varices. However, none of these 4 patients had large varices in need for primary prophylaxis of variceal bleeding.

CONCLUSIONS: Using the Baveno VI guidelines to avoid screening endoscopy in patients with TE < 20 kPa and PLT > 150 G/L would have missed 40% of patients with small varices. However, exclusion of large varices can accurately be made by using Baveno VI criteria.

20. Poster (#THU-384)
Cirrhosis: Clinical aspects – Hall 8.1
Date & Time: Thursday, April 14, 2016 - 08:00 - 18:00
PORTAL HEMODYNAMICS PREDICTS THE OUTCOME IN SEVERE ALCOHOLIC HEPATITIS PRESENTING AS ACUTE-ON-CHRONIC LIVER FAILURE
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BACKGROUND AND AIMs: During acute-on-chronic liver failure (ACLF), the progressive liver failure is associated with rise in portal pressure. Development of variceal bleed, sepsis and organ failures often related to the severity of portal hypertension in addition to the inciting acute injury. The aim is identify the changes in portal and systemic hemodynamics in patients of ACLF caused by Severe Alcoholic Hepatitis (SAH) or other etiologies and their influence on organ failure and survival.

METHODS: ACLF patients as by APASL were enrolled into the AARC database and followed prospectively for initial 90 days. Clinical events, laboratory parameters, disease severity score, survival were compared for the acute insult i.e. SAH against other etiologies. Median stiffness (KPa), Transient elastography (Fibroscan™), Transjugular portal hemodynamic parameters (HVPG), cardiac catheterization [mean Pulmonary Artery pressure (MPAP), PCWP, and formula based systemic hemodynamic variables [SVRI, PVRI, Cardiac Output (CO), Cardiac Index (CI)] were compared in SAH against other
Results: 308 patients (150 SAH, 158 other etiologies) with TJB were analyzed. At baseline the MELD, SOFA, bilirubin, creatinine, mortality (51.5% vs 48.5%, p = 0.29) were comparable. SAH group were younger [(40.8 ± 8.7) vs. (46.6 ± 12.8) years, p < 0.001] with higher portal pressure i.e. HVPG [(18.5 ± 5.0) vs. (16.7 ± 5.1) mm of Hg, p = 0.003] and lower Hb [(10.6 ± 1.7) vs. (11.3 ± 1.9) gm/dL, p = 0.001]. HR, MAP, CO, CI, SVRI, PVRI were comparable in both the groups. LSM, HVPG, PCWP, MPAP, variceal grade, INR, serum Na were predictors of 90 days mortality. In multivariate analysis HVPG [OR = 1.02, 95CI (1.01–1.13), p = 0.01], MPAP [OR = 1.04, 95CI (1.03–1.12)] were independent predictor of mortality. HVPG > 17.2 mm Hg correlate to variceal bleed (p = 0.03), AKI (p = 0.09) and sepsis (p = 0.07) within 15 days. HVPG correlated to low platelet (p = 0.02) and presence of RCS (p = 0.003) but not to the grade of varicices, TNF-alpha, CRP and Ferritin. The HVPG > 19.5 mm Hg was associated with mortality 28% vs. 42%, p=

Conclusions: SAH is associated with higher portal pressure than other etiologies irrespective of variceal grade and is an independent predictor of mortality. Presence of RCS on varices or low platelet, not the inflammatory markers correlate to portal hemodynamics.

22. Poster (#THU-394)
Cirrhosis: Clinical aspects – Hall 8.1
Date & Time: Thursday, April 14, 2016 - 08:00 - 18:00
PREDICTIVE POWER OF CLINICAL STIGMATA IN DETECTING ADVANCED LIVER DISEASE
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Background and Aims: Non-invasive tools for detection of liver fibrosis are increasingly utilized; however the additional diagnostic value of these tools in the setting of a thorough clinical examination remains unknown. This prospective study aims to determine the prevalence and utility of clinical stigmata of chronic liver disease (CLD) in a high-risk cohort.

Methods: Patients with chronic hepatitis B (CHB) and hepatitis C (CHC) undergoing liver stiffness measurement (LSM) using transient elastography (Fibroscan® 402) were recruited consecutively between November 2014 and October 2015 and assessed by one clinician for clinical stigmata associated with CLD according to a standardized assessment criteria. The clinician was blinded to prior clinical assessment and investigations results. Liver stiffness measurements (LSM)>8kPa, >13kPa and >21kPa were taken as cut-offs for significant liver disease, cirrhosis and portal hypertension.

Results: A total of 682 patients were recruited, 64.2% were male with a mean age of 43 ± 10.4 years. The primary indication of assessment was CHC in 66.1%. Significant alcohol (>140 g/wk) and tobacco use was noted in 31.7% and 55.9% respectively. Frequency of LSM < 8, LSM≥ 8 and <13, LSM ≥ 13 and <21 LSM ≥ 21 were 477
of the prospective trial is 12 months with assessments being performed at baseline (enrolment) and at 6 and 12 months following baseline visit. Physical examination, blood and urine sampling, completion of quality of life questionnaire, completion of the Unified Wilson Disease Rating Scale (UWDRS), liver assessments (including noninvasive fibrosis), neurological status, adverse events and concomitant medications assessments will be performed during the three study visits.

Results: The primary endpoint to be evaluated will be the percentage of patients with stable disease after 12 months of treatment with trientine based on the investigators score. Unified Wilson Disease Rating Scale (UWDRS) will be measured at 6 and 12 months and compared to the baseline data. Additionally assessment of serum and urinary parameters of copper metabolism will be made at these time points. Quality of life will also be measured. The time to discontinuation of treatment due to adverse events and/or inadequate response will also be assessed.

Conclusions: Complementing the retrospective study, the results from this prospective study will inform on the efficacy and safety of trientine, as well as provide valuable quality of life data in Wilson Disease patients treated with trientine following withdrawal of d-penicillamine.

24. Poster (#THU-488)
Clinical trials in progress
Date & Time: Thursday, April 14, 2016 - 08:00 - 18:00
REGENERATE: A PHASE 3, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED MULTICENTER STUDY OF OBITICHOLIC ACID THERAPY FOR NONALCOHOLIC STEATOHEPATITIS
V. Ratziu1, A.J. Sanyal2, L. MacConell3, R. Shringarpure4, T. Marmon5, D. Shapiro3, Z.M. Younossi4,5

Background and Aims: Nonalcoholic Steatohepatitis (NASH) is a slowly progressive chronic liver disease without approved therapies. Patients with NASH and fibrosis are at high risk of increased mortality. Obeticholic Acid (OCA) is a selective and potent farnesoid X receptor (FXR) agonist, that has been shown to improve liver histology, including NAFLD activity score (NAS) and fibrosis, in a Phase 2 clinical trial (FLINT). Furthermore in FLINT, OCA treated patients had significant improvements in select liver biochemistries, markers of inflammation, and select cardiometabolic parameters. The ongoing, randomized, global, Phase 3 clinical trial REGENERATE, will further evaluate the effect of OCA on liver histology and clinical outcomes in patients with biopsy-confirmed NASH with stage 2-3 fibrosis.

Methods: 2065 patients will be randomized 1:1:1 to 10 mg OCA, 25 mg OCA or placebo (Figure), each added to standard of care. Patients with NAS and fibrosis are at high risk of increased mortality. Obeticholic Acid (OCA) is a selective and potent farnesoid X receptor (FXR) agonist, that has been shown to improve liver histology, including NAFLD activity score (NAS) and fibrosis, in a Phase 2 clinical trial (FLINT). Furthermore in FLINT, OCA treated patients had significant improvements in select liver biochemistries, markers of inflammation, and select cardiometabolic parameters. The ongoing, randomized, global, Phase 3 clinical trial REGENERATE, will further evaluate the effect of OCA on liver histology and clinical outcomes in patients with biopsy-confirmed NASH with stage 2-3 fibrosis.

Methods: 2065 patients will be randomized 1:1:1 to 10 mg OCA, 25 mg OCA or placebo (Figure), each added to standard of care. An interim analysis at 18 months will evaluate the effect of OCA on liver histology. Total study duration is driven by time required to accrue a total of 264 outcome events and is estimated to be ~6 years. Safety assessments will include adverse events (AEs), adjudicated cardiovascular events, and hepatic events as well as laboratory assessments. The effect of OCA on NASH and fibrosis severity will also be assessed by multiple noninvasive methods (FIB-4, APRI, transient elastography, magnetic resonance elastography, etc.).

Results: The co-primary liver histology endpoints at 18 months include: (I) improvement in fibrosis by ≥2 stage with noworsening of NASH and (II) resolution of NAS with noworsening in fibrosis stage. Further, confirmation of clinical benefit of OCA will be assessed at the end of the study by comparing the time to first occurrence of any of the following adjudicated events: histological progression to cirrhosis;
uncontrolled ascites; hospitalization for: variceal bleed, hepatic encephalopathy or spontaneous bacterial peritonitis; hepatocellular carcinoma; liver transplant or eligibility for liver transplant (defined by model for end stage liver disease (MELD) score ≥15); and death.

Conclusions: REGENERATE is the first pivotal study in NASH, designed in conjunction with FDA and meant to support approval of OCA for NASH with fibrosis. This robust Phase 3 study is designed to evaluate the effect of OCA on liver histology and effects on progression to cirrhosis, liver-related clinical outcomes and mortality.

25. Poster (#FRI-116)
Viral hepatitis: Hepatitis B & D – clinical (therapy, new compounds, resistance)
Date & Time: Friday, April 15, 2016 - 08:00 - 18:00
USING OFF-TREATMENT HBV DNA LEVELS TO PREDICT ALT RELAPSE AFTER NUCLEOS(T)IDE ANALOGUE DISCONTINUATION: A PROSPECTIVE COHORT STUDY
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Background and Aims: Most studies regarding nucleos(t)ide analogue (NA) discontinuation in chronic hepatitis B (CHB) patients are retrospective without pre-defined stopping criteria, frequent off-treatment follow-up and standardized retreatment criteria. The optimal off-treatment management also remains unknown. The aim of this prospective study was to investigate whether sustained off-treatment response can be predicted by end-of-treatment or offtreatment factors.

Methods: This prospective study enrolled non-cirrhotic Asian CHB patients who stopped NA. HBeAg-positives had to achieve HBeAg seroconversion and undetectable HBV DNA followed by consolidation ≥12 months, while HBeAg-negatives required undetectable HBV DNA followed by consolidation ≥18 months. Patients were followed every month for the first 3 months, and then every 3 months with extensive assessments. Patients with HBV DNA > 2,000 IU/mL and ALT > 2x ULN (clinical relapse) were retreated.

Results: 82 patients (mean age 35 years, 89% males, 39% entecavir) were enrolled. Median follow-up was 1.9 years in patients without clinical relapse. 60 patients were HBeAg-positive and 22 HBeAg-negative at NA initiation. At end-of-treatment all patients were HBV DNA negative with mean HBSAg 2.7 log IU/mL and mean fibroscan 5.5 kPa. Clinical relapse was observed in 28 patients (37% at year 2). Adjusted for pre-treatment HBeAg-status, age was associated with clinical relapse (≥35 vs. ≤35 years: HR 2.80, p = 0.021). 58 (74% at year 2) patients developed a virological relapse (HBV DNA > 2,000 IU/mL) with a following biochemical relapse (ALT > 2x ULN) more often observed in patients with HBV DNA > 200,000 IU/mL at the initial HBV DNA elevation (2 year: 100%) than patients with HBV DNA > 20,000 – <200,000 IU/mL (65%) or HBV DNA > 2,000 – ≤20,000 (51%; p < 0.001). Furthermore, patients with persistent HBV DNA elevation (confirmed >2,000 IU/mL within 3 months) were at higher risk of biochemical relapse (HR 4.0, p = 0.004) than patients without. HBsAg seroclearance occurred in 5 patients (10% at year 2). Patients with end-of-treatment HBsAg ≤100 IU/mL were more likely to clear HBsAg (HR 7.1, p = 0.033).

Conclusions: This prospective stop study demonstrated that the level and persistency of off-treatment HBV DNA elevation can be used to predict relevant ALT elevation, and may thus guide the clinical management of CHB patients who stopped long-term NA.

26. Poster (#FRI-121)
Viral hepatitis: Hepatitis B & D – clinical (therapy, new compounds, resistance)
Date & Time: Friday, April 15, 2016 - 08:00 - 18:00
FIBROTIC BURDEN, NOTANTIVIRAL AGENT, DETERMINES CLINICAL OUTCOME IN CHRONIC HEPATITIS B PATIENTS: A PROPENSITYSCORE MATCHED ANALYSIS
H.S. Kim1, B.K. Kim1, S.U. Kim1, J.Y. Park2, D.Y. Kim1, S.H. Ahn1, K.J. Song1, J. Won Park1, Y.J. Kim1, O. Baatarkhuu2, K.H. Han1.
1. Yonsei University College of Medicine, Seoul, South Korea;
2. Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia

Background and Aims: We investigated whether entecavir (ETV) can reduce the risk of hepatocellular carcinoma (HCC) development compared to lamivudine (LAM) among patients with chronic hepatitis B (CHB) after adjusting for fibrotic burden.

Methods: To adjust for the imbalance between LAM-treated and ETV-treated patients, propensity-score matching (PSM) was performed at 1:1 ratio using seven [PSM-1: age, gender, hepatitis B e antigen (HBeAg), alanine aminotransferase, serum albumin, platelet count, and liver stiffness (LS) by transient elastography] and eight [PSM-2: seven variables of PSM-1 plus ultrasonographic cirrhosis] variables. Rescue therapy was performed for resistant strains.

Results: Four hundred thirty-five and 644 patients received LAM and ETV, respectively, as first-line therapy. During follow-up, 91 (8.4%) patients developed HCC. In multivariate analyses, fibrotic burden (as assessed using LS value; adjusted hazard ratio 1.02, p < 0.05), not antiviral agents independently predicted HCC risks. Propensity-score matching resulted in 342 pairs using PSM-1 variables and 338 pairs using PSM-2 variables. The cumulative rates of HCC development in LAM-treated and ETV-treated patients were similar in both models (PSM-1: 9.7% vs. 9.9% at 5-years and 10.5% vs. 9.9% at 7-years; PSM-2: 10.2% vs. 10.3% at 5-years and 11.9% vs. 12.0% at 7-years; all p > 0.05). When propensity-score matching was applied in the same manner in sub-cohorts with LS ≤ 13 kPa and LS > 13 kPa, cumulative risks between LAM-treated and ETV-treated patients remained similar overall (all p > 0.05).

Conclusions: Underlying fibrotic burden, not antiviral agent, independently influenced HCC risk. Therefore, fibrotic burden should be assessed during antiviral therapy for effective surveillance.

27. Poster (#FRI-158)
Viral hepatitis: Hepatitis C – clinical (except therapy)
Date & Time: Friday, April 15, 2016 - 08:00 - 18:00
GENETIC AND METABOLIC FACTORS RELATED WITH INSULIN RESISTANCE IN CHRONIC HEPATITIS C
1. Gastroenterology, Hospital Clínico San Carlos, Madrid,
Background and Aims: Insulin resistance is more frequent in chronic hepatitis C than in other chronic liver diseases. It has been related with the progression of liver fibrosis and with a greater risk of complications. The reasons why hepatitis C promotes insulin resistance are partially known.

Aims: To evaluate a wide multitest panel including biochemical, metabolic, inflammatory, genetic and virologic parameters in patients with hepatitis C and to identify factors related with insulin resistance.

Methods: Patients with chronic hepatitis C without any antiviral therapy in the previous one year were included. Subjects with decompensated cirrhosis, hepatitis B or HIV coinfection, or previous diagnosis of diabetes mellitus were excluded. In 76 patients, we performed a blood laboratory test which include routine, metabolic and inflammatory parameters (retinol, retinol-binding protein 4, 25-OH vitamin D, Vitamin E, lipopolysaccharide-binding protein, interleukin-6 and cystatin C). Insulin resistance was established with a HOMA value higher than 3. We determined single nucleotide polymorphisms rs7041 and rs4588 GC (Group specific component-Vitamin D-binding protein), rs 738409 PNPLA3 (patatin-like phospholipase domain containing 3), and rs12979860 IL28B (interleukin-28 B) genes. Viral parameters like genotype o viral load were obtained and fibrosis staging was assessed with liver biopsy or transient elastography.

Results: After backward logistic regression analysis, independent variables associated with insulin resistance were: 1) Gc1s/Gc1S Vitamin D-binding protein phenotype, that results from the homozygous carriage of the rs7041G/rs4588C haplotype (p = 0.033); 2) low retinol/RBP4 ratio, reflecting a greater rate of unbound retinol-binding protein 4 (p = 0.005); 3) older age (p = 0.01); 4) high serum triglycerides (p = 0.026), and 5) advanced (F3-F4) fibrosis stage (p = 0.034). The AUROC provided by the multivariate model was 0.950 (95% IC = 0.906–0.993).

Conclusions: In addition to previously known ones, the Gc1s/Gc1s phenotype variant of vitamin D-binding protein and the unbound fraction of plasma retinol-binding protein 4 may be considered as factors related with the incidence, and possibly the risk, of insulin resistance in chronic hepatitis C patients.

28. Poster (#FRI-164)

Viral hepatitis: Hepatitis C – clinical (except therapy)

Date & Time: Friday, April 15, 2016 - 08:00 - 18:00

GLOMERULAR AND TUBULAR KIDNEY INVOLVEMENT IN HCV CHILD-A CIRRHOSIS

D. Palazzo1, E. Biliotti1, F. Tinti1, A. Bachetoni2, P. Perinelli1, A. Cappolli1, M.D. D’Alessandro2, S. Greco2, R. Labriola2, M. Subic3, I. Umbro3, P. Rucci4, A.P. Mitterhofer5, G. Taliani1.
1. Clinical Medicine; 2. Clinical Pathology; 3. Internal Medicine; 4. Biomedical and Neuromotor Sciences, Sapienza University Of Rome, Rome, Italy

Background and Aims: Several evidences suggest that HCV has a negative impact on renal function. In addition renal dysfunction is a complication of liver cirrhosis. The relation between HCV infection and glomerular damage is well recognized, but very limited data are available on HCV-mediated tubular damage. The aim of the study was to assess the presence of renal involvement (RI), glomerular or tubular, in patients with HCV cirrhosis.

Methods: 98 patients with HCV cirrhosis CPT-A were consecutively enrolled. Urinary albumin/creatinine (ACR) and α1microglobulin/creatinine (α1MCR) were calculated. Estimated glomerular filtration rate (eGFR) was calculated with CKD-EPI 2009 equation. Glomerular involvement was defined based on ACR > 20 μg/mg, tubular involvement based on α1MCR > 14 μg/mg plus fractional sodium excretion (FeNa) > 1. Urine concentration of Liver-type Fatty Acid-Binding Protein (L-FABP) and Kidney injury molecule-1 (KIM-1) were examined in morning midstream urine samples. Urine concentrations of KIM-1 and L-FABP were normalized to urine creatinine concentration.

Results: eGFR was ≥60 mL/min/1.73 m2 in 92 patients (93.8%) and between 45 and 59 mL/min/1.73 m2 in 6 patients (6.1%). Glomerular involvement was found in 19 patients (19.4%), tubular involvement in 31 patients (31.6%) and they co-occurred in 10 patients (p = 0.034). Patients with glomerular or tubular involvement, or both, showed significantly lower eGFR values (p = 0.005) (Table 1). A ROC curve was drafted and a cut point of 90 mL/min predicted renal involvement (RI) with increased levels of L-FABP and KIM-1, while glomerular involvement was associated only with high L-FABP level (Table 1).
Conclusions: Tubular and/or glomerular involvement are quite frequent in HCV cirrhotic patients. The occurrence of eGFR < 90 mL/min/1.73 m² allows to recognize patients with chronic renal involvement and should prompt to monitor renal function more closely.

29. Poster (#FRI-175)

Viral hepatitis: Hepatitis C – clinical (except therapy)

Liver stiffness measurement after successful anti-viral therapy in hepatocellular carcinoma risk assessment for chronic hepatitis C patients


1. Division of Hepato-Gastroenterology, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung City, Taiwan.

Background and Aims: Chronic hepatitis C (CHC) patients after successful antiviral therapy remain at risk of hepatocellular carcinoma (HCC). This study was to determine whether liver stiffness measurement (LSM) was useful in HCC risk assessment and develop a risk-score system for clinical use.

Methods: This retrospective study enrolled CHC patients achieved sustained virological response (SVR) after interferon-based therapy with LSM at/after SVR determination. The demographics, clinical characteristics and HCC development were obtained from medical chart reviews. The diagnosis of HCC was based on recommended criteria.

Results: A total of 376 (M/F: 185/191, mean age: 54.1 year) patients, including 278 with pre-treatment liver biopsy specimens, were enrolled. The median follow-up period was 5.7 years. Twenty-one patients, including 18 with pre-treatment biopsy, developed HCC. The 5-year cumulative HCC incidence was 5.1%. Multivariate analysis showed advanced fibrosis/cirrhosis (odds ratio: 12.38, 95% confidence interval: 1.56–98.14), diabetes (2.80, 1.03–7.65) and LSM (1.01, 1.04–1.16) were associated with HCC developments. For LSM in HCC prediction, the performance and cutoff was 0.783 and 12 kilopascal (kPa) respectively. A risk-score system (score 0–4) combining advanced fibrosis/cirrhosis, diabetes and LSM>12 kPa was developed for 278 patients with pre-treatment biopsy. With score 0 and 1 as a reference, patients with score 2 and 3 (hazard ratio: 11.67, 95% confidence interval: 1.48–92.13) and score 4 (112.20, 14.02–897.71) carried higher risk of HCC development.

Conclusions: For CHC patients in SVR, LSM was useful in HCC risk assessment. Patients with pre-treatment advanced fibrosis/cirrhosis, diabetes and LSM>12 kPa after SVR were at high risk of HCC development.

30. Poster (#FRI-178)

Viral hepatitis: Hepatitis C – clinical (except therapy)

Date & Time: Friday, April 15, 2016 - 08:00 - 18:00

HIGH RISK FOR HEPATOCELLULAR CARCINOMA IN CIRRHOTIC PATIENTS WITH SVR FOLLOWING IFN-FREE DAA TREATMENT WITHIN 1 YEAR FOLLOW-UP

K. Kozbial1, R. Stern1, C. Freissmuth1, S. Beinhardt1, A.F. Stattermayer1, P. Munda1, M. Trauner1, P. Ferenci1, H. Hofer1, and Viral Hepatitis.

1. Gastroenterology and Hepatology, Medizinische Universität Wien, Vienna, Austria

Background and Aims: IFN-free antiviral treatment with DAAs improves liver function in many patients with cirrhosis already at the end of therapy, however, results of long-term follow-up are not yet known. The aim of this study was to evaluate patients’ outcomes at follow-up week 48 after interferon-free DAA therapy.

Methods: 154 of 215 patients with cirrhosis treated with IFN-free DAA therapy at our centre completed 12 weeks of treatment free follow up (141[91.6%] SVR12). 28 of them completed ≥48 weeks of follow-up (at the time of abstract submission) and were evaluated in this study (m/f = 19/9; mean age 57.7 ± 7.5 yrs; genotype [GT]-1:19, GT-3:5; GT-4: 4, median baseline liver stiffness 23.4 kPa, 12/16 [75.0%] with clinical significant portal hypertension ≥10 mmHg, 5 listed for transplantation). One patient died on therapy, and one after SVR 4. Data will be updated for the EASL meeting.

Results: SVR was durable during long term follow up. One of the five patients listed for liver transplantation was transplanted four months after end of treatment, three improved markedly and were removed from the list, and one is still actively listed. The overall condition as well as albumin (37.8 vs. 41.2 g/L, p = 0.001), ALT (95.8 vs. 40.2 U/L, p < 0.001), and AFP (27.0 vs. 7.6 IU/mL, p = 0.001) improved in most patients from baseline to FUP48. Child Pugh Score (CPS) changed in 12 patients, it improved in 9 (CPS-B to A: 7, C to A:1, C to B: 1), and worsened in 3 (A to B: 1, B to C: 2). During follow-up HCC was diagnosed in six patients (21.4%) (time to diagnosis after end of treatment: median 8.5 months, range 1–13; m/f = 19/9; mean age 56.5 ± 8.9 yrs; GT-1:5; GT-4:1; HVPG at baseline: 16 mmHg (median); CPS at baseline: A1, B4, C1). At treatment initiation none of them had evidence of HCC by imaging methods and AFP had been in the normal range in three patients, and slightly elevated in the other three. Two additional patients are currently investigated for suspected HCC.

Conclusions: Liver function improved in patients with cirrhosis after successful DAA therapy; however, the risk of HCC remains high. Thus, a vigorous surveillance after achieving SVR in patients with cirrhosis is mandatory.

31. Poster (#FRI-190)

Viral hepatitis: Hepatitis C – clinical (except therapy)

Date & Time: Friday, April 15, 2016 - 08:00 - 18:00

Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Age (yr)</td>
<td>60.2±7.5</td>
<td>0.016</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73 m²)</td>
<td>89.8 (73.1–96.7)</td>
<td>0.015</td>
</tr>
<tr>
<td>KIDOS</td>
<td>3 (4.5±10m/min/1.73 m²)</td>
<td>0.015</td>
</tr>
<tr>
<td>ACR (mg/dL)</td>
<td>3.3 (1.3–9.4)</td>
<td>0.015</td>
</tr>
<tr>
<td>e-timolol ataxinurina (mg/µg)</td>
<td>18.4 (8.8–24.2)</td>
<td>0.015</td>
</tr>
<tr>
<td>L-FABP (ng/mL)</td>
<td>3.61 (1.52–6.16)</td>
<td>0.015</td>
</tr>
<tr>
<td>KIV (ng/mL)</td>
<td>2.42 (1.57–6.17)</td>
<td>0.015</td>
</tr>
</tbody>
</table>

Conclusions: The one interval: 1.56 ± 0.07 evaluated in the other – 1.16 was associated with HCC developments. For LSM in HCC risk assessment, patients with cirrhosis already at the treatment biopsy, developed HCC. This study was to determine whether liver stiffness measurement (LSM) was useful in HCC risk assessment and develop a risk-score system for clinical use.

Methods: This retrospective study enrolled CHC patients achieved sustained virological response (SVR) after interferon-based therapy with LSM at/after SVR determination. The demographics, clinical characteristics and HCC development were obtained from medical chart reviews. The diagnosis of HCC was based on recommended criteria.

Results: A total of 376 (M/F: 185/191, mean age: 54.1 year) patients, including 278 with pre-treatment liver biopsy specimens, were enrolled. The median follow-up period was 5.7 years. Twenty-one patients, including 18 with pre-treatment biopsy, developed HCC. The 5-year cumulative HCC incidence was 5.1%. Multivariate analysis showed advanced fibrosis/cirrhosis (odds ratio: 12.38, 95% confidence interval: 1.56–98.14), diabetes (2.80, 1.03–7.65) and LSM (1.01, 1.04–1.16) were associated with HCC developments. For LSM in HCC prediction, the performance and cutoff was 0.783 and 12 kilopascal (kPa) respectively. A risk-score system (score 0–4) combining advanced fibrosis/cirrhosis, diabetes and LSM>12 kPa was developed for 278 patients with pre-treatment biopsy. With score 0 and 1 as a reference, patients with score 2 and 3 (hazard ratio: 11.67, 95% confidence interval: 1.48–92.13) and score 4 (112.20, 14.02–897.71) carried higher risk of HCC development.

Conclusions: For CHC patients in SVR, LSM was useful in HCC risk assessment. Patients with pre-treatment advanced fibrosis/cirrhosis, diabetes and LSM>12 kPa after SVR were at high risk of HCC development.
INTERFERON-FREE DAA REGIMENS DECREASE PORTAL PRESSURE AND HALT HISTOLOGICAL NECROINFLAMMATION IN HIV/HCV-COINFECTED PATIENTS

P. Schwabl1, M. Mandorfer1, S. Steiner1, B. Scheiner1, T. Bucsic1, M. Aichelburg2, K. Grabeimer-Pfistershammer2, W. Sieghart1, A. Ferlitsch3, M. Trauner1, T. Reiberger1, M. Peck-Radosavljevic1.

1. Division of Gastroenterology and Hepatology, Department of Internal Medicine II; 2. Division of Immunology, Allergy and Infectious Diseases, Department of Dermatology, Medical University of Vienna, Vienna, Austria

Background and Aims: Patients with HIV/HCV confection show increased fibrosis progression and are at risk for complications of portal hypertension (PHT). We measured changes in liver stiffness and portal pressure and evaluated liver histology after successful interferon (IFN)-free DAA therapy.

Methods: HIV/HCV patients undergoing IFN-free DAA treatment and who had paired hepatic venous pressure gradient (HVPG) and liver stiffness (LS) measurements at baseline and three months after end treatment (SVR12) were included. LS and HVPG were measured in a fasted, non-sedated state. Concomitant beta-blocker treatment was stopped for all measurements. Post-treatment liver biopsies were assessed by METAVIR score.

Results: Of 19 patients (56% male, age: 53.4 ± 6.7 years, 95% concomitant antiretroviral therapy), 16 received SOF/DCV, 2 SOF/RBV, and 1 SOF/LED. Seven (37%) patients were treatment naïve. Of 19 patients (56% male, age: 53.4 ± 6.7 years, 95% concomitant antiretroviral therapy), 16 received SOF/DCV, 2 SOF/RBV, and 1 SOF/LED. Seven (37%) patients were treatment naïve. Of 19 patients (56% male, age: 53.4 ± 6.7 years, 95% concomitant antiretroviral therapy), 16 received SOF/DCV, 2 SOF/RBV, and 1 SOF/LED. Seven (37%) patients were treatment naïve. Of 19 patients (56% male, age: 53.4 ± 6.7 years, 95% concomitant antiretroviral therapy), 16 received SOF/DCV, 2 SOF/RBV, and 1 SOF/LED. Seven (37%) patients were treatment naïve.

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BIPHASIC KINETICS OF HCV-RNA DECAY IS ACCOMPANIED BY AN EVEN FASTER AMINOTRANSFERASES NORMALIZATION IN ALL-DAA TREATED CIRRHOTIC PATIENTS: A DIFFERENT SCENARIO FROM INTERFERON-BASED THERAPIES


Background and Aims: With pegylated Interferon-Ribavirin (PR) treatment, alanine aminotransferase (ALT) normalization is slow and follows HCV-RNA clearance, driven by the cytotoxic effect of PR. The new mode of action of direct-acting antivirals (DAAAs), prompted us to explore, in cirrhotic patients (pts), the potential of a rapid “cure” of infected cells.

Methods: 140 HCV-infected pts (36% GT1a, 64% GT1b and 0.7% GT1g) and cirrhosis (11% Child-B; median[IQR] stiffness = 21[16–33] kPa) were treated: 108 with all-DAA regimens, and 32 with telaprevir (TVR) + PR. HCV-RNA and ALT kinetics during treatment (4–8:24–48–72 h, 1–2–3–4 weeks) were studied using a standard biphasic model and an exponential model, respectively. Normal ALT were defined as <45 IU/mL in women and <55 IU/mL in men.

Results: Viral kinetics (VK) fitted into a standard biphasic model. All-DAA treatment showed an impressive first-phase VK: 42.9% of pts had >1 log decay after only 8 h, and the median(QR) decay at 24 h was 2.4 (2.1–2.8) logIU/mL. NSSA-receiving pts had higher values of free virus clearance (c = 7.47 vs 4.86 in NSSA-free regimes), and a more rapid first-phase decline. Second-phase VK was slower and led to HCV-RNA clearance at week-4 (RVR) only 45% all-DAA, similarly to 53% of TVR-PR pts (p = .44). SVR12 rates were lower in non-RVR pts receiving TVR + PR (47% vs 88% in RVR, p = .01), but not in non-RVR all-DAA (96% vs 91%, p = .28). In contrast with VK parameters (not different in all-DAA vs TVR-PR regimes), ALT normalization rate λ was much lower in TVR-PR (0.118 vs 0.244 day−1; p < .001) vs all-DAA. The probability of ALT normalization by week-2 was 98% in all-DAA (vs 68% in TVR-PR, p < .001), while HCV-RNA at week-2 was undetectable in only 11% of all-DAA pts, indicating that ALT normalization precedes HCV-RNA clearance (see Figure). Of interest, HCV-RNA at the time of ALT normalization was higher in all-DAA (median[IQR] = 88[15–336] IU/mL), than TVR-PR (17[0–50] IU/mL; p = .004). Individual parameters of VK and ALT kinetic models had no reciprocal influence (all correlation coefficients <0.4), even comparing the loss rate of infected cell δ and the ALT normalization rate λ.

Conclusions: In cirrhotic pts, all-DAA regimens induce an excellent VK and a remarkably fast ALT normalization. ALT kinetics was much faster than in TVR-PR; their normalization precedes full HCV-RNA clearance. The DAA-driven “sparing” of liver cells (differently by their PR-mediated elimination) provides a rationale for a potentially faster improvement of liver function after HCV curing.

34. Poster (#FRI-205)
Liver immunology including viral hepatitis
Date & Time: Friday, April 15, 2016 - 08:00 - 18:00
LONG-TERM EFFICACY OF RECOMBINANT HEPATITIS B VACCINATION ON PERSISTENT HBS ANTIGENEMIA, RECURRENT OF VIREMIA AND INSULIN RESISTANCE AFTER OFF TREATMENT RESPONSE IN CHRONIC HEPATITIS B PATIENTS
A.S. Hanafi1.
1. Internal Medicine-Hepatology Division, Zagazig University, Zagazig, Egypt

Background and Aims: After disappearance of DNA, the decline in HBsAg is less frequent and level >1000 IU/mL was associated with possibility of viral reactivation and risk of HCC in 8% mainly in HBe negative patients. Patients after anti-HBe serocconversion can present with persistent HBs antigenemia for a long period and find difficulty in indefinite treatment due to financial or compliance issues.

Methods: 220 patients with chronic hepatitis B were enrolled. Group I: inactive carriers (n = 100). Group II: CHB exposed to NAs till 6 months after HBe serocconversion and HBV DNA disappearance (n = 120); HBeAg positive patients (n = 60) and HBeAg negative patients (n = 60), all show persistent HBs antigenemia. Control group (n = 100) with undetectable HBV DNA and persistence of HBs antigenemia, they did not receive HBV vaccine and were followed up for 3 years. Laboratory analysis included quantitative PCR at base line, every 3 months during therapy, then every 6 months after the last dose of HBV vaccine for 3 years. Determination of HbsAb titre 1 month post vaccination. HOMA-IR and Fibroscan before therapy and 3 months
Results: Highly significant reduction in HBsAg (p = 0.000), HOMA-IR (p = 0.000) and fibroscan (p = 0.000). 37 patients (16.8%) were vaccine nonresponders. 183 patients were vaccine responders (83.2%). 62 patients (28.2%) cleared HBsAg, 143 patients showed marked reduction of HBsAg (65%), 15 patients (6.8%) showed non-significant reduction in HBsAg with persistence of HBsAg > 1000 IU/mL. Vaccinated patients were followed up for 3 years by HBsAg quantification and HBV DNA every 6 months; only 4 patients (1.8%) showed recurrence of viremia. Patients with HBsAb titre > 100 IU/mL showed further reduction in the mean HBsAg and another 10 patients in treatment exp eAg negative group with low post vaccination HBsAg (114.5 ± 23 IU/mL) cleared it completely. In control group, 30 patients (30%) showed return of viremia; this highlights the highly significant protective effect of vaccination (χ2 = 57.5, p = 0.000).

Conclusions: HBV vaccination was highly efficient, safe, and cost effective in enhancing HBsAg clearance, causes its reduction to a favorable level less than 1000 IU/mL and halts HBsAg effect on fibrosis progression with durable off treatment response.

Results: 400 patients (280 males and 120 females) were enrolled in our study. The mean age 35.5 ± 4.7 years, they were overweight; mean BMI 27.7 ± 1.7 kg/m², patients with higher fibroscan reading (9 ± 1.01 kPs) showed a statistically highly significant values as regards AST, ALT, GGT (p = 0.000). A statistically highly significant difference in FBS, Insulin, HbA1c, HOMA-IR (p = 0.000), MPV and NLR were significantly higher (p = 0.000). The metabolic biomarkers as RBP4, Ferritin, Uric acid and triglycerides were significantly higher (p = 0.000). Serum level of AFP was significantly higher (8 ± 1.1 ng/dL). Cutoff value of fibroscan associated with severity of fatty liver was 6.85 kPs with sensitivity 90%, specificity 91.8%, AUC 0.94, 95% CI 0.93–0.97. Based on largest β coefficients from regression analysis, fibrosis progression was independently associated with RBP4 (β = 0.416, p = 0.000) at cutoff 48 µg/mL, AFP (β = 0.169, p = 0.000) at cutoff 7.5 ng/mL, MPV (β = 0.083, p = 0.000) at cutoff 9.4 fl, NLR (β = 0.091, p = 0.000) at cutoff 2.05, ferritin (β = 0.242, p = 0.000) at cutoff 321 ng/mL and uric acid (β = 0.215, p = 0.000) at 6.95 mg/dL.

Conclusions: The index correlated efficiently with fibroscan reading and should be applied in wider scale.

### 36. Poster (#FRI-279)

**Fatty liver disease: Clinical**

**Date & Time:** Friday, April 15, 2016 - 08:00 - 18:00

**ASSOCIATION OF INVASIVE ATTENUATION PARAMETER (CAP) AND HBA1C IN PATIENTS WITH FATTY LIVER**

A. Arslanow1, A. Eid2, J. Geisel3, F. Lammert4.

1. Department of Medicine II; 2. Institute of Clinical Chemistry and Laboratory Medicine, Saarland University Medical Center, Homburg, Germany

**Background and Aims:** Chronic liver diseases and serum glycosylated hemoglobin (HbA1c) levels are linked to one another through the metabolic syndrome. Our aim now was to analyze for the first time the potential association between hepatic steatosis, as determined quantitatively with the controlled attenuation parameter (CAP), and HbA1c.

**Methods:** At a tertiary referral center in Germany, we evaluated a group of 212 outpatients with hepatic steatosis retrospectively, of whom 93.4% presented with non-alcoholic liver disease. Hepatic steatosis was assessed non-invasively using controlled attenuation parameter (CAP), which quantifies the degree of ultrasound attenuation based on vibration-controlled transient elastography (VCTE, Fibroscan). Serum HbA1c and liver function tests were measured with standardized clinical chemistry assays. The prosteatotic gene variant PNPLA3 p.I148M was genotyped using Taqman assays.

**Results:** Overall in this cohort (113 men, median age 52 years), median CAP was 293 dB/m (100–400), and 171 (80.7%) patients presented with elevated CAP ≥238 dB/m, indicating marked hepatic steatosis. Median BMI was 30.2 kg/m² (17.2 ± 4.74), median HbA1c ws 5.6% (3.7–10.4) and serum ALT activities were 45 U/l (9–301). The frequency of elevated CAP increased with higher serum HbA1c levels (rs = 0.230, p = 0.001). Patients with both hepatic steatosis and increased HbA1c levels (HbA1c ≥ 6.0%) displayed significantly (p = 0.001) higher CAP values as compared to those with normal levels (312 vs. 286 dB/m). In our cohort, 104 patients (49.0%) carried at least one PNPLA3 p.I148M risk allele. When stratifying for the patient’s PNPLA3 genotype, the genetic association was maintained for carriers of the risk allele p.I148M and normal levels of HbA1c (p < 0.001) but not for those with increased levels. Overall, the risk for hepatic steatosis was independently associated with HbA1c, BMI, ALT and age as determined by multivariate linear regression analysis (all p ≤ 0.013).

**Conclusions:** Non-invasive risk stratification and follow-up of fatty liver in patients with metabolic syndrome is needed because of
potential progression to steatohepatitis. Steatosis as assessed by CAP is associated with HbA1c in non-diabetic individuals, and the combination of these non-invasive markers improves individual risk assessment of patients with chronic liver diseases.

Results: 452 (31.5%) of 1437 eligible patients were managed on the pathway. 114 patients (25.2%) required ELF test (FIB-4 1.30–3.25). Overall, 338 (74.8%) were stratified as having low risk of < F3 fibrosis. 111 patients (25.2%) were stratified as high risk of ≥F3 fibrosis and were eligible for referral. To date hospital data are available for 57 cases. 19 patients are awaiting investigations or have normal LFTs (thus were inappropriate for pathway). In the remaining 38 patients, a diagnosis of ≥F3 fibrosis was made in 20 patients (52.6%) compared to 3/79 (3.8%) for non-pathway referrals, and 6/85 (7.1%) pre-pathway (Figure 1). Cirrhosis detection increased by 250%. For 5/8 (62.5%) cirrhotics detected via the pathway, CLD was not evident from clinical examination, bloods or ultrasound.

Conclusions: Early analysis of the C&I NAFLD pathway demonstrates NAFLD risk-stratification using FIB-4 & ELF in primary care increases detection of ≥F3 fibrosis & cirrhosis, and reduces referrals of patients with <F3 disease. The pathway displays early promise in addressing an important clinical challenge.

37. Poster (#FRI-280)
Fatty liver disease: Clinical
Date & Time: Friday, April 15, 2016 - 08:00 - 18:00
PRIMARY CARE SEQUENTIAL USE OF FIB-4 AND THE ENHANCED LIVER FIBROSIS TEST TO STRATIFY PATIENTS WITH NONALCOHOLIC FATTY LIVER ACIDE DOUBLES CIRRHOSIS DETECTION AND REDUCES REFERRALS OF PATIENTS WITH MILD DISEASE
A. Srivastava1,2, R. Gailer3,4, S. Demma1,2, A. Warner3,4, D. Suri3, S. Morgan4, S. Tanwar3, K. Sennett5, D. Thorburn1,2, J. Parkes1,7, E. Tsochatzis1,2, W. Rosenberg1,2 and Camden and Islington Liver Working Group.

Background and Aims: Identifying patients with non-alcoholic liver disease (NAFLD) who may develop cirrhosis in primary care is challenging. Patients with advanced fibrosis remain undiagnosed until presenting with decompensated cirrhosis, whilst many with mild disease are referred to busy specialist clinics. In March 2014, Camden & Islington (C&I) Healthcare commissioned a risk stratification pathway using FIB-4 followed by ELF test for indeterminate cases. We present effectiveness data at 1 year.

Methods: Patients with NAFLD & abnormal transaminases were eligible for pathway entry from March 2014. Patients were stratified to low risk (FIB-4 < 1.30; or FIB-4 1.30–3.25 & ELF < 9.5) or high risk (FIB-4 > 3.25; or FIB-4 4.130–3.25 & ELF > 9.5) indicative of ≥F3 fibrosis. Only high-risk patients were recommended for referral. After one year, the C&I electronic database was interrogated for aggregate pathway data. Hospital records were reviewed at Royal Free London, UCLH & Whittington Hospital to determine outcomes of all referred patients. The primary endpoint was “consultant’s final fibrosis assessment” - a binary outcome: Advanced fibrosis/Cirrhosis vs. lesser degree/no fibrosis based on composite of liver histology (when available), imaging, Fibroscan, bloods & clinical judgement. Diagnostic performance was compared between pre-pathway (2012–2013) & those referred on the pathway and outside the pathway (2014–15).

38. Poster (#FRI-297)
Fatty liver disease: Clinical
Date & Time: Friday, April 15, 2016 - 08:00 - 18:00
QUANTIFICATION OF LIVER STEATOSIS USING THE NEW SCORE ULTRASOUND FLI (FATTY LIVER INDEX) AND CAP (CONTROLLED ATTENUATED PARAMETER): A COMPARATIVE ANALYSIS
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Background and Aims: Ultrasound FLI (US-FLI) is a new scoring system ranging 2–8 based on the intensity of liver/kidney contrast (0–3), posterior attenuation of ultrasound beam (0–1), vessel blurring (0–1), difficult visualization of gallbladder wall (0–1), difficult visualization of the diaphragm (0–1) and areas of focal sparing (0–1). So far, US-FLI was correlated with severity and the presence NASH assessed histologically. The association between US-FLI and CAP values has not been described. The aim of this study was to compare the US-FLI with CAP in detection and quantification of liver steatosis and correlated with clinical, anthropometric and laboratory parameters.

Methods: We studied patients with metabolic syndrome or type 2 diabetes mellitus in outpatients from october 2013 to august 2014. Other liver diseases, alcohol consumption ≥20 g/day and use of drugs associated with liver steatosis were excluded. Were evaluated: US-FLI (medical operator was blinded both to clinical information and to CAP value), liver elastography with CAP, weight, BMI, waist circumference, glycated hemoglobin, total cholesterol, LDL, HDL, triglycerides, GGT, platelet. The US-FLI was categorized as <4 and ≥4 and CAP categorized into <296 dB/min and ≥296 dB/min (≥66% steatosis).

Results: Overall, 102 patients with US FLI score were included (mean age 61 ± 10; 70% female), 93 with CAP value. 73% had diagnosis of DM, 83% had hypertension, 81% had dyslipidemia and 25% had HbA1c ≥6.0%.

Comparative analysis of US FLI and CAP was performed in 93 patients. The FLI was categorized as <4 and ≥4 and CAP was categorized into <296 dB/min and ≥296 dB/min (≥66% steatosis). The FLI distribution was 93.6% and 6.4%, while the CAP distribution was 97.8% and 2.2%. There was a strong correlation between US FLI and CAP. Differences in mean values between groups were significant for all parameters.
95% had metabolic syndrome. The weight was 80 ± 16 kg, BMI 32 ± 10 kg/m2 and the waist circumference of 104 ± 15 cm. 56% had FLI US ≥4 and 46% steatosis ≥66% by CAP. Variables associated with FLI US ≥4 were: fibrosis (kPa) (p = 0.008); BMI (p = 0.003); triglycerides (p < 0.001). The sensitivity (S), specificity (SP), positive predictive value (PPV), negative predictive value (NPV) of US-FLI ≥4 for steatosis ≥66% by CAP were: 88%, 72%, 73% and 88%. The AUROC of US-FLI ≥4 for steatosis ≥66% by CAP was 0.86. The agreement between the US FLI ≥4 with CAP ≥ 66% steatosis was significantly (p < 0.001; k = 0.59). US FLI ≥4 obtained S = 92%, E = 80% PPV = 85% and NPV = 89% in the detection of CAP ≥279, with highest concordance (p < 0.001; k = 0.73) and highest AUROC (0.90).

Conclusions: US-FLI have good accuracy in detecting severe steatosis and was as effective as the CAP. As the ultrasound tool easily accessible, the US-FLI should be better studied for diagnosis and quantification of liver steatosis.

### 39. Poster (#FRI-299)

**Fatty liver disease: Clinical**

**Date & Time:** Friday, April 15, 2016 - 08:00 - 18:00

**STEATOMETER: A NEW ULTRASOUND IMAGING SYSTEM FOR NON INVASIVE, NON-IONIZING FATTY LIVER MEASUREMENT**


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**Background and Aims:** Fatty-liver is increasing worldwide with overall healthcare-costs, mainly from cardiometabolic-diseases. Reliable non-invasive, cheap and non-ionizing imaging measurement systems are needed. We developed a software system (Steatometer) to analyse ultrasound (US) images for the liver fat quantification.

**Methods:** Liver fat was measured by Steatometer, CAP (Fibroscan, Echosense) and Magnetic Resonance Spectroscopy (MRS) in 52 (median age 55, range 35–74; 25 males) consecutive subjects undergoing abdominal US-scan because of metabolic-syndrome. Steatometer measures were obtained in all, Cap in 45 and MRS in 7. MRS was used as gold-standard and obtained with a 3-T clinical scanner (Philips Medical Systems, Eindhoven, the Netherlands). Capindex measures the US-attenuation-rate (decreased amplitude of USwaves propagating through the liver) obtained with a dedicated equipment. Steatometer B-mode images were acquired using standard-US-scanners in right inter/subcostal views (in supine/lateral position) and elaborated to calculate 5 parameters (hepaticrenal ratio, hepatic-portal-vein ratio, attenuation-rate, diaphragm and portal-vein-wall visualization) and an overall score as their linear combination.

**Results:** Steatometer-score (3.39, [−2.1+10.84]) was significantly related to MRS-measures (13.71, [0.45+39.62]) and CAP-score (281.33, [152÷394]) [r = 0.810, p < 0.005 and r = 0.574, p < 0.01, respectively]. Regression-analysis of the relationship between Steatometer and MRS/CAP fat measurements defined the Steatometer-score as 0.841 + (0.25*MRS-score) and −5.833 + (0.032*CAP-score), respectively. The model-R2 were 0.91 for MRS and 0.32 for CAP and effect-size Cohen’s f were 3.18 and 0.68 for the two models, respectively. The stronger link between Steatometer/MRS than Steatometer/CAP could be explained by the fact that MRS measures fat directly, Steatometer relies on multiple indirect parameters associated with steatosis while CAP on just one of them, the attenuation-rate.

**Conclusions:** The ultrasound imaging system Steatometer is a reliable tool for non invasive, non-ionizing quantification of fatty liver applicable to any standard US scanner. The Steatometer score shows the highest correlation with MRS and can be used for screening and monitoring fatty liver in both clinical trials and clinical practice.

### 40. Poster (#FRI-303)

**Fatty liver disease: Clinical**

**Date & Time:** Friday, April 15, 2016 - 08:00 - 18:00

**NON-INVASIVE TESTS FOR THE DIAGNOSIS OF LIVER FIBROSIS ARE ALSO PROGNOSTIC MARKERS IN NON-ALCOHOLIC FATTY LIVER DISEASE**

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**Background and Aims:** Last 2015 EASL guidelines state that noninvasive tests of liver fibrosis require further validation in nonalcoholic fatty liver disease (NAFLD). We aimed to evaluate the prognostic accuracy of 4 blood fibrosis tests and, for the first time, liver stiffness measurement by Fibroscan (LSM) in patients with NAFLD.

**Methods:** All consecutive patients who had a non-invasive evaluation of liver fibrosis in our Department between January 2005 and December 2009 were retrospectively enrolled. Patient follow-up started the day of the non-invasive testing and ended November 15, 2014. The date and cause of death were obtained by consulting the national death registry. The prognostic accuracy of fibrosis tests was evaluated using the C-index of Harrell that is interpreted as follow: 1: perfect prediction, 0.5: random prediction, and <0: prediction in the opposite direction that expected.

**Results:** 614 patients were enrolled. 556 patients had LSM with Fibroscan (M probe), and 418 had blood sampling that allowed for the calculation of APRI, FIB4, Hepascore, and FibroMeterV2G. LSM and the 4 blood tests were all available in 360 patients. The median follow-up of these 360 patients was 6.4 years (1st and 3rd quartiles: 5.1–7.8) during which 83 died (17 from liver-related cause). For the prediction of overall death, C-indexes of Harrell were: APRI: 0.544 [0.463–0.614], FIB4: 0.696 [0.636–0.752], LSM: 0.725 [0.659–0.782], Hepascore: 0.732 [0.665–0.791], and FibroMeterV2G: 0.789 [0.742–0.834] (APRI vs others: p < 0.001, FibroMeterV2G vs others: p ≤ 0.013). For the prediction of liver-related death, C-indexes of Harrell were: APRI: 0.689 [0.490–0.839], FIB4: 0.778 [0.663–0.880], FibroMeterV2G: 0.844 [0.753–0.925], Hepascore: 0.853 [0.738–0.938], LSM: 0.885 [0.818–0.947] (APRI vs LSM or FibroMeterV2G: p < 0.045). The diagnostic fibrosis classifications of LSM (7 classes) and FibroMeterV2G (6 classes) individualized several subgroups of patients with significant different prognosis: the higher was the class of the fibrosis classification, the worse was the prognosis. Pattern of the survival curves thus obtained was similar to previously published for the pathological fibrosis stages.

**Conclusions:** The non-invasive tests initially developed for the diagnosis of liver fibrosis are also prognostic markers in NAFLD. In clinical practice, these tests identify the patients with an impaired prognosis for whom a specific management is required.

### 41. Poster (#FRI-308)

**Fatty liver disease: Clinical**

**Date & Time:** Friday, April 15, 2016 - 08:00 - 18:00

**THE ROLE OF SYSTEMIC INFLAMMATION AND ENDOTHELIAL DYSFUNCTION IN PATHOGENESIS OF CARDIOVASCULAR DISEASE IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE**

K. Pivtorak1.
42. Poster (#FRI-311)

Fatty liver disease: Clinical
Date & Time: Friday, April 15, 2016 - 08:00 - 18:00

THE USE OF AN INULIN-TYPE PREBIOTIC IN NON-ALCOHOLIC STEATOHEPATITIS

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Background and Aims: Liver steatosis is one of the most common diseases of the liver, triggered and influenced by a series of factors and in strong connection to cardiovascular risk factors (metabolic syndrome). This prospective study aims to analyze the effects of an inulin type prebiotic in patients with non-alcoholic steatohepatitis.

Methods: We included 64 patients, 28 of which were males, with a mean age of 54.83 ± 20.15 years. The patients were evaluated with serologic markers, transient elastography and abdominal ultrasonography to determine the degree of steatosis/steatohepatitis. All of them were given 16 g Sinergin® (Innergy), an inulin type prebiotic, daily, for two months. Before and after the treatment we performed abdominal ultrasonography, transient elastography (Fibroscan®), serum determination of tumor necrosis factor alpha and glycaemia, serum insulin and glycosylated haemoglobin for the diabetic patients.

Results: 46 patients had diabetes mellitus, 13 of them requiring insulin treatment. According to the body mass index, 15 patients were of normal weight (8 men and 7 women), 32 were overweight (13 men and 19 women) and 17 were obese (7 men and 10 women). In all patients the echographic aspect of the liver improved after treatment. Furthermore, the degree of liver fibrosis quantified by Fibroscan® decreased significantly, both in patients with diabetes and patients with higher body mass index. NASH score evaluated by Fibromax also improved in all patients. Patients undergoing treatment with oral antidiabetic agents had a higher response than those treated with insulin (p = 0.03). Also, women had a better response than men (p = 0.001). Obese patients had a significantly higher decrease in liver stiffness than overweight patients (p = 0.02) and patients with normal body mass index (p < 0.001). In terms of diabetic control, lower levels of glycaemia and glycosylated haemoglobin were noticed in all patients, in absence of any other chance in the therapeutic scheme. Better results were noticed in patients with oral anti diabetic treatment. Serum levels of tumor necrosis factor alpha were lowered in all categories of patients, particularly in obese patients (p = 0.004) and patients undergoing treatment with insulin (p = 0.03).

Conclusions: We conclude that the use of an inulin type prebiotic is associated with a better fibrosis score and decreased levels of inflammation markers particularly in patients with diabetes mellitus regardless of treatment and in patients with high body mass index.

43. Poster (#FRI-312)

Fatty liver disease: Clinical
Date & Time: Friday, April 15, 2016 - 08:00 - 18:00

THE ACCURACY OF TRANSIENT ELASTOGRAPHY AND COMPARISON OF NON-INVASIVE MARKERS FOR ASSESSING FIBROSIS IN KOREAN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Background and Aims: The prevalence of non-alcoholic fatty liver disease (NAFLD) is growing worldwide. We investigated whether liver stiffness (LS) and controlled attenuation parameter (CAP), assessed using transient elastography (TE), could assess liver steatosis and fibrosis accurately.

Methods: In a total 214 patients who underwent liver biopsy and concomitant TE were recruited from a tertiary hospital in Korea and finally analyzed between November 2011 and December 2014. We assessed liver fibrosis using APRI, NAFLD fibrosis score, and FIB-4.

Patients with NAFLD exhibited a mean age of 39.7 years and male predominance (n = 103) and NAFLD group (n = 111) according to the results of liver biopsy. Patients with NAFLD exhibited an average age of 39.7 years and male predominance (n = 85, 76.6%). The accuracy of CAP in detecting ≥S1, ≥S2, and ≥S3, assessed by the area under the receiver operating curve (AUROC), were 0.882, 0.906, and 0.870, respectively. The optimal cut-off values for steatosis were 248 dB/m for S1, 281 dB/m for S2, and 315 dB/m for S3. Also, the AUROC of LS in detecting ≥F2, ≥F3, and ≥F4 were 0.887, 0.958, and 0.986, respectively. The optimal cut-off values for fibrosis in patients with NAFLD were 7.65 dB/m for F2, 8.75 dB/m for F3, and 14.45 dB/m for F4. The sensitivity and specificity of the optimal cut-off for detecting ≥F3 and F4 were good (100 and 72% vs. 80.0 and 98.0%, as well as better than other non invasive markers such as APRI, NAFLD fibrosis score and FIB-4. About 24 (21.6%) patients with NAFLD showed discordance between TE and histology. The predictive factors for discordance were age, body mass index (BMI), and the grade of steatosis.

Conclusions: TE showed the accurate detection of body mass index (BMI) and the grade of steatosis.
showed better sensitivity and specificity for detecting advanced fibrosis and cirrhosis than other noninvasive markers.

44. Poster (#FRI-313)
Fatty liver disease: Clinical
Date & Time: Friday, April 15, 2016 - 08:00 - 18:00
THE SIGNIFICANT ASSOCIATION BETWEEN CONTROLLED ATTENUATION PARAMETER MEASURED BY TRANSIENT ELASTOGRAPHY AND VISCERAL FAT, NOT BODY MASS INDEX
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**Background and Aims:** Visceral fat area (VFA) measured by computed tomography (CT) can assess the amount of visceral fat tissue precisely and accurately, representing central obesity. Controlled attenuation parameter (CAP) is noninvasive method of measuring hepatic steatosis with high accuracy. Although the central obesity significantly contribute to occurrence of hepatic steatosis, but the relationship between CAP value and VFA is not investigated yet.

**Methods:** A total of 304 consecutive subjects who underwent general health examination including abdominal ultrasonography, transient elastography and abdominal fat CT at one tertiary center in Korea were enrolled prospectively. In this study, significant steatosis was diagnosed when patients have both 1) abdominal ultrasonography finding suggestive of hepatic steatosis and 2) CAP value ≥250 dB/m.

**Results:** The mean age (165 male, 139 female) were 56.5 years. Multivariate linear regression analysis revealed that visceral fat area (VFA) was significantly related with CAP value, together with triglycerides (TG), and alanine aminotransferase. In the multiple logistic regression analysis, VFA (odd ratio [OR], 0.99; 95% confidence interval [CI], 0.97–1.01; p = 0.028) and TG (OR, 1.00; 95% CI, 1.00–1.01; p = 0.02) were selected as independent risk factors for significant hepatic steatosis. When the study population was stratified into three groups (VFA ≤ 100 cm2, VFA 100.1–200 cm2, VFA >200 cm2), patients with a higher VFA were at a greater risk of significant hepatic steatosis with OR of 4.838 (p < 0.001; 95% CI, 2.912–8.039) for VFA 100.1–200 cm2; OR of 7.474 (p < 0.001; 95% CI, 1.32–12.69); p = 0.02. In the validation set, 216 patients were included. Fibrosis distribution was F0: 58.8% (127/216), F1: 19.0% (41/216), F2: 11.6% (25/216), F3: 9.7% (21/216) and cirrhosis 1% (2/216). 12% (26/216) of patients showed a NAS score higher than 5. Rs1421085 genotype distribution was: CC 14.4% (31/216), CT 43.5% (94/216) and TT 42.1% (91/216). Genotype CC was found associated with NAS score >5 [OR: 5.19 (95% CI 1.03–5.19); p = 0.04].

**Conclusions:** Our data demonstrated that VFA was significantly related with significant hepatic steatosis assessed by CAP, suggesting that surveillance of hepatic steatosis is needed for patients with central obesity.

45. Poster (#FRI-318)
Fatty liver disease: Clinical
Date & Time: Friday, April 15, 2016 - 08:00 - 18:00
THE FTO RS1421085 T > C POLYMORPHISM IS ASSOCIATED WITH THE SEVERITY OF NON-ALCOHOLIC FATTY LIVER
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**Background and Aims:** It has been recently described the role of FTO rs1421085 T > C polymorphism in the down-regulation of adipocyte thermogenesis and its association with obesity development. The aim of our study was to evaluate the role of FTO rs1421085 variant in NAFLD severity in a cohort of Spanish patients.

**Methods:** Cross-sectional multicentre study including a cohort of consecutive NAFLD patients. Patients from a single centre as well as a subset of healthy controls composed estimation cohort. Diagnosis of NAFLD was established according to clinical, ultrasonography, and transient elastometry criteria, and also histological evaluation when available. FTO rs1421085 SNP was determined by allelic discrimination using Taqman probe. A set of biopsy-proven multicentre NAFLD patients was used as validation cohort.

**Results:** 393 subjects were genotyped: 185 NAFLD patients and 208 healthy volunteers. Genotype frequency was similar between both groups. Rs1421085 genotype distribution in NAFLD patients was: CC 22.2% (41/185), CT 49.2% (91/185) and TT 28.6% (53/185). In 88/185 cases (47.6%) liver biopsy was performed. Of them, 60% (53/88) of patients confirmed NASH diagnosis according Brunt’s classification. Additionally, in absence of histological data, the diagnosis of NASH was established in 5/97(5.2%) cirrhotic patients according to transient elastometry, biochemistry and clinical criteria. A statistically significant higher proportion of CC genotype was found among NASH compared to steatosis simple patients (32.8% (19/58) vs 17.3% (22/127); [O.R. 2.33 (95%CI 1.14–4.76); p = 0.03]. In the subset of patients with BMI ≤ 40 kg/m2 40.54% (75/185), these differences were remarkable (40%/10/25) vs 14%/7(50); [O.R. 4.10 (95%CI 1.32–12.69); p = 0.02]. In the validation set, 216 patients were included. Fibrosis distribution was F0: 58.8% (127/216), F1: 19.0%(41/216), F2: 11.6% (25/216), F3: 9.7%(21/216) and cirrhosis 1% (2/216). 12% (26/216) of patients showed a NAS score higher than 5. Rs1421085 genotype distribution was: CC 14.4% [31/216], CT 43.5% (94/216) and TT 42.1% (91/216). Genotype CC was found associated with NAS Score >5 [O.R. 2.55 (95% CI 0.97–6.69); p = 0.05] and lobular inflammation [O.R. 2.32 (95%CI 1.03–5.19); p = 0.04].

**Conclusions:** To our knowledge, this is the first study showing an association between FTO rs1421085 and NAFLD severity. The reduction in adipocyte mitochondrial thermogenesis of this polymorphism could be associated, with the severity of liver injury in non-morbid obese NAFLD.

46. Poster (#FRI-327)
Fatty liver disease: Clinical
Date & Time: Friday, April 15, 2016 - 08:00 - 18:00
PERFORMANCE OF FIBROSCAN® IN THE ASSESSMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE/NON-ALCOHOLIC STEATOHEPATITIS PATIENTS: INTERIM RESULTS OF A PROSPECTIVE MULTICENTRE VALIDATION STUDY
1. NHRI Liver Biomedical Research Unit and Centre for Liver Research, University of Birmingham, Birmingham; 2. Institute of cellular medicine – Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne; 3. NHRI Nottingham Digestive Diseases Biomedical Research Unit, NHS Trust and University of Nottingham, Nottingham; 4. UCL Institute for Liver and Digestive Health, Royal Free Hospital, London, United Kingdom; 5. Department of Pathology, Physiology and Imaging, Beaujon Hospital Paris Diderot University, Paris, France

**Background and Aims:** The aim of this study is to prospectively evaluate the feasibility and diagnostic performance of liver stiffness (LS) as measured by a FibroScan (Echosens, France) system equipped

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EASL 2016 | Communications about FibroScan®
with both M and XL probes in patients with non-alcoholic fatty liver disease (NAFLD).

**Methods:** Patients fulfilling the following inclusion criteria were prospectively enrolled between March 2014 and May 2015: liver biopsy (LB) for investigation of suspected NAFLD and FibroScan examination within 2 weeks, absence of viral hepatitis, alcohol consumption <16 g/day for women and <24 g/day for men. LB were read in a blinded manner by two expert pathologists. LS was measured using either the M or the XL probe depending on the automatic recommendation made by the device based on the skin to liver capsule distance.

**Results:** 117 patients (57% male, age 52.7 ± 13.3 years, BMI 33.2 ± 6.2 kg/m² range [19.9–47.8]) were recruited. In 56% of patients LS was performed with the XL probe and BMI of these patients was higher (36.5 ± 5.8) than for those measured with the M probe (28.8 ± 3.6; p < 10–12). Ten valid LS readings were obtained for all of these patients, and according to Boursier’s [1] criteria only four were considered as unreliable (all with BMI above 40). Consensus Kleiner fibrosis stage (F) and steatosis grades (S) were F0 21%, F1 25%, F2 21%, F3 23%, F4 9% and S0 10%, S1 23%, S2 34%, S3 32% respectively. NAS score was 0–26%, 3–4 33% and 5–8 40%. Fibrosis stage was significantly associated with LS (p < 10–10) by 2-way ANOVA and was not influenced by steatosis grade (p = 0.86). Of the 117 cases measured either by M or XL probe, the AUROC values (95% CI) for LS were 0.81 (0.72–0.89), 0.80 (0.72–0.88), 0.84 (0.76–0.91) and 0.92 (0.86–0.98) for F ≥ 1, F ≥ 2, F ≥ 3 and F = 4, respectively. The cut-off values maximizing the Youden index were 8.5 kPa (Se 0.61, Sp 0.92, NPV 0.39, PPV 0.97), 8.6 kPa (Se 0.70, Sp 0.78, NPV 0.69, PPV 0.79), 9.7 kPa (Se 0.79, Sp 0.78, NPV 0.89, PPV 0.64) and 10.5 kPa (Se 1.00, Sp 0.75, NPV 1.00, PPV 0.30) for F ≥ 1, F ≥ 2, F ≥ 3 and F = 4, respectively.

**Conclusions:** These data indicate that with the M/XL probe reliable LS readings can be obtained in 97% of patients across a range of BMI up to 48 kg/m², and that a common cut-off can be used for both probes. Moreover, these data indicate that steatosis does not adversely influence assessment of liver fibrosis.

**Reference**

### 47. Poster (#FRI-328)

**Fatty liver disease: Clinical**

**Date & Time:** Friday, April 15, 2016 - 08:00 - 18:00

**ELEVATED MEAN PLATELET VOLUME IMPROVES CURRENT NON-INVASIVE MARKERS OF FIBROSIS AND PREDICTS ACUTE CARDIOVASCULAR EVENTS IN NON-ALCOHOLIC FATTY LIVER DISEASE PATIENTS**

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**Background and Aims:** The purpose of this study was to investigate whether elevated Mean Platelet Volume (MPV) could predict advanced fibrosis stage and/or increased cardiovascular risk in nonalcoholic fatty liver disease (NAFLD) population.

**Methods:** Consecutive patients with biopsy proven NAFLD were evaluated: Anthropometric tests, medications, concomitant diseases, biochemistry were prospectively collected. QRISK2 score which predicts cardiovascular risk over a 10-year period was used. Acute vascular events included acute coronary syndrome, intervention, pulmonary embolism, strokes and transient ischaemic attacks. Biopsies were scored using Kleiner classification. APRI, FIB4, NAS and BARD scores were calculated. Liver Stiffness was measured by FibroScan®.

**Results:** 198 patients were included: Median age 53(19–78); 132 (67%) male. Median follow up was 63(14–89) months. 107(54%) had DM, 90(46%) hypertension, 125(63%) on a statin. Median BMI was 29 (21–53). Liver Stiffness was available in 188 patients with median values 8.1(3–34) kpa. 72(36%) patients had elevated MPV values (11.5–13.8 fl). Elevated MPV values were associated with lower platelet counts (p < 0.001) and higher total bilirubin (p = 0.024). Seventeen (9% of population) acute vascular events (AVE) were recorded over the follow up time. Univariately, age, male gender, hypertension and elevated MPV were associated with AVE. Logistic regression showed that MPV is an independent predictor of acute vascular events, with a HR of 7.2 (p = 0.011; 95% CI, 1.58–32.5). The area under the receiver-operating characteristics (AUROC) curves of QRISK2, MPV and QRISK2*MPV (combination of QRISK2 with MPV) for predicting AVE were 0.73 (p = 0.015, 95%CI 0.57–0.89), 0.88 (p = 0.011, 95%CI 0.57–0.89) and 0.90 (p = 0.0001, 95%CI 0.84–0.97) respectively. At a cut-off value of 2.9 for QRISK2*MPV, we could predict AVE with 81% sensitivity, 81% specificity, PPV 80% and NPV 84%. Fibrosis stage 4 was found in 25 (13%), and stage 3 in 97 (49%) patients. AUROCs for APRI, BARD, NAS, MPV, FIB4, stiffness and FIB4*MPV of predicting F ≥ 3 were 0.59, 0.7, 0.76 (p = 0.016), 0.73 (p = 0.0001), 0.77 (p = 0.0001), 0.826 and 0.827 (p = 0.0001) respectively. At a cut-off value of 11 for FIB4*MPV, we could predict F ≥ 3 with 82% sensitivity, 71% specificity, PPV of 79% and NPV of 55%.

**Conclusions:** Elevated MPV is strongly associated with advanced fibrosis and cardiovascular risk. Accommodating MPV in QRISK2 and FIB4 significantly improves their performance in selecting patients at risk of cardiovascular events and advanced fibrosis.

### 48. Poster (#FRI-340)

**Fatty liver disease: Clinical**

**Date & Time:** Friday, April 15, 2016 - 08:00 - 18:00

**EFFICACY OF GLUTATHIONE FOR THE TREATMENT OF NONALCOHOLIC FATTY LIVER DISEASE: AN OPEN-LABEL, MULTICENTER, PROSPECTIVE STUDY**

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Background and Aims: Non-alcoholic fatty liver disease (NAFLD) can progress to non-alcoholic steatohepatitis (NASH), cirrhosis and hepatocellular carcinoma. NAFLD/NASH is considered a hepatic manifestation of metabolic syndrome and is particularly associated with insulin resistance, obesity, and oxidant stress. However, no effective drug therapy for NAFLD has been established yet. Glutathione (GSH) is the most prevalent low-molecular-weightthiol in mammalian cells. It is crucial for antioxidant defense and the regulation of pathways essential for whole body homeostasis. Therefore we evaluated the efficacy of GSH treatment in NAFLD patients in this present study.

Methods: Thirty-one NAFLD patients (15 men and 16 women: mean age, 50.8 ± 13.3) seen between September 2013 and October 2015 were enrolled in the present study. All the patients received GSH (300 mg/body/day) for 4 months. We compared the alterations of not only clinical parameters but also image-view observations (steatosis and liver fibrosis) by follow-up transient elastography before and after the treatment of GSH. The reduced form of L-Glutathione (KOJIN Life Sciences, Tokyo) was produced by fermentation with Torula yeast by KOJIN Life Sciences, a subsidiary of Mitsubishi Corporation Life Sciences (Tokyo, Japan). This product has been qualified for Generally Recognized As Safe status by the U.S. Food and Drug Administration (U.S. FDA GRAS notified GRN00293).

Results: The serum ALT, γ-glutamyl transpeptidase, LDL cholesterol, triglyceride, free fatty acid, and ferritin levels were significantly improved by the treatment with GSH for four months. In image-view observations, follow-up Transient Elastography revealed that steatosis grade were also significantly improved. The fibrosis stage did not change significantly. As a result of sub-analysis, the effect of GSH on NAFLD patients with diabetes mellitus and severe fibrosis were poor.

Conclusions: Major clinical parameters and image-view observation (steatosis) were significantly improved by the treatment with GSH. Our pilot study demonstrated the efficacy of GSH for drug therapy of NAFLD/NASH and may lead large-scale clinical trial in future. (Funding) KOJIN Life Science provided Glutathione and partial financial support for this work. However, they were not involved in any data analysis or manuscript preparation.

50. Poster (#FRI-342)
Fatty liver disease: Clinical
Date & Time: Friday, April 15, 2016 - 08:00 - 18:00

DUODENAL-JEJUNAL BYPASS LINER (ENDOBARRIER®) TREATMENT IMPROVES NON-ALCOHOLIC FATTY LIVER DISEASE
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Background and Aims: Non-alcoholic fatty liver disease (NAFLD) is strongly associated with the metabolic syndrome. The duodenaljejunal bypass liner (DJBL), a temporarily placed barrier in the upper gastrointestinal tract, is a new endoscopic method for treatment of type 2 diabetes mellitus (T2DM) and obesity. Recent studies show promising effects of DJBL treatment on weight loss and glycemic control. However, the impact of DJBL on NAFLD has not been studied so far.

Methods: Patients undergoing DJBL treatment (EndobARRIER®, GI dynamics, Lexington/MA, USA) for T2DM and/or obesity were noninvasively assessed for the presence and severity of NAFLD. Body mass index (BMI), laboratory values, and liver stiffness measurement (transient elastography, TE, using M- and XL-probe as appropriate) including steatosis assessment with controlled attenuation parameter (CAP) were evaluated before and 24 weeks after DJBL placement.

Results: DJBL was successfully placed in 31 patients. In two cases, the device was removed after <2 weeks due to discomfort. The remaining cohort (59% female, median age/range 57/35–65 years) achieved a significant weight loss (BMI baseline 39.5 ± 8.6 vs. 35.6 ± 8.5 kg/m2, p < 0.001) and improved glycemic control (glycated hemoglobin 7.3 ± 1.3 vs. 6.9 ± 1.2%, p = 0.049) after 24 weeks of DJBL treatment, which was associated with a significant decline of median alanine aminotransferase levels (p < 0.001). Serial TE assessment was feasible in 22 patients, whereas repetitive TE failed in seven cases due to high skin-to-liver capsule distances at the measuring site. Liver stiffness (6.3/2.9–16.8 vs. 4.7/2.5–10.8 kPa, p = 0.021) and CAP score, CAP and TE were defined as previously published. Patients were categorized according to NAS and Metavir indexes in absence (S < 2) or presence of significant steatosis (S ≥ 2) and absence (F < 2) or presence of significant fibrosis (F ≥ 2). Univariate and multivariate analysis were performed to identify independent variables of significant steatosis and fibrosis. Diagnostic accuracy (AUROC) of CAP and TE was evaluated to identify S ≥ 2 and F ≥ 2.

Results: We evaluated 802 patients with BMI ≥28 kg/m2. We exclude 88 (11%) patients with inadequate TE using M probe. Patients with suitable values of TE (probe M), CAP, NAFLD fibrosis score and liver biopsy (n = 85) were included in the study. Liver disease was CHC in 41 (48%) patients, CHB in 23 (27%) and NAFLD in 21 (25%). Median age was 49 years, 69% were men, 34% with metabolic syndrome and median BMI 31 kg/m2. Liver biopsies showed that 24% of patients had S ≥ 2 and 35% F ≥ 2. The only variable independently associated (OR, 95%CI, P) with steatosis was the CAP (1.02, 1.0–1.03; p = 0.002). Variables related to F ≥ 2 were TE (1.4; 1.2–1.7, p < 0.001) and the NAFLD fibrosis score (2.0, 1.02–3.9; p = 0.04). Diagnostic accuracy (AUROC) of CAP to identify S ≥ 2 was 0.77 (p < 0.001). Diagnostic precision of TE to identify F ≥ 2 was 0.92 (p < 0.001). A value of CAP ≥ 268 dB/m identified 86% of patients with S ≥ 2 and a TE ≥ 7.6 kPa identified 87% of F ≥ 2.

Conclusions: CAP and TE identify in a single procedure more than 85% of obese patients with significant steatosis and/or significant fibrosis regardless of the etiology of liver disease.
51. Poster (#FRI-345)

Autoimmune and hepato biliary disease 1
Date & Time: Friday, April 15, 2016 - 08:00 - 18:00

VALUE OF TRANSIENT ELASTOGRAPHY (FIBROSCAN®) IN PATIENTS WITH AUTOIMMUNE HEPATITIS ON IMMUNOSUPPRESSIVE TREATMENT

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Background and Aims: Autoimmune hepatitis (AIH) is characterized by elevated serum immunoglobulin G (IgG) levels, presence of serum autoantibodies and inflammation of the liver leading to liver fibrosis and cirrhosis. Immunosuppressive treatment improves liver function tests, ameliorates symptoms and prolongs survival. Moreover, regression of fibrosis during immunosuppressive treatment has been demonstrated. However, the value of non-invasive measurement of fibrosis by transient elastography (Fibroscan®) during treatment of AIH is not well established yet.

Methods: 122 AIH patients (female: n = 92 [75.4%]; age at biopsy: 46.3 ± 1.6 [mean ± SE] years; definite AIH: n = 85 [69.7%], probable AIH: n = 37 [30.3%] according to simplified score) with a baseline liver biopsy were included. Fibrosis was staged according to Ludwig score on a four-point scale. All patients received immunosuppressive treatment and evaluation by transient elastography (TE; Fibroscan®, Echosens, France) during follow-up was performed in 50 (41.0%) patients (female: n = 34 [68.0%]; age at biopsy: 39.8 ± 2.3 years; definite AIH: n = 34 [68.0%], probable AIH: n = 16 [32.0%]). A liver stiffness ≤6.5 kPa was considered as absence of significant fibrosis (stage 2–4). ALT, AST and quantitative IgG were determined at time of treatment.

Results: Fibrosis stages as assessed by liver biopsy were: stage 1: n = 5 (10.0%), 2: n = 21 (42.0%), 3: n = 13 (26.0%), 4: n = 11 (22.0%). Follow up time between liver biopsy and TE was 8.6 ± 0.9 years (range: 0.4–26.5 years). Mean liver stiffness was 9.5 ± 1.0 kPa. Overall, 27 patients (54.0%) had a liver stiffness ≤6.5 kPa. In patients with advanced fibrosis at baseline (stage 3–4; n = 24 [48.0%]) nine subjects (37.5%) had a liver stiffness ≤6.5 kPa during follow-up. Patients with biochemical remission (normal ALT, AST and IgG levels) had significantly lower liver stiffness (n = 23 [46.0%], 6.7 ± 0.7 kPa) than patients without (n = 27 [54.0%], 12.0 ± 1.5, p = 0.007). In multivariate logistic regression liver stiffness ≤6.5 kPa was significantly and independently associated with female sex (OR: 76.9, CI95%; 4.9–100.0, p = 0.002), mild fibrosis at baseline (OR: 14.3, CI95%; 1.6–100.0, p = 0.017) and biochemical remission (OR: 35.8, CI95%; 2.8–100.0, p = 0.006).

Conclusions: Treatment-induced remission improves liver fibrosis in a substantial number of AIH patients. In addition to biochemical parameters, determination of liver stiffness by TE might be a useful tool in evaluating response to immunosuppressive therapy.

52. Poster (#FRI-347)

Autoimmune and hepato biliary disease 1
Date & Time: Friday, April 15, 2016 - 08:00 - 18:00

UTILITY OF UK-PBC RISK SCORES AS AN ALTERNATIVE TO TRANSIENT ELASTOGRAPHY IN ASSESSING RISK IN PRIMARY BILIARY CHOLANGITIS (CIRRHOSIS) PATIENTS


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Background and Aims: The performance of transient elastography (TE) in PBC has been well established but due to the high equipment cost its availability is restricted to specialised centres limiting its utility in normal clinical care. The UK-PBC Risk Score is a new, validated, scoring system for long-term prediction of risk of death or need for liver transplantation in PBC. To assess: 1) the association between TE and the UK-PBC Risk Scores, 2) to evaluate the reliability of UK-PBC Risk scores and thus utility in identifying low and high risk PBC patients in the centres where TE is not available (primary care and non-specialist hospitals).

Methods: We enrolled sixty (n = 60) PBC patients attending outpatient clinic and recorded their median liver stiffness (Fibroscan®) during treatment of AIH is not well established yet.

Results: 88% were females (mean age 58 yr). The mean (±SD) LSM was 11.63 ± 13.98 kPa and mean 5 yr, 10 yr and 15 yr UK-PBC Risk Scores were 2.51 ± 6.4, 8.21 ± 17.63 and 10.52 ± 19.42 respectively. Frequency of mild, moderate and severe fibrosis and cirrhosis were 47.4%, 22%, 18.6% and 12%. There were significant correlations between TE and the 5 yr (Spearman correlation, r = 0.47, p = 0.002), 10 yr (r = 0.43, p = 0.009), and 15 yr (r = 0.47, p = 0.002) UK-PBC Risk Scores. The ROC for 5 yr, 10 yr and 15 yr UK-PBC Risk Scores for moderate fibrosis were 0.73 (95% CI 0.60–0.86, p = 0.0029), 0.69 (95% CI 0.55–0.83, p = 0.011) and 0.73 (95% CI 0.60–0.86, p = 0.0029) respectively. For severe fibrosis the ROC was 0.78 (95% CI 0.65–0.91, p = 0.0008), 0.75 (95% CI 0.61–0.88, p = 0.003) and 0.78 (95% CI 0.65–0.91, p = 0.001) respectively. Table shows diagnostic performance of the UK-PBC Risk Score cut-offs for moderate fibrosis.

Conclusions: The UK-PBC Risk Score positively correlated with the liver stiffness as measured by transient elastography. The ROC for UK-PBC Risk Scores could identify both moderate and severe fibrosis. The high sensitivity and negative predictive values of the UK-PBC Risk Score cut-offs for moderate fibrosis suggest they can be reliably utilised as alternative to transient elastography in the settings where the latter is not available.
53. Poster (#FRI-375)

Autoimmune and hepato biliary disease 1

Date & Time: Friday, April 15, 2016 - 08:00 - 18:00

LIVER STIFFNESS MEASUREMENT BY TRANSIENT ELASTOGRAPHY FOR THE PREDICTION OF FIBROSIS IN PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS IN A RANDOMIZED TRIAL OF SIMTUZUMAB


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Background and Aims: Our objective was to assess the diagnostic performance of liver stiffness measurement (LSM) by transient elastography (TE) for the prediction of fibrosis in patients with primary sclerosing cholangitis (PSC).

Methods: Liver stiffness was measured by TE ( FibroScan, Echosens, Paris, France) in subjects with PSC enrolled in a sub-study of a phase 2b trial of simtuzumab, a monoclonal antibody directed against lysyl oxidase-like-2 (LOXL2). Liver stiffness was staged according to the Ishak classification and hepatic collagen in sirius red-stained biopsies was quantified via computer-assisted morphometry. The correlations between liver stiffness and Ishak fibrosis stage, hepatic collagen, serum biopsy markers (LOXL2, FibroTest, ELF), and Mayo Risk Score were determined. The diagnostic performance of TE for predicting bridging fibrosis ( Ishak stages 3–6 vs. 0–2) and cirrhosis ( stages 5–6 vs. 0–4) was determined using AUROCs and compared to biopsy markers; sensitivity analyses were conducted according to biopsy length (≥ vs. <2.0 cm). The operating characteristics of TE were determined at published cut-offs (Corpechot, et al. Gastro 2014).

Results: 56 of 234 randomized patients (24%) participated in the TE sub-study (median age, 43 years; 61% male; 61% with UC, 64% on UDCA, and median alkaline phosphatase, 255 U/L [IQR 122–339]). The median biopsy length was 2.0 cm (IQR 1.6–2.4); 57% of biopsies were ≥2.0 cm. 48% (n = 27) had bridging fibrosis and 11% (n = 6) had cirrhosis. Liver stiffness was strongly correlated with Ishak fibrosis stage (r = 0.67), hepatic collagen (r = 0.51), serum LOXL2 (p = 0.66), FibroTest (p = 0.74), ELF (p = 0.75), and Mayo Risk Score (p = 0.60; all p < 0.001). For bridging fibrosis, the AUROC of TE was 0.79 (95% CI 0.67–0.91); at a cut-off of ≥9.6 kPa, TE was 67% sensitive, 72% specific, and had positive predictive value (PPV) of 69% and 70%, respectively. For cirrhosis, the AUROC of TE was 0.95 (95% CI 0.88–1.00); the sensitivity, specificity, PPV, and NPV of TE at a cut-off of ≥14.4 kPa were 100%, 82%, 40%, and 100%, respectively. The AUROCs for TE were similar to those of LOXL2, FibroTest, and ELF, and did not differ according to biopsy length (data not shown).

Conclusions: Liver stiffness measurement by TE can effectively exclude PSC-related cirrhosis, but has sub-optimal accuracy for the prediction of bridging fibrosis.

54. Poster (#FRI-426)

EU and public health

Date & Time: Friday, April 15, 2016 - 08:00 - 18:00

ECONOMIC EVALUATION OF A COMMUNITY BASED DIAGNOSTIC PATHWAY TO SCREEN ADULTS FOR NON-ALCOHOLIC FATTY LIVER DISEASE


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Background and Aims: Current diagnostic algorithms for detecting non-alcoholic fatty liver disease (NAFLD) are based in secondary care and associated with considerable costs and late diagnosis. We have created an integrated community based pathway utilising transient elastography and a community hepatologist review, to stratify patients at risk of developing NAFLD. This study investigated the cost-effectiveness from an NHS England perspective of this innovative diagnostic pathway (IDP).

Methods: Markov modelling of the natural history of NAFLD was combined with results from a prospective cross sectional feasibility study of IDP and compared to standard care. Patients were stratified into the health states, no/ mild liver disease, significant liver disease or compensated cirrhosis and could progress to decompensated cirrhosis, hepatocellular carcinoma, liver transplant and death. Different transition probabilities were used dependent on whether early stages of liver disease were diagnosed or not. Transition probabilities, utility and resource use data were preferentially chosen from up-to-date UK sources or published literature which reflected the population. An expert panel of hepatologists was consulted to generate indicative estimates when data could not be identified. Starting age was 68, cycle length 1 yr, time horizon lifetime and cost year 2014. An incremental cost-effectiveness ratio (ICER) was estimated and one-way sensitivity (OSA) and probabilistic sensitivity analyses (PSA) were performed to assess robustness of the results.

Results: We found an ICER of £2,138 per extra quality adjusted life year (QALY). OSAs demonstrated ICERs were most sensitive to varying the rate of fibrosis progression and the effect of treatment on reducing this. PSA demonstrated a 37% probability that IDP dominates SC and an 85% probability of cost effectiveness at the UK willingness to pay threshold of £20,000/QALY.
Conclusions: We have not considered other likely health benefits such as reduced cardiovascular events and improved diabetic control and are probably underestimating the true impact of the pathway. Further work is also needed to improve specification of transition probabilities. However, despite the presence of significant uncertainty around estimates, the implementation of our pathway for earlier identification and management of NAFLD appears cost effective compared to standard care.

55. Poster (#FRI-473)
Liver transplantation / surgery: Clinical
Date & Time: Friday, April 15, 2016 - 08:00 - 18:00

LACK OF IMPROVEMENT OF LIVER STIFFNESS DURING SOFOSBUVIR-TREATMENT IN DECOMPENSATED CIRRHOTIC PATIENTS LISTED FOR LIVER TRANSPLANT SEEMS TO BE ASSOCIATED WITH MORE SEVERE HISTOLOGICAL DAMAGE IN THE NATIVE LIVER
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Background and Aims: Sofosbuvir/Ribavirin-based regimens (SOF/R) prevent HCV graft reinfection in listed patients with HCV-RNA undetectability 4 weeks before liver transplant (LT). SOF/R-induced HCV clearance could also improve liver function in listed patients resulting in a possible delisting for clinical improvement while also reducing list drop-out due to disease progression. The aim was to investigate in listed cirrhotic patients the effect of HCV clearance on liver disease severity before transplant and the rate of SOF-induced prevention of HCV graft reinfection.

Methods: From June 2014 to September 2015, 35 patients listed for HCV-related cirrhosis ± HCC received SOF/R until transplant or for 48 weeks. Clinical-laboratory tests and liver stiffness by transient elastography (TE) were sequentially assessed and compared with histology of native liver, blindly reviewed by two pathologists who subclassified cirrhosis (F4) by Laennec (4A,B,C) according to histological severity.

Results: 25 patients (71%) were transplanted. Among them, 18 (72%) were HCV-RNA(-) for >4 weeks and stopped SOF/R, while 7 (28%) with suboptimal viral response extended treatment post-transplant for 24 weeks. Median treatment duration was 4 months (range 1–10); waiting list 4 months (1–8) and post-transplant follow-up 8 weeks (2–14). Most patients had GT-1 (60%), 64% HCC, HCV-RNA median values were 5 log10 UI/mL (2–7), MELD 11 (7–25) CPT 10 (5–14), esophageal varices detected in 16 (64%) cases, ascites in 16 (64%), encephalopathy in 12 (48%). TE baseline value was 34 Kpa (14–75). LT candidates who were classified as decompensated (Child 7–14, n = 16) and compensated cirrhotics (n = 9) significantly differed for MELD score (16 vs 9, p < 0.003) and HCV-RNA levels (5 vs 6 log10, p = 0.05). Liver stiffness value did not improve during therapy in decompensated patients (34 vs 36 Kpa, p = 0.75) who showed more advanced stages of cirrhosis by Laennec (4B-C = 100%). In contrast, liver stiffness significantly decreased in compensated patients (31 vs 22 Kpa, p = 0.04) and 5 patients (56%) resulted as Laennec stage 4A. SVR12 was achieved in 92% of overall treated recipients.

Conclusions: Liver stiffness did not improve during anti-HCV treatment in decompensated cirrhotics on waiting list and was associated with more advanced histological stages of cirrhosis at transplant. Effective prevention of HCV graft reinfection by SOF/R was achieved in the large majority of listed patients.

56. Poster (#FRI-475)
Liver transplantation / surgery: Clinical
Date & Time: Friday, April 15, 2016 - 08:00 - 18:00

CLINICAL AND FUNCTIONAL CHANGES ASSOCIATED WITH THE ACHIEVEMENT OF SUSTAINED RESPONSE IN HCV GENOTYPE-1 INFECTED LIVER TRANSPLANT RECIPIENTS: DOES SOFOSBUVIR DIFFER FROM PEG-INTERFERON THERAPY?
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Background and Aims: The introduction of direct antiviral agents (DAAs) has radically changed the treatment of recurrent HCV infection after liver transplantation (LT), allowing to reach sustained virological response (SVR) rates much more often that with conventional peg-interferon alfa (P) and ribavirin (R) therapy and with minimal side-effects. We aimed to assess whether the clinical and functional liver changes associated with the achievement of SVR differ when this is obtained after DAA or PR.

Methods: Fifteen HCV genotype-1 LT recipients (M/F 11/4, median age 56.2) who achieved SVR with sofosbuvir (S), 400 mg/day, and R (800 mg/day) therapy were compared with a matched group (M/F 9/6, median age 60.4) who achieved SVR after P (180 mcg/wk) and R (1000–1200 mg/die) therapy. Liver function tests and liver stiffness (transient elastometry) were assessed at baseline, 4 week, 12 week, end of treatment (EOT) and at week 24 after EOT. Portal vein main velocity was assessed at baseline, EOT and at week 24 after EOT by abdominal Doppler ultrasound scan.

Results: Baseline characteristics were comparable in the two groups. Aminotransferase (ALT) showed a significantly greater decrease after SR than after PR during treatment (week 12: 30.4 ± 11.3 vs 44.5 ± 15.1 IU/L; p = 0.008) as well as at week 24 after EOT (21.2 ± 5.4 vs 26.9 ± 4.9 IU/L; p = 0.001). Liver stiffness decreased at week 24 after EOT by an average of 38% and 23% in the SR and PR group, respectively (p = 0.04) compared to baseline values. Portal vein velocity was significantly higher in the SR than in the PR group both at EOT (23.1 ± 2.3 vs 19.7 ± 2.9 cm/sec and at week 24 after EOT (23.4 ± 2.8 vs 20.3 ± 1.6 cm/sec; p < 0.001).

Conclusions: In patients who obtain SVR, SR therapy determines an earlier and greater on-treatment improvement of liver function and portal hemodynamics compared to PR therapy. Achievement of SVR24 is associated with significantly lower ALT levels (to below the normal values), lower liver stiffness and higher portal blood velocity following SR compared to PR therapy. Whether these differences are long-lasting and reflect distinct mechanisms of action of S (inhibition of viral replication) vs P (immune-stimulatory effect) requires further studies.

57. Poster (#SAT-003)
Cirrhosis: Bleeding, hepatorenal syndrome and ascites
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

THE COMBINATION OF HEPATIC ELASTOGRAM AND DOPPLER ULTRASOUND CAN PREDICT THE RISK OF UPPER GASTROINTESTINAL BLEEDING IN PATIENTS WITH CIRRHOSIS
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Background and Aims: In the past we studied the role of ultrasound and elastography in assessing the severity of esophageal varices and the risk of upper gastrointestinal bleeding (UGIB), and
none of the methods was satisfactory and did not enter the medical practice.

Aims: Evaluating a method in assessing the risk of UGIB in patients with cirrhosis that combines the results from elastography with those from the Doppler evaluation of the portal circulation.

Methods: The study group comprised 68 patients diagnosed with CHILD A or B cirrhosis based on clinical and laboratory criteria. From each patient were noted the hemodynamic parameters of the portal blood flow (velocity, flow, congestion index) and liver elastography values (it excluded the patients with ascites, CHILD C stage). Patients were followed on an average of 16 months (12–23 months) and were monitored for episodes of UGIB.

Results: The correlation between the results of liver elastography and portal vein velocity allowed dividing the lot of cirrhotic patients in three groups: low risk group (24 patients, liver stiffness >20 kPa and portal vein velocity >15 mm/sec) in which UGIB occurred at only one patient (annual average frequency of UGIB = 3.0%); the high risk group (12 patients, liver stiffness >30 kPa and portal vein velocity <12 mm/sec) in which UGIB occurred in 5 patients (annual average frequency of UGIB = 31.2%); and intermediate risk group (32 patients that do not fit in the above groups) in which UGIB occurred in 6 patients (annual average frequency of UGIB = 14.0%).

Conclusions: The combination of liver stiffness and values obtained by Doppler ultrasound can select high-risk patients to be referred for endoscopic examination and prophylactic treatment for UGIB.

58. Poster (#SAT-029)
Cirrhosis: Bleeding, hepatorenal syndrome and ascites
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00
EVALUATION AND IMPROVEMENT OF BAVENO 6 RECOMMENDATION FOR NON-INVASIVE DIAGNOSIS OF ESOPHAGEAL VARICES
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Background and Aims: Screening for esophageal varices (EV) is recommended in cirrhosis. The Baveno6 recommendations allow ruling out EV if platelets >150 G/L and Fibroscan <20 kPa. However, primary prevention focuses on large EV (LEV) and it is unknown in which etiology this rule applies. Therefore, we evaluated this rule and tried to improve it with the aim of 100% predictive values (NPV, PPV).

Methods: 287 patients with cirrhosis of various causes were prospectively included. Diagnostic tools were UGI endoscopy, 16 blood fibrosis tests, and Fibroscan. Patient characteristics were: men: 72%, age: 55 ± 11 years, causes: alcohol: 64%, virus: 26%, NAFLD: 6%, others: 4%; EV: none: 56%, small: 27%, large: 17%.

Results: Evaluation: NPV of Baveno6 rule was: EV: 87.1%, LEV: 100%. The spared endoscopy rate was only 16.4%. This rate was 38% with the best performing blood test (CirrhotiMeter (CM), p < 0.001 vs Baveno6) for a missed LEV rate not significantly different (0%, 7%, respectively, p = 0.157). Improvement: A modified Baveno6 rule (different cut-offs for platelets and Fibroscan) for EV had NPV100% in 18.2% of patients and even a PPV100% in 10.3% of patients. For LEV, there was a NPV100% in 37.0% of patients but no PPV100%. Finally, CM and Fibroscan combination had, respectively EV and LEV, NPV100% in 17.6% and 24.2% of patients and PPV100% in 6.7% and 3.0% of patients.

Discussion: The Baveno6 rule has only a fair NPV for EV whereas it is very specific and poorly sensitive for LEV. New cut-offs provide NPV100% for LEV in more patients (37% vs 16%, p < 0.001). By replacing platelets by a blood test, one can also get a 100% PPV. Thus, the best strategy is to use the modified Baveno6 rule to rule out LEV and replace platelets by CM to rule in LEV. This algorithm has 100% accuracy with 0% missed LEV and 53.2% spared endoscopy. In practice, one measures platelets and stiffness in all patients; if the NPV100% cut-off is not reached, CM is performed; if the CM PPV100% cut-off is not reached, endoscopy is performed. The non-invasive strategy can be made in 1 or 2 steps knowing that the 2 non-invasive tests are already part of EASL and AASLD 2015 recommendations for fibrosis staging.

Conclusions: The Baveno6 rule can be notably improved. With 2 simple non-invasive tests and without additional cost, it is possible not only to rule out but also to rule in LEV, which is original, with any missed LEV and half of endoscopies spared. These results have to be validated in another population.

59. Poster (#SAT-103)
Viral hepatitis: Hepatitis C – clinical (therapy)
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00
TREATMENT WITH SOFOSBUVIR + SIMEPREVIR FOR 12 WEEKS IN HCV COMPENSATED CIRRHOSIS (GENOTYPES 1 AND 4); THE USE OF RIBAVIRIN DOES NOT INFLUENCE SUSTAINED VIRAL RESPONSE
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Background and Aims: The COSMOS study reported a high rate of sustained viral response (SVR) with Sofosbuvir + Simeprevir ± Ribavirin in patients with advanced liver fibrosis; however the number of cirrhotic patients included was small. Our aim was to assess the efficacy and safety of this therapeutic combination in patients with compensated cirrhosis.

Methods: We analyze the outcome of our patients with HCV genotype 1 and 4 infection treated with Sofosbuvir + Simeprevir ± Ribavirin during the last year. The decision about use Ribavirin or not was a personal choice of the prescriber. The presence of Q80K polymorphism in HCV-genotype 1a infection was not explored in our patients. Cirrhosis (Stage 4 fibrosis) was defined by a transient elastography result ≥14 Kpsacal.

Results: A total of 79 patients were treated (45 Men/34 Women; mean age: 58.9 ± 9.9 years). Sixty-nine patients (87.3%) had cirrhosis. Baseline characteristics were: Child-Pugh A/B 89.9%; MELD 7.7 ± 1.9; Presence of esophageal varices: 40.5%; History of hepatic decompensation: 13.9%; and previous hepatocellular carcinoma: 10%. Patients had infection by HVC-Genotype 1b/1a/4: 67.1%/21.5%/8.9% and they were Naïve 32.9%, Relapsers 13.9%, and Null responders 39.3%. Among cirrhotic patients Ribavirin was added to Sofosbuvir + Simeprevir in 49.2% and SVR was similar with and without Ribavirin (93.5% vs 88.8%, p = 0.65). In patients with cirrhosis SVR-4 was 93.7% and SVR-12 was 91.4%. No significant differences in SVR-12 were observed between patients treated with or without Ribavirin according to HCV-genotype or previous treatment response. SVR-12 with and without RBV in genotype 1a (n = 12/2) was 100% vs 100%, in genotype 1b (n = 13/25) was 84.6% vs 88%; All patients with genotype 4 (n = 5) were treated with Ribavirin and reached SVR-12 (100%). SVR-12 with or without Ribavirin was 91.6% vs 83.3% in naïves (n = 12/6), 100% vs 100% in relapers and partial responders (n = 6/5), and 90.9% vs 85.7% in null responders (n = 11/14). Three patients (3.8%) suffered severe adverse events, including one death and one discontinuation of therapy. Patients treated with Ribavirin presented a higher number of mild adverse events.
High Efficacy and Favorable Safety of ABT-493 and ABT-530 Co-Administration for 12 Weeks in HCV Genotype 1-Infected Patients with Cirrhosis (SURVEYOR-I)


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Background and Aims: Next generation direct-acting antivirals (DAAs), including ABT-493, an NS3/4A protease inhibitor (identified by AbbVie and Enanta) and ABT-530, an NSSA inhibitor, have demonstrated potent antiviral activity against all major HCV genotypes (GTs) in vitro, with little or no loss of potency against common resistance-associated variants. Furthermore, the ABT-493/ABT-530 combination was well-tolerated and achieved high sustained virologic response (SVR) rates in patients with HCV GT1, GT2 and GT3 infection without cirrhosis (SURVEYOR-I/Ii, Part 1). Here we present data from Part 2 of the SURVEYOR-I study, evaluating the safety and efficacy of ABT-493 and ABT-530 administered for 12 weeks in HCV GT1-infected patients with compensated cirrhosis.

Methods: Treatment-naïve or pegylated interferon/ribavirin treatment-experienced patients with cirrhosis received ABT-493 200 mg + ABT-530 120 mg once daily for 12 weeks. Cirrhosis was determined by either liver biopsy (Metavir F4), Fibroscan (liver stiffness >14.6 kPa) or serum markers (Fibrotest score ≥0.75 and an APRI > 2). SVR at post-treatment week 12 (SVR12; HCV RNA levels determined using Roche COBAS TaqMan® RT-PCR assay [lower limit of detection of 15 IU/mL and lower limit of quantification of 25 IU/mL]) and safety are reported.

Results: A total of 27 patients were enrolled and the population was 74% male, 89% white, 74% GT1a, 85% non-CC IL28B, 26% HCV treatment-experienced, and all reported baseline fibrosis scores of F4. The median (range) HCV RNA log10 IU/mL was 6.7 (5.6–7.3), and 93% had HCV RNA ≥6,000,000 IU/mL at baseline. SVR12 was achieved in 26 out of 27 (96%) patients, with one patient experiencing relapse at post-treatment week 4. All adverse events (AEs) were deemed mild or moderate in severity, with no patients reporting severe or serious AEs considered related to study drugs. No patients discontinued treatment prematurely due to AEs and the most frequent AEs reported in >10% of patients were fatigue (11%) and headache (11%). No clinically meaningful abnormal liver function or other laboratory results were observed.

Conclusions: Treatment with the IFN- and ribavirin-free combination of next generation HCV DAAs, ABT-493 and ABT-530, was well-tolerated and achieved high SVR12 rates of 96% following a 12-week treatment regimen in GT1-infected patients with compensated cirrhosis regardless of baseline viral load or prior treatment history.

62. Poster (#SAT-144)

Viral hepatitis: Hepatitis C – clinical (therapy)

Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

High SVR Rates with SMV + SOF in HCV GT1 and GT4 Patients with Cirrhosis or Advanced Fibrosis: A Real Practice Analysis from a Large Regional Database in Tuscany, Italy

R WITHOUT RIBAVIRIN IN PATIENTS – 8-27

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-25

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-7 vs 22.4, p = 0.008), absence of clinical

12

impairment.

94.9% (316/333) and 91.6% (263/287). SVR12 is associated with

13

gt1 (1a = 0.8%) post

14

transplant recurrence. Among them, 325 (87.8%) were

15

the performance of this therapy in the real practice.

Methods: From February 2015 a total of 370 pts (age 58.6 ± 10.4 yrs, 66.5% males) were treated for 12 weeks with SMV + SOF (54.1%) or SMV + SOF + RBV (45.9%) in 15 referral centres covering the whole region of Tuscany. The stage of fibrosis was assessed by histology (4.3%) or transient elastography (96.8%). Clinical cirrhosis was defined by presence of decompensated disease and/or oesophageal varices and/or platelets <100,000/μL.

Results: Overall, 300 (81.1%) pts had cirrhosis (169 clinical), 57 (15.4%) F3 fibrosis, 10 (2.7%) cryptogallengiroma/lipoma and 3 (0.8%) post transplant recurrence. Among them, 325 (87.8%) were GT1 (1a = 20.8%; 1b = 64.9%) and 45 (12.2%) GT4 infected; 39 were HIV coinfected, 181 (48.9%) failed pegIFN + RBV and 14 (3.8%) 1st generation protease inhibitors. Actual SVR4 and SVR12 rates are 94.9% (316/333) and 91.6% (263/287). SVR12 is associated with higher BMI (median 24.7 vs 22.4, p = 0.008), absence of clinical cirrhosis (94.7% vs 86.1%, p = 0.037) and, in previously treated patients, with relapse as compared to PR/NR (100% vs 85%, p = 0.006). Age, gender, fibrosis (F3 or F4), HCV genotype-subtype, HCV coinfection, RBV, baseline Log HCV-RAA, ALT, AST, Bilirubin, Albumin and INR, are not significantly associated. At multifactor analysis (193 pts), only BMI and clinical cirrhosis are independently associated to SVR12 (p = 0.007 and 0.030). HCV-RNA Log decline is greater in SVR12 patients at week 2 (5.29 vs 4.46, p = 0.008) and atweek 4 (6.01 vs 5.55, p = 0.073). Most frequent adverse events are total bilirubin increase (52.2%, median 1.7 (1.1–6.8 mg/dL), more frequent with RBV (60% vs 43.3%, p = 0.005), and anaemia (23.8%, median haemoglobin: 11.0, range: 7.6–11.8 g/dL), requiring RBV dose reduction/withdrawn in 19% of the cases. Three patients with clinical cirrhosis did not complete treatment: one died for pneumonia and liver failure, one had leukaeemia, and one with lymphoma had renal function impairment.

Conclusions: SMV + SOF efficacy in HCV GT1,4 pts with advanced fibrosis and cirrhosis is high (91.6%) in every day clinical practice and not influenced by RBV. Low BMI and advanced cirrhosis are negative predictors of SVR, whereas the HCV-RNA Log decline at week 2 is a positive predictor of SVR.
statistical significance (p = 0.05). No serious adverse events were detected.

Conclusions: At the EOT, HCV-RNA was suppressed in 99% of HIV/HCV co-infected patients treated with Daclatasvir and Ombitasvir/Paritaprevir/Ritonavir + Ribavirin. Treatment was generally well tolerated, compatible with a wide range of antiretrovirals and didn’t compromise HIV control.

64. Poster (#SAT-150)
Viral hepatitis: Hepatitis C – clinical (therapy)
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00
HIGH Efficacy OF INTERFERON-FREE TREATMENTS IN REALWORLD PATIENTS WITH CHRONIC HepatITIS C A MULTICENTRIC STUDY

Background and Aims: The development of new, direct-acting antivirals (DAA) for the treatment of chronic hepatitis C virus (HCV) infection has led to rates of sustained virological response (SVR) >90%, according to registry studies. Few studies have assessed the efficacy of these treatments in clinical practice.

Methods: A multicentric, descriptive, observational, and prospective study was conducted to analyze the data of 410 HCV patients who received interferon (IFN)-free treatments (December 1, 2014 to August 31, 2015). The SVR was evaluated 4 and 12 weeks after completing treatment (SVR4 and SVR12).

Results: Baseline characteristics: 68% males, mean age 55 ± 11 years, BMI 26.5 ± 4.67, hemoglobin 14.3 ± 1.9 mg/dL, platelets 155,278 ± 71,698/mm³, alanine transaminase (ALT) 81 ± 63 UI/mL, and HCV RNA 3,349,042 ± 954,222 UI/mL. The IL28B polymorphisms were: CT (71%), CC (16%), and TT (13%). Seventy-eight percent of the patients had genotype (G)1 (67 subtype 1b, 31% 1a, and 2% 1c), 10% had G3, 5% G4, and 3% G2. The mean fibrosis level determined by transient elastography (TE) (n = 372) was 19 ± 14.2 kPa; 62% presented F4 cirrhosis (>12.5 kPa), and 5% had no significant fibrosis (<7.2 kPa). A total of 62% had received previous treatment; the majority with IFN and ribavirin (RBV) (73%). The most often used combinations of DAA included sofosbuvir (SOF) + simeprevir (SMV) (42%); SOF + ledipasvir (22%); ombitasvir/paritaprevir/ritonavir (OBV/PTV/r) + dasabuvir (18%); and SOF + daclatasvir (DCV) (13%). RBV was administered to 44% of the patients. The most often used treatment combination for G1 and G4 patients was SOF + SMV (47% and 57, respectively), and for G3 and G2 patients, SOF + DCV (79% and 50, respectively). The majority of the G1, G3, and G4 patients (90%, 63, and 89, respectively) were treated for 12 weeks, and 58% of the G2 patients were treated for 24 weeks. RBW was administered to 37%, 58%, 76%, and 45% of the G1, G2, G3, and G4 patients, respectively. The SVR4 rate (n = 278) was 96%, and SVR12 rate (n = 186) was 90%. According to the data available to date, the rates of SVR4 for G1, G2, G3, and G4 patients are 96%, 100%, and 89%, respectively, and the rates of SVR12 are 90%, 100%, and 81%, respectively.

Conclusions: In our clinical practice, patients with HCV who received IFN-free treatments presented high rates of SVR4. The SVR12 rate was approximately 90%, which is similar to the results of other registry studies (except in for G4 patients).

65. Poster (#SAT-151)
Viral hepatitis: Hepatitis C – clinical (therapy)
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00
EFFICACY OF INTERFERON-FREE THERAPY IN CIRRHOTIC AND NON-CIRRHOTIC CHRONIC HepatITIS C PATIENTS IN CLINICAL PRACTICE


Background and Aims: The effectiveness of treatment regimens of chronic hepatitis C (CHC) with interferon (IFN)-free therapy has been proven in clinical trials. Little data is available on the efficacy of this treatment in clinical practice, especially for difficult-to-treat population, such as cirrhotic patients.

Methods: A multicenter observational prospective study was performed between 1/12/2014 and 31/8/2015 on 401 patients undergoing an IFN-free treatment. Variables analyzed: age, sex, BMI, IL28B CC polymorphism genotype, previous treatments, treatment regimens and their duration, use of ribavirin (RBV) and sustained virological response for 4 (SVR4; n = 301) and 12 weeks (SVR12; n = 189) after end of treatment. The level of basal fibrosis (no-F4/F4/F4) was determined by transient elastography (372 patients with a cut-off value for F4 of 12.5 kPa), a biopsy and/or an abdominal ultrasound (29 patients).

Results: The preliminary results of 153 (38%) patients without cirrhosis and 248 (62%) with cirrhosis, were analyzed. Non-significant differences in age, sex, BMI, or IL28B CC polymorphism were observed. Of the non-cirrhotic patients, 76 (50%) were treatment-experienced compared with 166 (67%) of the cirrhotic patients (p = 0.0006). The most common drug combinations used in non-cirrhotic patients compared to cirrhotic patientswere sofosbuvir (SOF) + ledipasvir (29% vs 17%; p = 0.0036) and paritaprevir + ombitasvir + dasabuvir (28% vs 11%, respectively; p = 0.0001). The simeprevir (SMV) + SOF combination was more frequently used in cirrhotic (54%) than in non-cirrhotic patients (22%) (p = 0.0001). In addition, the use of RBV was more frequent in cirrhotic (49%) than in non-cirrhotic patients (33%) (p = 0.0024), and a 24-week extension of the treatment was more frequent in cirrhotic (14%) than in noncirrhotic patients (4%) (p = 0.0011). Non-significant differences were observed in the SVR4 (noncirrhotic, 98%; cirrhotic, 91%), or the SVR12 (non-cirrhotic, 98%; cirrhotic, 89%), although a trend indicating a lower response in the cirrhotic patients was observed.

Conclusions: In this CHC-patient cohort undergoing IFN-free treatment, use of SMV + SOF treatment, extension to 24 weeks and association with RBV was more frequent in cirrhotic than in noncirrhotic patients. Furthermore, the SVR4 and SVR12 rates of approximately 90% in the cirrhotic patients are lower than rates in non-cirrhotic patients, although these differences are not significant using the data available to date.
Background and Aims: Several direct-acting antiviral combinations are recommended for the treatment of genotype 1 (G1) chronic hepatitis C (CHC) patients. Simeprevir (SMV) and sofosbuvir (SOF) with or without ribavirin (RBV) has been shown to be highly efficient in some clinical trials. This study was conducted to assess the effectiveness and safety of this regimen in real-world patients with G1 CHC.

Methods: A multicenter study was performed including 115 patients with G1 CHC who were undergoing a SMV/SOF combination for 12 weeks (with or without RBV at their doctor’s discretion). Variables analyzed: age, sex, BMI, genotype, subtype, baseline fibrosis (transient elastography), presence of cirrhosis (>12.5 kPa and/or biopsy F4 and/or ultrasound diagnosis), analytical parameters, previous treatment experience, RBV use and the 12-week post-treatment sustained virological response (SVR12).

Results: Baseline characteristics: 78 (68%) males, mean age of 57.6 ± 9.6 years, BMI of 25 (18–47) and G1 subtypes 1a and 1b were found in 26 (23%) and 83 (73%) of the patients, respectively. HCV-RNA was detected in 1,080,000 UI/mL (11,390–17,000,000). The median age is 47 years (range 21–90), 74% and 16% of the patients, respectively. The platelet count was 128,000/mm3 (13,200–347,000); the ALT value was 61 UI/mL (10–75). The median age is 47 years (range 21–90), 74% and 16% of the patients, respectively. The assessment of fibrosis was 17.3 (4.4–75) kPa with cirrhosis in 93 (82%) patients. Treatment-experienced and treatment-naïve patients were 98 (87%) and 27 (23%), respectively. SVR12. All 28 patients with undetectable viral load and 30 with undetectable viral load at the end of treatment were 100%. SVR12 100% (2/2).

Conclusions: These results provide the first efficacy data with SOF/LDV in Spanish prison population and show a response similar to that of general population.
Background and Aims: HCV genotype-4 (G4) comprises 90% of HCV infections in Egypt. Recent studies with DAAAs have often shown suboptimal rates of sustained virologic response (SVR) in cirrhotic patients. We report a Phase 3 trial of ravidasvir (RDV), a pan-genotypic HCV NS5A inhibitor, plus sofosbuvir (SOF), a nucleotide HCV inhibitor, in 300 Egyptian patients (43% with cirrhosis).

Methods: Patients were 18–65 y with HCV-G4 infection, HCV RNA >4 log10 IU/mL, without compensated cirrhosis or other liver disease. Three patient groups were enrolled: interferon (IFN)–naive non-cirrhotic and cirrhotic, by FibroScan & FIB-4 score (Group 1); IFN experienced non-cirrhotic (Group 2); and IFN-experienced cirrhotic (Group 3). Groups 1 and 2 were treated QD with RDV 200 mg + SOF 400 mg for 12 wk, randomized 1:1 to add RBV or no RBV. Group 3 received RDV + SOF + RBV, randomized 1:1 to 12 vs. 16 wk treatment. The primary endpoint is SVR12, defined as non-detectable HCV RNA (<12 IU/mL) by the Abbott Real-Time™ PCR assay at 12 wk posttreatment.

Results: 300 patients were enrolled (150 in Group 1, 80 in Group 2, and 70 in Group 3); 170 were non-cirrhotic and 130 (43%) were Childs A cirrhotics. At the time of this abstract all patients have completed treatment-period evaluations, and only 31/300 have not yet completed their SVR12 evaluation. Treatment has been well tolerated, with 1 serious adverse event possibly related to treatment (transient bradycardia). HCV RNA declined rapidly and was undetectable by Wk 8 in all patients. For the 264 patients who have reached their SVR12 evaluation point, 164/164 (100%) noncirrhotic patients and 94/100 (94%) cirrhotic patients achieved SVR12. There have been no viral breakthroughs. All 6 treatment failures have been post-treatment relapses in cirrhotics receiving 12 wk treatment (1 had only 8 wk). Five patients discontinued unrelated to study treatment.

Conclusions: Overall per protocol, 98% of 264 patients achieved SVR12 with SOF + RDV +/- RBV treatment, with SVR12 in all noncirrhotic patients and failures limited to 6 relapses in cirrhotic patients. RBV did not improve responses in non-cirrhotics or IFN naive cirrhotics. All (100%) 20 patients in Group 3 cirrhotics treated for 16 wk have achieved SVR12 (data pending on another 15), suggesting that 16 wk treatment may be sufficient for optimizing viral clearance in IFN-experienced G4 cirrhotics, the most refractory patients. Final study data will be available at the Congress.

70. Poster (#SAT-186)

Viral hepatitis: Hepatitis C – clinical (therapy)

Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

HEPATIC FIBROSIS MEASURED BY ELASTOGRAPHY AMONG PEOPLE WHO INJECT DRUGS WITH CHRONIC HCV IN COMMUNITY SETTINGS: THE TAP STUDY

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Background and Aims: The HCV Treatment and Prevention (TAP) Study is a community-based trial involving people who inject drugs (PWID) using a networks-based approach to treatment. We describe fibrosis and drug taking behaviour prior to treatment among the first fifty participants.

Methods: Eligible PWID were those with chronic HCV monoinfection, who injected drugs in the same time and place with ≥1 person in the previous six months, and without significant medical or concomitant medication interactions to sofosbuvir/ledipasvir ± ribavirin therapy. Participants were recruited via mobile streetbased vans or primary health clinics for PWID. Hepatic fibrosis was measured by transient elastography (FibroScan) and alcohol and other drug use was documented at screening. The study protocol (clinicaltrials.gov NCT02363517) requires participants with advanced fibrosis receive treatment program marked the beginning of a new era in HCV therapy in Egypt. The real-life results of this therapy for HCV genotype 4 is not known.

Methods: Through aweb-based registration system, the Egypt multicenter national treatment program started including compensated patients with advanced fibrosis or cirrhosis (F3-F4 by biopsy or fibroscan and FIB-4) in October 2014. Till November 2015, 175,000 patients have started treatment, and data are available at 12 weeks follow-up after end of therapy for 5,243 patients with advanced fibrosis-cirrhosis (F3-F4) (3,615 interferon eligible patients treated with SOF-PEG-RBV for 12weeks (69%), and 1,628 interferon ineligible patients treated with SOF-RBV 24 weeks (31%)). Patients older than 60 years, and those with platelets <100,000, leucocyte count <3,000, neutrophils <1,500, or albumin <3 g/ml were also selected for “selected” for SOF-RBV treatment for 24 weeks. Response to therapy was assessed 12 weeks after end of treatment and SVR was considered if HCV-RNA was <15 IU/mL.

Results: Patients in the SOF-RBV group were older, and more had cirrhosis and had lower platelets and albumin (a result of the selection criteria). By end of treatment, 163 (3.1%) patients failed to respond (3.2% with SOF-PEG-RBV, and 2.8% with SOF-RBV) and 5,080 patients had HCV-RNA below level of quantification (15 IU/mL) (96.9%). Subsequently, 543 patients (10.41%) relapsed (175 in the SOFPEG-RBV group (4.5%) and 371 in the SOF-RBV group (27.1%). By 12 weeks after end of treatment, 4,534 (86.5%) patients had achieved SVR (3,572 (92.2%) in the SOF-PEG-RBV group and 962 (70.3%) in the SOF-RBV group).

Conclusions: These real-life results from the largest national treatment program using SOF based therapy in patients with advanced fibrosis/cirrhosis showed a high SVR rate for 12 weeks of SOF-PEG-RBV and a lower SVR rate for 24 weeks of SOF-RBV, both being lower than results of clinical trials using same treatment regimens for HCV-genotype 4. More patients will reach SVR 12, and their results will be presented in the meeting.

69. Poster (#SAT-165)

Viral hepatitis: Hepatitis C – clinical (therapy)

Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

REAL-LIFE RESULTS OF SOFOSBUVIR BASED THERAPY FOR EGYPTIAN PATIENTS WITH HEPATITIS C AND ADVANCED FIBROSICIRRHOSIS

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1. Kasr Al-Aini School of Medicine; 2. Kasr Al-Aini School of Medicine; 3. Ain Shams School of Medicine; 4. National Hepatology and tropical Medicine Research Institute; 5. Faculty of Medicine, Helwan University, Cairo; 6. National Liver Institute, Shebeen El-Kom, Egypt

Background and Aims: Egypt faces the largest burden of HCV infection in the world, and infection is predominantly with genotype 4. Triple therapy with sofosbuvir (SOF), pegylated interferon (PEG) and ribavirin (RBV) for 12 weeks, and dual therapy with SOF-RBV for 24 weeks have shown high sustained virological response (SVR) rates (97% and 90% respectively) in clinical trials that included HCV-genotype 4 patients, and their introduction in late 2014 in a national...
Patients with advanced liver cirrhosis, defined by at least one of the following criteria: FibroScan >20 kPa, thrombocytes <90,000/μL, albumin <35 g/L or signs of liver decompensation, were analyzed.

Results: 567 patients had advanced liver cirrhosis (median MELD score 9; range 6–32), 383 patients with FU week 12 were included. The majority of patients was infected with HCV-genotype 1 (n = 442); HCV-genotypes 2, 3, 4 and 6 were present in 14, 92, 18 and 1 patient, respectively. Patients received different treatment regimens (Table 1). Overall, SVR was achieved in 82.8% of the patients (ITT). SVR rates according to the regimen ranged from 66 to 100%. DAA therapy lead to SVR rates (ITT) of 86.3%, 75.0%, 68.5% and 60.0% for HCV-genotype 1 (n = 65), 2 (n = 9), 3 (n = 37) and 4 (n = 6), respectively. Liver function parameters including albumin, bilirubin and prothrombin time improved in the majority of patients during antiviral therapy/follow-up. The median platelet count, as a clinical marker of portal hypertension, increased from 86,000/μL at baseline to 100,000/μL during follow-up (p < 0.05). Creatinine levels were stable during antiviral treatment. SAEs were reported in 8.1% and 4 patients died from cirrhosis associated complications.

Conclusions: This real-world cohort confirms that DAA treatment is feasible in patients with advanced liver cirrhosis leading to a restoration of liver function. A broad spectrum of individual treatment regimens was applied reflecting individualization of treatment in this difficult-to-treat cohort.

Table 1: Treatment regimens of HCV patients with advanced cirrhosis

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>%</th>
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<tbody>
<tr>
<td>SOF+RBV</td>
<td>56</td>
<td>9.9</td>
</tr>
<tr>
<td>SIM+SOF</td>
<td>114</td>
<td>20.1</td>
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<tr>
<td>SIM+SOF+RBV</td>
<td>16</td>
<td>2.8</td>
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<tr>
<td>DCV+SOF</td>
<td>142</td>
<td>25.0</td>
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<tr>
<td>DCV+SOF+RBV</td>
<td>55</td>
<td>9.7</td>
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<tr>
<td>LDV/SOF 12 W</td>
<td>53</td>
<td>9.3</td>
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<tr>
<td>LDV/SOF 24 W</td>
<td>31</td>
<td>5.5</td>
</tr>
<tr>
<td>LDV/SOF+RBV 12 W</td>
<td>48</td>
<td>8.5</td>
</tr>
<tr>
<td>LDV/SOF+RBV 24 W</td>
<td>25</td>
<td>4.4</td>
</tr>
<tr>
<td>OBV/PTV/sofosbuvir/daclatasvir 12 W</td>
<td>2</td>
<td>0.4</td>
</tr>
<tr>
<td>OBV/PTV/sofosbuvir/daclatasvir 12 W</td>
<td>22</td>
<td>3.9</td>
</tr>
<tr>
<td>OBV/PTV/sofosbuvir/daclatasvir 12 W</td>
<td>3</td>
<td>0.6</td>
</tr>
<tr>
<td>Total</td>
<td>567</td>
<td>100</td>
</tr>
</tbody>
</table>

72. Poster (#SAT-195)

Viral hepatitis: Hepatitis C – clinical (therapy)

Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

SOF/VEL FOR 12 WEEKS RESULTS IN HIGH SVR12 RATES IN SUBJECTS WITH NEGATIVE PREDICTORS OF RESPONSE TO TREATMENT: AN INTEGRATED ANALYSIS OF EFFICACY FROM THE ASTRAL-1, ASTRAL-2 AND ASTRAL-3 STUDIES


1. Institute of Liver Studies, Kings College Hospital, London, United Kingdom;
2. University Health Network Liver Clinic, Toronto, Canada;
3. Centre Hepato-Bilio-Pancreatique, Vannes;
4. Hôpital Saint Joseph, Marseille, France;
5. GastroOne, Germantown;
6. VAMC Long Beach, Long Beach, United States;
7. Royal Prince Alfred Hospital, Camperdown;
8. Royal Brisbane and Women’s Hospital, Brisbane, Australia;
9. Gilead Sciences, Inc, Foster City;
10. Beth Israel Deaconess Medical Center, Boston, United States

Background and Aims: The once-daily fixed-dose combination tablet of sofosbuvir/velpatasvir (SOF/VEL) was evaluated for the treatment of genotype 1–6HCV infection in three phase 3 studies in patients with and without compensated cirrhosis (ASTRAL-1, ASTRAL-2, ASTRAL-3). Overall SVR12 rates were >95% across all HCV genotypes.
37. Poster (#SAT-201)

Viral hepatitis: Hepatitis C – clinical (therapy)

Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

RAPID CHANGES IN CHOLESTEROL IN CHRONIC HEPATITIS C PATIENTS TREATED WITH ANTIVIRALS AND POTENTIAL IMPACT ON CARDIOVASCULAR RISK


1. Internal Medicine Department & Liver Transplantation Unit, Puerta de Hierro University Hospital; 2. Infectious Diseases Unit, La Paz Hospital; 3. Biostatistics Unit, Puerta de Hierro Research Institute, Madrid, Spain

Background and Aims: Chronic HCV infection influences the host lipid metabolism. Within infected hepatocytes, HCV proteins interact with lipid droplets to facilitate virion assembly and production. Lipid disturbances tend to normalize following HCV eradication with interferon-based therapies. Little is known about the effect of interferon-free therapies.

Methods: Clinical data from all patients who completed interferon-free DAA at two clinics in Madrid were analyzed. A repeated GEE (generalized estimation equation) analysis was performed, using Gaussian family with an identity link, in order to estimate the association between three different dependent variables (total, LDL and HDL cholesterol) and diagnosis of Diabetes, HIV coinfection, HIV + treated with ritonavir-boosted protease inhibitors (PIs), Liver Cirrhosis and liver transplantation, respectively.

Results: A total of 174 chronic hepatitis C patients received DAA and were analyzed. Overall, 71.3% were male; median age 54.5 years old; baseline HCV-RNA 6.17 log IU/mL; 27.6% had diabetes, 30% had received a liver transplant and 44.3% were HIV+, of whom 37.7% were on PIs. More than half of patients were cirrhotic (mean fibroscan value in them: 28 Kpa). A total of 92.5% of individuals were treated with sofosbuvir-based combinations. Serum HCV-RNA was <15 IU/mL in 84% of patients at week 4. Overall, mean total cholesterol increased 7.3 mg/dL at week 4 of DAA treatment (p = 0.042). There was a major interaction with diabetes (+25.23 mg/dL; p = 0.007) and with HIV+ individuals on PIs (+23.3 mg/dL; p = 0.007). By contrast, cirrhosis and transplantation behaved as the rest of patients. Whereas mean increases in LDL-cholesterol at week 4 were of 12.4 mg/dL (p < 0.001) and of 1.14 in HDL-cholesterol of (p = 0.4). Interestingly, these figures were of +12 and 9.27 mg/dL, respectively (p < 0.01) in diabetic patients. At weeks 8 and 12 of DAA therapy, total and LDL cholesterol tended to return to baseline values in all groups whereas HDL-cholesterol kept rising up (+8.04 at week 12; p < 0.001).

Conclusions: Clearance of HCV using DAA results in rapid increases in circulating cholesterol particles, most likely reflecting a direct effect of HCV inhibition on the lipid metabolism. This effect is more pronounced in diabetic patients. Interestingly HDL-cholesterol continuous to rise, perhaps contributing to reduce the cardiovascular risk in cured HCV patients.

74. Poster (#SAT-205)

Viral hepatitis: Hepatitis C – clinical (therapy)

Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

REAL-LIFE EXPERIENCE OF DAA-BASED REGIMENS PLUS RIBAVIRIN IN CIRRHOTIC PATIENTS CONFOCTED WITH HCV AND HIV-1

E. Messina1, C. Uberti-Foppa2, M. Merli2, L. Galli3, D. Barbantotti1, A. Poli2, S. Salpietro2, G. Morisica1, S. Bagaglio3, A. Andolina1, A. Castagna1, A. Lazzarin2, H. Hasson1.

1. Infectious Diseases Clinic, IRCCS Ospedale S. Raffaele; 2. Università Vita-Salute San Raffaele, Milano, Italy

Background and Aims: Despite the availability of interferon(IFN)-free direct-acting antivirals (DAAs) regimens, ribavirin (RBV) remains an important treatment component, although it is associated with increased toxicities. We evaluated the safety and efficacy of RBV including DAA regimens in HCV/HIV cirrhotic patients (pts) in real life setting.

Methods: HIV/HCV co-infected cirrhotic (Metavir F4) pts, on antiretroviral therapy (ART), treated with DAs plus RBV weight based between March/August 2015 for 12 or 24 weeks were considered. Clinical, biochemical, virological and immunological parameters were recorded at baseline, week 4, 12/EOT, 16, 24/EOT and PT4, PT12 for pts on 12 weeks regimen. Results reported as median (IQR) or frequency (%).

Results: 62 pts were included: 29 and 33 pts treated for 12 and 24 weeks, respectively. Baseline characteristics: age 52 (51–55) yrs, duration of HIV infection 25 (23–32) yrs, nadir CD4+ 129 (71–229) cells/μL, HCV RNA 5.8 (5.1–6.2) log10 cps/mL; HCV genotype (GT) was: 34 (55%) GT1 (23 [37%] GT1a, 8 [13%] GT1b, 3 [5%] GT1c), 3 (5%) GT2, 14 (23%) GT3a; 11 (18%) GT4; 57 (92%) pts had Child-Pugh (CTP) A, 5 (8%) had CTP B; liver stiffness was 20.2 (14.6–28.4) Kpa, 27 (44%) pts were naive to IFN and RBV. Pts were mainly treated with the following DAA regimens: 26 (42%) simeprevir/sofosbuvir (SOF), 12 (19%) daklatasvir/SOF, 11 (18%) SOF, 7 (11%) SOF/ledipasvir. Main (>10%) ART regimens were: 11 (18%) delugetavir/tenofovir/emtricitabine, 9 (15%)
raltegravir/tenofovir/emtricitabine. Thirty-seven (60%) pts completed anti-HCV treatment (Table 1): 36/62 (58%) achieved HCV-RNA <12 IU/mL by week 4 and 37/37 (100%) at the end of treatment. Thirty-six (58%) pts experienced ≥1 adverse event (Table 1); the most common AEs were: anaemia (17%), total bilirubin elevations (29%), bacterial infections (3%). During anti-HCV treatment, 29 (47%) pts reduced RBV dosage, 13 (21%) required erythropoietin. Up to date, no discontinuation of DAA regimens occurred. HIV immuno-virological outcomes are shown in Table 1: 2 viral blips and 1 virological failure (2 consecutive HIV-RNA > 50 cps/mL) were observed during follow-up. No AIDS defining events occurred.

Conclusions: DAA-associates with RBV weight-based were effective, generally well tolerated and also with favorable HIV immuno-virological outcomes suggesting that the use of DAA regimens plus RBV can be safely used in cirrhotic pts co-infected with HCV.

Table 1. HCV and HIV outcomes

<table>
<thead>
<tr>
<th>12-week DAA regimens</th>
<th>Treatment</th>
<th>Post treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BL (n=29)</td>
<td>Week 4 (n=29)</td>
</tr>
<tr>
<td>HCV-RNA&lt;12 IU/mL (%)</td>
<td>0 (40%)</td>
<td>27 (100%)</td>
</tr>
<tr>
<td>HIV-RNA&lt;50 copies/mL (%)</td>
<td>26 (100%)</td>
<td>28 (97%)</td>
</tr>
<tr>
<td>CD4+ (cells/µl)</td>
<td>667 (452-722)</td>
<td>581 (403-756)</td>
</tr>
<tr>
<td>CD4+ change since BL (cells/µl)</td>
<td>0 (24)</td>
<td>(-154 - 147)</td>
</tr>
<tr>
<td>Number of pts with ≥1 AE grade 3-4</td>
<td>0 (14%)</td>
<td>3 (3%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>24-week DAA regimens</th>
<th>Treatment</th>
<th>Post treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BL (n=32)</td>
<td>Week 4 (n=32)</td>
</tr>
<tr>
<td>HCV-RNA&lt;12 IU/mL (%)</td>
<td>0 (22)</td>
<td>21 (100%)</td>
</tr>
<tr>
<td>HIV-RNA&lt;50 copies/mL (%)</td>
<td>33 (100%)</td>
<td>31 (94%)</td>
</tr>
<tr>
<td>CD4+ (cells/µl)</td>
<td>466 (324-668)</td>
<td>463 (157-567)</td>
</tr>
<tr>
<td>CD4+ change since BL (cells/µl)</td>
<td>0 (0)</td>
<td>(-140 / 40)</td>
</tr>
<tr>
<td>Number of pts with ≥1 AE grade 3-4</td>
<td>0 (13)</td>
<td>4 (1%)</td>
</tr>
</tbody>
</table>

Table (abstract: SAT-205)

75. Poster (#SAT-206)

Viral hepatitis: Hepatitis C – clinical (therapy)
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00
DIFFERENCES BETWEEN HEPATITIS HCV-MONoinFECTED AND HCV-HIV-COinfECTED PATIENTS TREATED WITH NEW DAA-BASED THERAPIES


Background and Aims: Our aim was to compare HCV mono (HCV) and HIV-coinfected (HIV/HCV) individuals treated with DAA in two large cohorts in Madrid.

Methods: Prospective analysis comparing characteristic and outcomes of HCV vs. HIV/HCV patients treated (Apr/15–Oct/15) at our centers.

Results: 1,240 HCV and 490 HIV/HCV individuals were treated (Table 1). HIV/HCV individuals were younger (mean age: 51.4 vs. 58.4 years), more frequently male (76.5% vs. 55.2%) and were more commonly infected with genotypes 1a (36.7% vs. 17.2%), 3 (14.7% vs. 6.6%) and 4 (23.5% vs. 4.6%). No significant differences were found in the child-Pugh category, liver stiffness (LS) and HCV-RNA level. LS > 14 Kpa were observed in 42.3% of the HCV and in 48% of the HIV/HCV individuals. DAA-regimens differed between HCV and HIV/HCV. The main difference was that Abbvie-3D regimen was most commonly used in HCV individuals with genotype 1a vs. 1b, p < 0.001. Data of SVR at W12 was already available only in 266 HCV and 98 HIV/HCV individuals: 96.6% for HCV vs. 95.5% for HIV/HCV. Updated data will be giving during the conference.

Conclusions: Approximately half of the patients treated with DAA-regimens had advanced liver disease. No significant differences between HCV and HIV/HCV were seen in severity of liver disease, although HIV/HCV were ten years younger. Significant differences between groups were also found in gender and genotype distribution. The type of DAA-regimens according to genotype was similar between both groups, except in genotype 1a, in with the Abbvie-3D regimen was more frequently used in HCV than HIV/HCV individuals.

76. Poster (#SAT-210)

Viral hepatitis: Hepatitis C – clinical (therapy)
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00
MODELING EARLY HCV KINETICS TO INDIVIDUALIZE DIRECT ACTING ANTIMVIRALS TREATMENT DURATION IN PATIENTS WITH ADVANCED CIRRHOSIS


1. Liver Unit, Hospital Clinic, IDIBAPS, CIBERehd., Barcelona, Spain; 2. The Program for Experimental & Theoretical Modeling, Division of Hepatology, Loyola University Medical Center, Maywood, Illinois, United States; 3. Centre for Immunity, Infection and Evolution, University of Edinburgh, Edinburgh, United Kingdom; 4. Center for Modeling and Simulation in the Biosciences, Brown University, Providence, Rhode Island, USA

Background and Aims: While recent direct acting antiviral (DAAs)-based regimens achieve sustained virological response (SVR) rates of over 90%, there is still substantial interest in optimizing length (and cost) of therapy, particularly in difficult-to-cure populations, such as advanced cirrhotic patients. We aimed to investigate whether modeling of very early HCV-RNA kinetics after therapy initiation could
be helpful for estimating the optimal treatment duration to achieve cure.

Methods: We included 90 patients with HCV-related chronic liver disease who received DAAs-based treatments for 12, 16 or 24 weeks, in a single centre. HCV genotype, liver disease stage [Child-Pugh (CTP)], MELD, hepatic venous pressure gradient [HVPG], liver stiffness [LS], platelets count [PLT], albumin level [ALB], IL28B, and treatment regimen were registered. Viral load was assessed at baseline, at 4, 8 and 24 hours after treatment initiation, as well as at days 2, 3, 4, 7 and at weeks 2, 3 and 4 (or until target-not-detected [TND]). HCV-RNA < 15 IU/mL. A mathematical modeling approach was used to estimate cure, i.e., <1 virus copy in the entire extracellular body fluid and <1 infected cells in the body.

Results: Ninety patients (90% cirrhotics) received different treatment regimens: sofosbuvir (SOF)/simeprevir (SMV) + RBV (n = 32), SOF/ledipasvir (LDV) + RBV (n = 16), SOF/daclatasvir (DCV) + RBV (n = 15), ombitasvir (OBV)/paritaprevir-ritonavir (PTV)/r + RBV (n = 14), DCV/SMV + RBV (n = 9) and SOF + RBV (n = 4). Among patients 37% had a MELD ≥ 12, 25% were CTP ≥ B7 and 70% had an HVPG ≥ 12 mmHg. Treatment outcomes are: 81% SVR12, 8% SVR4, 5% treatment failure, 6% pending. Modeling results are currently available in 52 patients. The median time to reach TND was 14 days (range 0.3–49). Modeling indicated that the median time to cure was 8.7 (range 2.5 to 20.2) weeks. Median time to cure was significantly longer in patients with CTP ≥ B7 compared to those with CTP<B7 (9.1 weeks [range 4.7–20.2] vs 7.5 weeks [range 2.5–17.3], p = 0.002) and in patients with ALB < 35 compared to those with ALB ≥ 35 (9.2 weeks [range 4.2–15.1] vs 7.9 weeks [range 2.5–20.2], p = 0.048).

Conclusions: Based on very early kinetic modeling, most cirrhotic patients will be cured by treatment regimens ranging from 8 [44%] to 10 [25%] weeks with higher proportion [29% vs 8%] of those with more advanced disease (CTP ≥ B7 vs CTP < B7) requiring >12 week treatment durations to achieve cure. The use of early viral-kinetic analysis has the potential to individualize duration (and cost) of DAA therapy.

77. Poster (#SAT-213)
Viral hepatitis: Hepatitis C – clinical (therapy)
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

INTERFERON-FREE TREATMENT WITH SOFOSBUVIR PLUS DACLATASVIR ACHIEVES SUSTAINED VIROLOGIC RESPONSE IN 100% OF DIFFICULT-TO-TREAT HIV/HCV-COINFECTED PATIENTS AND DECREASES LIVER STIFFNESS

M. Mandorfer1, on behalf of Vienna HIV & Liver Study Group, P. Schwabi1, S. Steiner1, B. Scheiner1, D. Chromy3, T. Bucsis3, A.F. Staettermayer1, M.C. Aichelburg2, K. Grabmeier-Pfistshammer2, M. Trauner1, T. Reiberger1, M. Peck-Radosavljevich1 and Vienna HIV & Liver Study Group.

Background and Aims: We aimed to investigate the safety and efficacy of interferon (IFN)- and ribavirin (RBV)-free therapy with sofosbuvir plus daclatasvir (SOF/DCV) in HIV/HCV-coinfected patients (HIV/HCV), who have an urgent need for effective antiviral therapy. We also assessed its impact on liver stiffness.

Methods: Thirty-four thoroughly documented HIV/HCV with advanced liver disease (advanced fibrosis and/or portal hypertension; n = 31) or severe extrahepatic manifestations (n = 3) who received SOF/DCV were retrospectively studied. The following treatment durations were applied: HCV-genotype (HCV GT1)/4 without cirrhosis: 12 weeks; HCV-GT1/4 with cirrhosis: 24 weeks; HCV-GT3: 24 weeks; if HCV-RNA was detectable 4 weeks before the end of treatment, treatment was extended by 4 weeks at a time.

Results: Fifty percent of patients were treatment-experienced. The majority of patients had HCV-GT1 (67%), while HCV-GT3 and HCV-GT4 were observed in 24% and 9% of patients, respectively. Eighty-five percent had liver stiffness >9.5 kPa or METAVIR stage ≥F2 and 41% had liver stiffness >12.5 kPa or METAVIR stage F4. Portal hypertension (HVPG ≥ 6 mmHg) and clinically significant portal hypertension (HVPG ≥ 10 mmHg) were observed in 68% (18/28) and 25% (7/28) of patients, respectively. The patients with severe extrahepatic manifestations had cryoglobulinemia with leg ulcers or end-stage renal disease, and Non-Hodgkin lymphoma (n = 1 each). Sustained virologic response 12 weeks after the end of treatment (SVR12) was achieved in 100% (34/34) (see Figure panel A). Treatment with SOF/DCV was generally well-tolerated and there were no treatment discontinuations.

Among 33 patients with paired liver stiffness measurements, liver stiffness decreased in 88% (29/33) of patients, while it increased in 12% (3/33) of patients (see Figure panel B). There was a decrease in liver stiffness between BL and FU (11.4 [10] vs. 6.9 [7.3] kPa; mean change: -4.41 ± 0.79 kPa; p < 0.001; see Figure panel B). The mean relative change in liver stiffness was -27 ± 4%.

Conclusions: IFN- and RBV-free treatment with SOF/DCV was well tolerated and achieved SVR12 in all difficult-to-treat HIV/HCV. It also significantly improved liver stiffness, suggesting anti-fibrotic and anti-portal hypertensive effects.

78. Poster (#SAT-228)
Viral hepatitis: Hepatitis C – clinical (therapy)
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

THE EFFECT OF SOFOSBUVIR CONTAINING REGIMES IN PATIENTS WITH HCV GENOTYPE 3 INFECTION – A SCANDINAVIAN REAL-LIFE EXPERIENCE


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2. Infectious Disease Department, Karolinska Universityhofsudding, Stockholm, Sweden;
3. Dept of Gastroenterology, Sønderborg sykehus, Arendal;
4. Dept of Gastroenterology, Stavanger University Hospital, Stavanger, Norway;
5. Department of Infectious Medicine/Virology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden;
6. Infectious Disease Department, Vestre Viken HF, Drammen, Drammen, Norway;
7. Gastroenterology, Helsinki University Hospital, Helsinki, Finland;
8. Department of Infectious Diseases, Malmö University Hospital, Malmö, Sweden;
9. Department of Infectious Diseases, Aalborg University Hospital, Aalborg, Denmark;
10. Infectious Disease Department, Odense University Hospital, Odense;
11. Dept of Hepatology, Copenhagen University Hospital, Rigshospitalet, Copenhagen;
12. Dept of Gastroenterology, Aalborg University Hospital, Aalborg;
13. Department of Infectious Diseases, Odense Hospital, Odense;
14. Department of Infectious Diseases, Copenhagen University Hospital, Copenhagen;
15. Department of Gastroenterology, Aalborg Hospital, Aalborg;
16. Infectious Disease Department, Copenhagen University Hospital, Hvidovre, Copenhagen, Denmark
Methods: We included 229 patients. The mean age was 55 years (range 31–77), 68% were men, 46% were treatment experienced and 67% of 220 with available staging were cirrhotic.

Results: SVR4 was achieved in 213 (92%), 11 (5%) experienced virological relapse, 4 (2%) non-response and 1 (0.4%) viral breakthrough. Two patients died during treatment (unrelated to therapy). SVR4 was achieved in 140/154 cirrhotics (91%) compared to 63/66 (96%) of non-cirrhotics. Among those with a transient elastography available those with liver elasticity below 12.5 kPa, between 12.5 and 25 kPa, between 25 and 37.5 kPa and above 37.5 kPa the SVR4 rates were 100%, 93%, 96% and 75%, respectively (n = 144). Among all patients SVR 4 was obtained in 16/19 (84%) treated with SOF + RBV for 24 weeks, 53/55 (92%) of those treated with SOF + pegIFN + RBV for 12 weeks, 14/16 (88%) of those treated with Harvoni +/- RBV and 78/79 of those treated with SOF + DCV +/- RBV for 12 weeks and 44/49 (90%) of those treated SOF + DCV +/- RBV for 24 weeks.

Conclusions: With SOF containing regimes for genotype 3 infected patients SVR 4 rates over 90% were achieved in a real world setting.

### Table 1: Baseline Demographic and Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57.3 ± 10.3</td>
</tr>
<tr>
<td>Male, no. (%)</td>
<td>149 (65%)</td>
</tr>
<tr>
<td>Race, no. (%)</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>129 (56%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>54 (23%)</td>
</tr>
<tr>
<td>African-American</td>
<td>44 (19%)</td>
</tr>
<tr>
<td>Other</td>
<td>15 (6%)</td>
</tr>
<tr>
<td>Asian</td>
<td>7 (3%)</td>
</tr>
<tr>
<td>History of previous treatment, no. (%)</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>230 (99%)</td>
</tr>
<tr>
<td>Treatment-experienced</td>
<td>15 (6%)</td>
</tr>
</tbody>
</table>

### Table 2: Sustained virologic response

<table>
<thead>
<tr>
<th>SVR 4 status</th>
<th>No.</th>
<th>SVR 12 status</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment-naive</td>
<td>99%</td>
<td>Treatment-experienced</td>
<td>99%</td>
</tr>
</tbody>
</table>

79. Poster (#SAT-231)

**Viral hepatitis: Hepatitis C – clinical (therapy)**

**Date & Time:** Saturday, April 16, 2016 - 08:00 - 18:00

**SOFOSBUVIR/DACLATASVIR/RIBAVIRIN FOR 12 WEEKS IN PATIENTS WITH GENOTYPE 3 HEPATITIS C AND ADVANCED FIBROSIS/CIRRHOSIS: RESULTS FROM A REALWORLD COHORT**

O.F. Ahmed1, F. Marra2, R. Fox1, M. Priest2, S. Datta2, M. Heydtmann3, S.T. Barclay1.

1. Walton Liver Clinic, Glasgow Royal Infirmary; 2. Gastroenterology and Hepatology, Queen Elizabeth University Hospital, Glasgow; 3. Gastroenterology and Hepatology, Royal Alexander Hospital, Paisley, United Kingdom

**Background and Aims:** The combination of Sofosbuvir/Daclatasvir/Ribavirin (Sof/Dac/Rbv) for 12 weeks has shown good clinical efficacy amongst genotype 3 (GT3) patients with advanced fibrosis in a clinical trial setting, and within expanded access programmes (EAP). Outcomes from the use of this combination in routine clinical care are limited. We sought to examine the sustained viral response rates (SVR) of non EAP patients with GT3 infection and F3/4 disease, treated in Glasgow treatment centres.

**Methods:** The Scottish Hepatitis C databases were examined to identify GT3 patients with F3 (liver stiffness (LSM) > =9.5 kPa <12.5 kPa) or F4 cirrhosis (LSM >12.5 kPa, liver biopsy or imaging) treated in Glasgow treatment centres with Sof/Dac/Rbv for 12 weeks. Demographics, Child’s score, baseline viral load, week 4 and 12 PCR, SVR 4 and SVR12 were recorded, as were adverse events and premature discontinuations. HCV RNA was performed using Abbott Realtime PCR (lower limit of quantification (LLOQ) 12 IU/mL).

**Results:** 27 patients met the inclusion criteria, 19 (70%) Male, mean age 49.3 (±7.4), 9 (33.3%) treatment experienced. 26/27 (96.3%) were cirrhotic of whom 15 (55.5%)/7 (25.9%)/4 (14.8%) were Child’s A/B/C respectively. 2 patients had HIV co infection, and one was post liver transplant. Median baseline viral load was 4.92 IU/mL (±1.1). At week 4 18 (69%) patients had RNA < 12 IU/mL (8 undetectable, 10 detectable), and 6 (31%) patients had quantifiable viraemia (median 22 IU/mL range 14–40 IU/mL). Treatment was well tolerated with no discontinuations due to drug related adverse events. One patient’s treatment was stopped after 3 weeks due to an attempted hanging and subsequent psychiatric admission (excluded from SVR analysis), not judged related to treatment. One patient was admitted with variceal bleeding but maintained on treatment and achieved SVR. All patients achieved an end of treatment response (21 undetectable, 5 detectable <LLOQ). To date 16/18 (84.2%) of patients have achieved SVR12, including 4/5 (80%) of those with quantifiable RNA at week 4, and 4/5 (80%) of those detectable <LLOQ at end of treatment. Full SVR data for the cohort will be presented.

**Conclusions:** Sof/Dac/Ribwas safe and effective when used in routine clinical care, amongst a cohort with advanced liver disease. Neither quantifiable viraemia at week 4, nor detectable viraemia <LLOQ at end of treatment appear to impact on SVR12.

80. Poster (#SAT-232)

**Viral hepatitis: Hepatitis C – clinical (therapy)**

**Date & Time:** Saturday, April 16, 2016 - 08:00 - 18:00

**SOFOSBUVIR/DACLATASVIR/RIBAVIRIN FOR 12 WEEKS IN PATIENTS WITH GENOTYPE 3 HEPATITIS C AND ADVANCED FIBROSIS/CIRRHOSIS: RESULTS FROM A REALWORLD COHORT**

O.F. Ahmed1, F. Marra2, R. Fox1, M. Priest2, S. Datta2, M. Heydtmann3, S.T. Barclay1.

1. Walton Liver Clinic, Glasgow Royal Infirmary; 2. Gastroenterology and Hepatology, Queen Elizabeth University Hospital, Glasgow; 3. Gastroenterology and Hepatology, Royal Alexander Hospital, Paisley, United Kingdom

**Background and Aims:** The combination of Sofosbuvir/Daclatasvir/Ribavirin (Sof/Dac/Rbv) for 12 weeks has shown good clinical efficacy amongst genotype 3 (GT3) patients with advanced fibrosis in a clinical trial setting, and within expanded access programmes (EAP). Outcomes from the use of this combination in routine clinical care are limited. We sought to examine the sustained viral response rates (SVR) of non EAP patients with GT3 infection and F3/4 disease, treated in Glasgow treatment centres.

**Methods:** The Scottish Hepatitis C databases were examined to identify GT3 patients with F3 (liver stiffness (LSM) > =9.5 kPa <12.5 kPa) or F4 cirrhosis (LSM >12.5 kPa, liver biopsy or imaging) treated in Glasgow treatment centres with Sof/Dac/Rbv for 12 weeks. Demographics, Child’s score, baseline viral load, week 4 and 12 PCR, SVR 4 and SVR12 were recorded, as were adverse events and premature discontinuations. HCV RNA was performed using Abbott Realtime PCR (lower limit of quantification (LLOQ) 12 IU/mL).

**Results:** 27 patients met the inclusion criteria, 19 (70%) Male, mean age 49.3 (±7.4), 9 (33.3%) treatment experienced. 26/27 (96.3%) were cirrhotic of whom 15 (55.5%)/7 (25.9%)/4 (14.8%) were Child’s A/B/C respectively. 2 patients had HIV co infection, and one was post liver transplant. Median baseline viral load was 4.92 IU/mL (±1.1). At week 4 18 (69%) patients had RNA < 12 IU/mL (8 undetectable, 10 detectable), and 6 (31%) patients had quantifiable viraemia (median 22 IU/mL range 14–40 IU/mL). Treatment was well tolerated with no discontinuations due to drug related adverse events. One patient’s treatment was stopped after 3 weeks due to an attempted hanging and subsequent psychiatric admission (excluded from SVR analysis), not judged related to treatment. One patient was admitted with variceal bleeding but maintained on treatment and achieved SVR. All patients achieved an end of treatment response (21 undetectable, 5 detectable <LLOQ). To date 16/18 (84.2%) of patients have achieved SVR12, including 4/5 (80%) of those with quantifiable RNA at week 4, and 4/5 (80%) of those detectable <LLOQ at end of treatment. Full SVR data for the cohort will be presented.

**Conclusions:** Sof/Dac/Ribwas safe and effective when used in routine clinical care, amongst a cohort with advanced liver disease. Neither quantifiable viraemia at week 4, nor detectable viraemia <LLOQ at end of treatment appear to impact on SVR12.
Efficacy of Sofosbuvir/Ledipasvir in Treating Genotype 1 and 4 Hepatitis C for 8/12 Weeks: Results from a Difficult to Treat Cohort


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Background and Aims: Sofosbuvir/Ledipasvir (SOF/LDV) is highly effective in treating patients with genotype (GT) 1, 4, 5 and 6 hepatic C. Real world cohort data from the United States have highlighted a reluctance to use 8 week treatment regimens in eligible non cirrhotic patients, and suggested that proton pump inhibitor (PPI) use may have a detrimental impact on sustained viral response (SVR) rates. We sought to examine the impact of these, and other baseline factors in patients attending our treatment centres.

Methods: The Scottish Hepatitis C database was examined to identify patients commencing treatment with SOF/LDV in Glasgow treatment centres prior to 01/10/2015. Patients were treated to a local protocol; Treatment naive FO-3 patients (liver stiffness <12.5 kPa/11.9 kPa [HIV co-infected]) were treated for 8 weeks, irrespective of baseline viral load and HIV status. All other patients were treated for 12 weeks with addition of Ribavirin (RBV) post liver transplant, in decompensated cirrhosis, treatment experienced cirrhosis, platelets <75 and protease inhibitor (PI) failures. All patients underwent a screen for drug-drug interactions (DDIs) and PPI dose was reduced to omeprazole 20 mg (or equivalent) with appropriate dosing instructions. Standard practice was to dispense SOF/LDV from a community pharmacy, with directly observed therapy where appropriate. Data on demographics, liver disease severity, methadone use, treatment regimens, on treatment response, SVR and premature discontinuation were obtained from the database augmented by chart review. Viral RNAs were tested using Abbott Realtime PCR, lower limit of quantification (LLOQ) 12 IU/mL.

Results: Demographics and baseline characteristics are displayed in Table 1. The cohort are predominantly male, over 80% have advanced fibrosis (1:10 Child’s B/C), around 1 in 3 are treatment experienced, and high levels of opiate substitution, PPI use and drug of abuse use were seen. To date 108 patients have completed treatment. 1 patient discontinued treatment early due to non-compliance; no discontinuations due to adverse events have been seen. 41/45 (91%) of patients have achieved SVR12 (8/8 (100%) treated for 8 weeks), 33/37 (89.1%) of those treated for 12 weeks. Full SVR12 data analysed according to baseline factors will be presented.

Conclusions: Sofosbuvir/Ledipasvir is well tolerated in a difficult to treat real world cohort, with SVR12 rates comparable to clinical trials.

Patient characteristics n=143

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>104 (72.2)</td>
</tr>
<tr>
<td>Mean Age (±Standard deviation)</td>
<td>50 (±8.4)</td>
</tr>
<tr>
<td>HIV co infection (%)</td>
<td>9 (6.3)</td>
</tr>
<tr>
<td>Post liver transplant (%)</td>
<td>2 (1.4)</td>
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<tr>
<td>On opiate substitution therapy (%)</td>
<td>51 (35.7)</td>
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<tr>
<td>Positive drugs of abuse screen within 12 months of treatment (%)</td>
<td>25 (17.5)</td>
</tr>
<tr>
<td>Prescribed PPI</td>
<td>42 (29.4)</td>
</tr>
<tr>
<td>F4 (%)</td>
<td>85 (59.4)</td>
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<tr>
<td>CPT A (%)</td>
<td>70 (48.9)</td>
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<tr>
<td>CPT B (%)</td>
<td>11 (7.7)</td>
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<tr>
<td>CPT C (%)</td>
<td>4 (2.8)</td>
</tr>
<tr>
<td>F3 (%)</td>
<td>31 (21.7)</td>
</tr>
<tr>
<td>F0-2 (%)</td>
<td>27 (18.9)</td>
</tr>
<tr>
<td>Median Viral load log (IQR)</td>
<td>5.91 (1.05)</td>
</tr>
<tr>
<td>Genotype (%)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>142 (99.3)</td>
</tr>
<tr>
<td>4</td>
<td>1 (0.7)</td>
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<tr>
<td>Treatment experienced</td>
<td>51 (35.7)</td>
</tr>
<tr>
<td>Prior PI failure</td>
<td>12 (8.4)</td>
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81. Poster (#SAT-241)

Viral hepatitis: Hepatitis C – clinical (therapy)

Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

Ledipasvir/Sofosbuvir Treatment for 8 Weeks in Genotype 1 Infected Patients Under Real Life Conditions: Data from the German Hepatitis C Register (DHC-R)


Background and Aims: Ledipasvir/Sofosbuvir (LDV/SOF) for 8–24 weeks is approved for the treatment of chronic hepatitis C. In the ION-3 study 8 weeks of LDV/SOF was non-inferior to 12 wks in previously untreated GT1 patients without cirrhosis. According to the summary of product characteristics (SmPC) a treatment duration of 8 wks may be considered in naïve non-cirrhotic HCV GT1 infected patients with viral load <6 Mio IU/mL. Aim of this analysis was to evaluate the virologic response rates of 8 wks treatment under real world conditions.

Methods: The DHC-R (Deutsches Hepatitis C Register) is a registry for the documentation of the HCV treatment situation in Germany. Data are collected in a centralized database and on-site monitoring is implemented. Data collection is ongoing. In this analysis data of patients with 8 or 12 wks treatment with LDV/SOF and available SVR12 data (until 9/2015) were included. Baseline characteristics, prior treatment history, safety and effectiveness were investigated.

Results: 262 (141 female) pts (8 week) and 444 (210 female) pts (12 week) met the inclusion criteria. One pt in the 8 week group (1) and 130 in the 12 week group (2) had weight-based ribavirin added to

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IMPACT OF SUSTAINED VIRAL RESPONSE ON RENAL FUNCTION IN PATIENTS WITH CHRONIC INFECTION BY HEPATITIS C VIRUS (HCV)

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Background and Aims: Chronic infection by hepatitis C virus (CHC) is often associated with extrahepatic manifestations including kidney disease. The glomerular filtration rate (GFR) is widely accepted as the best overall index of kidney function in health and disease. The aim of our study was to determine the proportion of patients with renal insufficiency and to evaluate the impact of the treatment with direct acting antivirals (DAA) on the renal function.

Methods: Design: Prospective study

Patients: All patients with CICHVC who initiated therapy with DAA between April and Sep/15 were included. Demographic, clinical and laboratory variables were prospectively collected. Fibrosis was evaluated by biopsy or Fibroscan (F2: 7.5–9.4 kPa, F3: 9.5–12.4 kPa and cirrhosis ≥12.5 kPa).

Treatment: DAWere given according to the EASL guidelines. Sustained virologic response (SVR12): undetectable viral load by COBAS Taqman 12 weeks after ending the treatment. Renal function. We calculated the glomerular filtration rate (GFR) with the CKD-EPI equation before and 12 weeks after the end of treatment and patients categorized according to the KDIGO classification. Primary endpoints. Proportion of patients with chronic renal insufficiency (CRI), defined as a GFR < 90 mL/min, and changes in the GFR 12 weeks after the end of treatment in those patients with CRI baseline.

Results: 124 individuals were included, 67.7% male, mean age 53.8 years. 84 (67.7%) were pre-treated with Peginterferon and ribavirin. (22 relapsers, 13 partial responders, 40 null responders and 9 intolerants).103 had genotype 1 (1a: 29.1%, 1b: 68.9% and others: 2%), 12 genotype 3 and 9 genotype 4. The baseline viral load was over 800,000 IU/mL in 94 (75.8%). Fibrosis staging: 10 were F0–F1; 29 F2; 34 F3 and 51 (41%) had cirrhosis. In this cohort, 70/71 (98%) who completed 12 weeks of follow-up had SVR12. 51/124 (41%) had a CRI baseline (44 categorie 2 and 6 categorie 3a). Out of them, 27 completed 12 weeks of follow-up with 100% SVR12. In this subgroup, the GFR baseline improved significantly after obtaining SVR12 (78.55 ± 8.96 ml/min vs 81.85 ± 12.87 ml/min; p = 0.037).

Conclusions: Under real world conditions, 8 wks LDV/SOF achieves comparable SVR rates to 12 weeks treatment, but relapses are more frequent in particular in patients who do not meet the selection criteria according to the SmPC.

83. Poster (#SAT-261)

Viral hepatitis: Hepatitis C – clinical (therapy)

THE REALWORLD EXPERIENCE OF DACLATASVIR AND ASUNAPREVIR COMBINATION THERAPY FOR MORE ELDERLY PATIENTS THAN THE CLINICAL TRIAL SUBJECTS WITH GENOTYPE 1B CHRONIC HEPATITIS C

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1. Hepatology, Sapporo Kosei General Hospital, Sapporo, Japan.

Background and Aims: The dual oral therapy with daclatasvir (DCV) and asunaprevir (ASV) for patients with HCV infection was accepted for the clinical application in July 2014 in Japan. The entry criterion for the subject’s age in the clinical trial of DCV + ASV was 75 years old or less. There exist many elderly patients who face a risk of development to cirrhosis or hepatocellular carcinoma (HCC), and the evaluation of DCV + ASV treatment for those patients seems urgent issue. In this study, we investigated the efficacy and the safety of DCV + ASV for cases over 75 years old in the real world.

Methods: From September 2014, total of 300 genotype 1 patients were treated with fixed daily dose of DCV (60mg) and ASV (200mg) for 24 weeks. Subjects were divided into 2 groups (Gr) with age: Gr.A ≤75yo and Gr.B >75yo. Final efficacy was determined as SVR12. Serum Wisteria floribunda agglutininpositive Mac-2 binding protein (WFA+M2BP) was measured with HiSCL™ M2BPG reagent (Sysmex Co., Kobe, Japan) for estimating liver fibrosis. Liver stiffness was measured by FibroScan™ (Echosens, Paris, France). Trough value of ASV was measured once a week after the start of DCV+ASV therapy with HPLC method. Resistance-associated variants (RAV) at D168 were performed in 39 cases and all RAVs were accepted for the clinical application in July 2014 in Japan. The dual oral therapy with daclatasvir and asunaprevir for patients with HCV infection was accepted for the clinical application in July 2014 in Japan.

Results: Eighty cases (26.7%) were over 75 years old (Gr.B) and the oldest case was 88 years old. Rate of female (66.3%), cirrhosis (52.5%), past history of HCC (30.0%), hypertension (35.0%), diabetes mellitus (15.0%), major I2B8 genotype (8099917: TT) (59.7%) and RAV (Y93H) in N53, L31 and Y93 in N53 were measured by PCR-Invader method.

Results: Eighty cases (26.7%) were over 75 years old (Gr.B) and the oldest case was 88 years old. Rate of female (66.3%), cirrhosis (52.5%), past history of HCC (30.0%), hypertension (35.0%), diabetes mellitus (15.0%), major I2B8 genotype (8099917: TT) (59.7%) and RAV (Y93H) in N53, L31 and Y93 in N53 were measured by PCR-Invader method.

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Conclusions: Despite the adverse conditions related to physiological functions, complications and biochemical abnormalities,
elderly patients over 75 years old could receive DCV + ASV combination therapy as safe as younger patients. Lower SVR rate was associated mainly with viral factor such as RAV.

84. Poster (#SAT-265)
Viral hepatitis: Hepatitis C – clinical (therapy)
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

RELAPSE AND TREATMENT-EMERGENT RAVS WITH DAA-BASED REGIMENS IN HEPATITIS C VIRUS (HCV) MONO- OR HUMAN IMMUNODEFICIENCY VIRUS (HIV)-HCV CO-INFECTED PATIENTS – A REAL CONCERN IN CLINICAL PRACTICE? RESULTS FROM THE GERMAN HEPATITIS C COHORT (GECCO)
S. Christensen1, P. Ingiliz2, K. Schewe3, J. Rockstroh4, D. Huppe5, A. Baumgarten5, T. Lutz6, G. Schmutz7, K.G. Simon8, H. Busch9, T. Kimhofer9, S. Mauss7.

Background and Aims: The first direct acting antivirals (DAAs) were approved in Europe 2014 based on limited study data. Although relapse with treatment-emergent resistance-associated variants (RAVs) were rare events in clinical studies, real-life data on virologic failure, RAVs and success of retreatment are lacking.

Methods: The GECCO cohort is a multicenter cohort from 8 sites in Germany. To date n = 1,170 (24% HIV-coinfected) patients started on a second generation DAA containing regimen. For the current analysis, only patients with data at least 4 weeks after the end of therapy (FU4) were included. All patients within the GECCO cohort are part of the German hepatitis C registry.

Results: Overall, n = 796 patients reached FU4, n = 619 FU12. N = 36 patients experienced a virologic relapse (4.5%). Of those n = 6 where HCV RNA negative at FU4 and relapsed until FU12. The majority of patients n = 23/36 (64%) were pretreated, n = 10/36 (28%) HIVcoinfected and n = 22/36 (61%) had liver cirrhosis defined by FibroScan ≥12.5 KPa or APRI ≥2. Virologic failure rate according to HCV genotype (GT)was: GT1 = n = 24/59 (4%), GT2 = n = 3/35 (9%), GT3 = n = 8/109 (7%) and GT4 = n = 1/46 (2%). Most patients relapsed on sofosbuvir (SOF) plus ribavirin n = 11/95 (11.6%), n = 13/149 (8.7%) relapsed on SOF, pegylated interferon (PEG) and RBV, n = 7/315 (2.2%) on SOF, ledipasvir (LDV) ± RBV, n = 3/116 (2.6%) on SOF and daclatasvir (DCV) ± RBV, n = 2/36 (5.6%) on SOF and simesperavir (SMV).

N = 7/36 relaper were tested for RAVS before treatment and n = 22/36 after failure. No NS3B or NS5B RAVS were found. In n = 7/22 RAVs could be detected at timeoff relapse.NS5Amutations were found in 6 of them, causing a broad resistance to currently available NSSA inhibitors. All failed on LDVorDCVcontaining regimens. Retreatmentwas initiated in n = 20/36 patients. So far n = 16/20 (80%) of retreated patients achieved SVR4 and 10/20 (50%) SVR12. To date neither relapse nor breakthrough or loss to follow up occurred in the retreated patients.

Conclusions: In this real life cohort the rate of relapse is low (4.5%) and most likely to occur in GT2 or GT3, pretreated patients, liver cirrhosis and being treated with SOF/RBV or SOF/PEG/RBV. Relapses after SOF/LDV or SOF/DCV containing regimens were associated with the emergence of RAVs causing a broad resistance to currently available NSSA inhibitors. Retreatment in this cohort is ongoing and so far successful.

85. Poster (#SAT-270)
Viral hepatitis: Hepatitis C – clinical (therapy)
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

DECREASE IN LIVER STIFFNESS IN CHRONIC HEPATITIS C PATIENTS AFTER DIRECT – ACTING ANTIVIRAL THERAPY
S. Kainth1, A. Jindal1, S.K. Sarin2 and ILBS.
1. Hepatology, ILBS, New Delhi, India

Background and Aims: Chronic hepatitis C virus infection leads to progressive liver fibrosis. Liver fibrosis, rather than serum viremia, is the most important prognostic factor in chronic HCV patients. The present study aimed to analyze the changes of liver stiffness and its associated factors in chronic hepatitis C after Direct acting antiviral therapy as the literature is lacking for the effect of DAA in improvement of liver fibrosis.

Methods: Patients with chronic HCV started on DAA therapy were enrolled. Liver stiffness was measured at the time of enrollment, and after completion of DAA therapy with FibroScan & changes of stiffness and its associated factors were analyzed. Patients with ETR and SVR were analysed for improvement in fibrosis. Patients with high and normal ALT were separately assessed and compared for improvement in fibrosis post DAA therapy and improvement in liver fibrosis was correlated with change in HVPG post therapy.

Results: One hundred and eleven patients of chronic HCV (age 51.5 ± 20 yrs, 54.7% males) who had completed DAA and achieved ETR, Fibroscan were compared which showed 79 (71.2%) patients with liver stiffness improvement & 32 patients (28.8%) had stiffness worsening. SVR at 4 weeks was seen in 23 patients with stiffness reduction in 17 (73.9%) patients vs 5 (83.3%) with SVR –ve at 4 weeks (p = 0.74). Cirrhotic (n = 83) patients showed liver stiffness reduction in 56 (67.5%) vs non cirrhotics (n = 22) 84.6%, p = 0.13. Of the compensated cirrhosis patients (n = 77), 56 patients (72.7%) had stiffness reduction as compared to 36.4% decompensated patients (p < 0.018). Comparison was also made between HCV patients post DAA with high vs low ALT (cut off-40U/L) at baseline. Of the 109 patients 20 patients had normal ALT with 17 (85%) patients having liver stiffness reduction as compared to 61 (68.5%) patients with high ALT (p = 0.14). HVPG at baseline was evaluated as a predictor for post DAA liver stiffness reduction with patients with HVPG <12 mHg (n = 19), LSM reduction in 13 patients (68.4%) vs 21 patients (65.6%) with HVPG >12 mHg. 5 patients were compared for pre and post DAA HVPG vs Fibroscan and showed mean 24% reduction in HVPG and mean 34.5% improvement in liver stiffness.

Conclusions: Liver stiffness decreased in End treatment response and Sustained virological response following DAA therapy in chronic HCV patients and liver stiffness reduction as measured by fibroscan is comparable with HVPG reduction post DAA therapy.

86. Poster (#SAT-367)
Autoimmune and hepatobiliary disease 2
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

CORRELATION OF NON-INVASIVE MARKERS OF LIVER FIBROSIS IN PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS: A VALIDATION COHORT
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1. National Institute for Health Research Birmingham Liver Biomedical Research Unit, University of Birmingham; 2. Department of Liver Medicine, University Hospitals Birmingham, Birmingham, United Kingdom

Background and Aims: Assessment of liver fibrosis remains an important component of patient care for those with primary sclerosing cholangitis (PSC). Liver biopsy is a “gold-standard” but non-invasive markers have been proposed by a number of groups, with greater patient acceptability. We sought to validate and compare

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simple non-invasive markers of liver fibrosis in a characterised pretransplant cohort of PSC patients.

Methods: 21 patients were prospectively recruited from the PSC clinic at University Hospital Birmingham between March and September 2014. The following data were recorded on a single visit: demographics, clinical phenotype, alkaline phosphatase (ALP), aspartate aminotransferase/platelet ratio index (APRI), fibrosis-4 (FIB-4) score, model for end stage liver disease (MELD) score, Mayo clinic PSC score, Enhanced Liver Fibrosis (ELF) score and liver stiffness as measured by FibroScan®. The Fibroscan® examinations were performed by a single operator (PE). Data were analysed by Spearman’s rho correlation coefficient. Statistical significance was taken as p < 0.05.

Results: Of the 21 participants, 20 (95%) were Caucasian with 15 (71%) male. Median (range) age was 50 (18–73) years. Inflammatory bowel disease was present in 19 (90%) and 10 (48%) were treated with ursodeoxycholic acid at a median (range) dose of 13.6 (8.5–20.0) mg/Kg. ALP and MELD score did not significantly correlate with any other marker of fibrosis or disease severity. Analysing ELF, liver stiffness, APRI and FIB-4 in a pairwise fashion revealed statistically significant, positive correlation in all six pairings. The strongest association was between liver stiffness and ELF score (r = 0.706, p = 0.001) (see Figure). In addition, Mayo score showed statistically significantly correlation with ELF (r = 0.592 p = 0.006), liver stiffness (r = 0.559 p = 0.010) and FIB-4 (r = 0.733 p < 0.001).

Conclusions: Our data validates the good correlation between noninvasive markers of fibrosis in patients with PSC. This supports the increasing use of non-invasive markers of fibrosis to stratify risk in PSC, including in the long term follow up of patients, as well as in clinical trial settings.

88. Poster (#SAT-393)
Autoimmune and hepato biliary disease 2
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00
A FUT2 POLYMORPHISM INFLUENCES RESPONSIVENESS TO VANCOMYCIN IN PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS
T. Murdoch1, J. Oshiomogho1, T. Vo1, G. Kaplan2, B. Eksteen1.
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2. D’Oliveira Institute for Public Health and Division of Gastroenterology, University of Calgary, Calgary, Canada

Background and Aims: Host genetic and microbiome factors have been invoked in the pathogenesis of primary sclerosing cholangitis (PSC). Previous work has suggested a role for vancomycin in PSC, however there is heterogeneity of response across patients. FUT2 is a glycosylation enzyme responsible for presentation/secretion of ABO antigens on mucosal surfaces. The G→A mutation at rs601338 results in non-secretor status of ABO antigens, which is a risk variant for PSC and known to influence biliary microbial composition. We hypothesized that FUT2 genotype could influence responsiveness to vancomycin in PSC.

Methods: PSC patients with concomitant IBD were genotyped for the rs601338 variant (AA genotype [non-secretor], n = 10; and GG genotype [secretor], n = 10). Patients were treated with a 12-week course of vancomycin 250 mg orally four times daily. Alkaline phosphatase (ALP) levels, Mayo PSC risk score, and transient elastography (TE) were evaluated at baseline and week 12. Vancomycin resistant enterococcus (VRE) testing was undertaken at weeks 0 and 12. Statistical analysis was undertaken using Mann-Whitney test for unpaired, Wilcoxon rank test for paired, and Fischer exact test for categorical data (data reported as mean+/−SEM). Figure:
ALP levels improved in both patients with AA (A) and GG (B) FUT2 genotypes, however the decline in ALP was significantly greater in AA genotype patients (C).

Results: Twelve week treatment with vancomycin led to improvement in ALP levels (n = 20, 332+/- 25 at week 0 versus 217+/-24 mmol/L, at week 12, p < 0.0001). Treatment did not result in change in Mayo risk score or TE. While ALP did not differ by genotype at baseline, after 12 weeks of treatment it was significantly lower in AA versus GG genotype patients (152+/-19 versus 281+/-33 mmol/L, p = 0.003) (Figure). Mayo risk score and TE did not differ at baseline or week 12. After vancomycin treatment, 45% patients versus 5% at baseline were VRE positive (p = 0.008); VRE status did not differ by genotype.

Conclusions: This study demonstrates the influence of a FUT2 polymorphism on response to vancomycin therapy in a cohort of patients with PSC. High levels of VRE, in combination with unclear clinical efficacy of vancomycin for PSC beyond improvement in ALP, suggest need for a longer clinical trial to determine efficacy of vancomycin in PSC cohorts with defined FUT2 genotypes.

89. Poster (#SAT-399)
Autoimmune and hepato biliary disease 2
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

CLINICAL MANAGEMENT OF AUTOIMMUNE HEPATITIS IN THE REAL WORLD

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4. Department of Medicine and Research Laboratory of Internal Medicine, School of Medicine, University of Thessaly, Larissa, Greece;
5. Department of Surgery, Oncology and Gastroenterology, University of Padova, Padova, Italy;
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10. University Medical Centre Eppendorf, Hamburg, Germany;
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90. Poster (#SAT-427)
Non-invasive markers of liver fibrosis
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

THE RELATIONSHIP BETWEEN FIB-4 INDEX VARIATIONS AND OUTCOME IN PATIENTS WITH CHRONIC HEPATITIS C AND CIRRHOSIS: COMPARISON WITH LIVER STIFFNESS MEASUREMENT
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1. Hepatology, Hôpital Cochin APHP;
2. Hepatology, Cochin APHP;
3. Virology;
4. Département Informatique, Hôpital Cochin APHP, Paris, France

Background and Aims: To evaluate the relationship between FIB-4 index variations and clinical outcomes in a cohort of patients with chronic hepatitis C virus (HCV) infection and cirrhosis. The performances of sequential FIB-4 and liver stiffness measurements (LSM) were compared.
**Methods:** A cohort of 341 patients (male 66%; median age: 56 years) with HCV and proven compensated cirrhosis underwent sequential FIB-4 and LSM measurements from September 2006 to July 2015. Disease progression was scored as a composite end-point of endstage liver disease (ESLD) and/or hepatocellular carcinoma (HCC). A mixed model analysis adapted for repeated measures and adjusted on gender, sustained virological response (SVR), HBsAg positivity, alcohol use disorders (AUD) and the metabolic syndromes was used to evaluate the relation between the annual FIB-4 and LSM variations and outcome.

**Results:** Overall, 14 (4%) patients had detectable HBsAg, 112 (33%) had AUD; 111 (32.6%) had the metabolic syndrome; 226 (66%) had received an interferon-based antiviral treatment and 45 (13%) had achieved SVR at first noninvasive test evaluation. The baseline median values of FIB-4 index and LSM were 4.26 (interquartile range [IQR], 2.28–8.36) and 16.3 (IQR, 10.2–27.5) kPa, respectively. After a median follow-up of 23.5 months (IQR, 11–51 months), disease progressed in 136 (40%) patients, including 57 (17%) with ESLD, 47 (14%) with HCC and 32 (9%) with ESLD and HCC. In a fully adjusted model, the risk of disease progression increased linearly with FIB-4 and LSM. A 2.7 unit increase or decrease of FIB-4 index or LSM increased or decreased the risk of disease progression by 14.5% (p < 0.0001) and 11.2% (p = 0.007), respectively. FIB-4 index and LSM variations were more closely related to ESLD than to HCC.

**Conclusions:** The variations of the inexpensive and readily available FIB-4 index, similarly to LSM, are related to disease progression, especially ESLD, in HCV-patients with cirrhosis, regardless of comorbidities and SVR.

91. Poster (#SAT-428)

**Non-Invasive markers of liver fibrosis**

**Date & Time:** Saturday, April 16, 2016 - 08:00 - 18:00

**USEFULNESS OF COMMON FIBROSIS MARKERS TO PREDICT VIREMIA IN PATIENTS WITH REACTIVE HEPATITIS C ANTIBODY TEST**

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**Background and Aims:** Hepatitis C (HCV) diagnosis involves two steps: antibody screening followed by confirmatory molecular testing to "out-screen" resolved infections and biologically false-positives. Molecular testing is not widely available in resource-poor settings. We explored the added value of Aspartate-to-Platelet Ratio (APRI) and FIB-4 scores to overcome this bottleneck in the HCV diagnostic cascade.

**Methods:** We analyzed data from a cross-sectional study examining the prevalence of chronic HCV in a large HIV cohort in Phnom Penh, Cambodia. (clinical trials.gov NCT02361541). APRI and FIB-4 were calculated for patients with HCV IgG antibody positive or borderline result. ROC curves of APRI and FIB-4 to diagnose current coinfection (HCV IgG positive/ borderline and HCV RNA positive) were established with corresponding area under curve (AUC) with 95% confidence interval (CI). Optimal cut-offs, chosen by weighing false negatives (FN) twice as harmful as false positives (FP), were defined as the point which minimizes number of FP + 2* number of FN. Sensitivity/Specificity was estimated with 95% CI for these cutpoints. Finally the performance of the APRI/FIB-4 combination was assessed.

**Results:** By 03 November 2015, 2,326 patients were screened for HCV. Hundreeds eighty-three (7.9%) patients had a positive (N = 181) or borderline (N = 2) HCV IgG result; 79 tested HCV-RNA positive. Baseline parameters to calculate scores were available for all. The AUC for diagnosis of chronic HCV was 0.78 (95% CI 0.71, 0.85) for APRI and 0.70 (95% CI 0.62, 0.78) for FIB-4. The optimal cut-points were 0.367 for APRI and 1.008 for FIB-4. The corresponding sensitivity was 81% (CI 70.6%, 89%) and specificity was 67.3% (CI 57.4%, 76.2%) for APRI; whilst being 79.7% (CI 69.2%, 88%) and 51.9% (CI 41.9%, 61.8%) for FIB-4. Ninety-eight patients scored positive for HCV IgG and APRI > 0.367. Targeting HCV viral load to this subgroup would half the need for confirmatory testing. Fifteen diagnoses would have been missed; none of those had advanced fibrosis on transient elastography. When combining both scores (APRI >= 0.367 or FIB-4 >= 1.008) the sensitivity was 87.3% (CI 78%, 93.8%) and specificity was 47.1% (CI 37.2%, 57.2%).

**Conclusions:** HCV antibody testing in combination with fibrosis markers as APRI and FIB-4 might have an interesting potential to identify the majority of chronic HCV patients. In contexts with limited availability, HCV viral load testing can be targeted to a subgroup of patients to confirm the presence of chronic infection.

92. Poster (#SAT-429)

**Non-Invasive markers of liver fibrosis**

**Date & Time:** Saturday, April 16, 2016 - 08:00 - 18:00

**NATIONAL SURVEY INVESTIGATING THE POTENTIAL ROLE OF NONINVASIVE LIVER FIBROSIS TESTS IN THE UK**

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**Background and Aims:** Liver fibrosis assessment (LFA) is important in the management of patients with chronic liver disease (CLD). Liver biopsy is the "gold standard" for LFA but has recognized limitations including pain, hazard, cost & scalability. The emergence of noninvasive tests (NIT) permits novel strategies for LFA. We aimed to assess the attitudes of UK specialists towards NIT and their use in healthcare.

**Methods:** An invitation for a web-based survey was sent to 1,761 GMC registered gastroenterologists/hepatologists, specialist trainees and nurses. Questions explored themes related to LFA, liver biopsy, NIT and their use in clinical pathways. Responses were analysed using SPSS for quantitative data and NVIVO for qualitative data.

**Results:** 214 (12.2%) responses were obtained from 107 specialist hepatologists (50%); 96 gastroenterologists (45%) & 11 virologists or specialists. 95.8% of respondents perform LFA, liver biopsy, NIT and their use in clinical pathways.

**Conclusions:** This national survey found that 97.5% of UK clinicians that responded support the use of NIT but highlights that only a quarter of UK specialists report having adequate access. This may explain the variability seen in the frequency of LFA. Availability of the tests and cost were cited as the principle barriers. However, clinical pathways using NIT are emerging, and their evaluation will inform future practice. This national survey demonstrates a national consensus regarding the importance of the use of NIT in the care of patients with liver disease. Barriers to the widespread use of these
Tests are identified and should be overcome in order to improve the identification and stratification of patients with CLD.

93. Poster (#SAT-433)
Non-Invasive markers of liver fibrosis
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

TRANSPORT ELASTOGRAPHY IS SUPERIOR TO FIB-4 IN ASSESSING THE RISK OF HEPATOCARCINOMA IN PATIENTS WITH CHRONIC HEPATITIS B
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Background and Aims: Liver stiffness (LS), assessed using transient elastography (TE), and FIB-4 can both estimate the risk of developing hepatocellular carcinoma (HCC). We compared prognostic performances of LS and FIB-4 to predict HCC development in patients with chronic hepatitis B (CHB).

Methods: Data from 1,308 patients with CHB, who underwent TE, were retrospectively analyzed. FIB-4 was calculated for all patients. The cumulative rate of HCC development was assessed using Kaplan-Meier curves. The predictive performances of LS and FIB-4 were evaluated using time-dependent receiver-operating characteristic (ROC) curves.

Results: The mean age (883 men) was 50 years. During follow-up (median 6.1 years), 119 patients developed HCC. The area under the ROC curves (AUROCs) predicting HCC risk at 3, 5, and 7 years were consistently greater for LS than for FIB-4 (0.791–0.807 vs. 0.691–0.725; all p < 0.05). Similarly, when the respective AUROCs for LS and FIB-4 at every time point during the 7-year follow-up were plotted, LS also showed consistently better performance than FIB-4 after 1 year of enrollment. The combined use of LS and FIB-4 significantly enhanced the prognostic performance compared with the use of FIB-4 alone (p < 0.05), but the performance of the combined scores was statistically similar to that of LS alone (p > 0.05).

Conclusions: LS showed significantly better performance than FIB-4 in assessing the risk of HCC development, and the combined use of LS and FIB-4 did not provide additional benefit compared with the use of LS alone. Hence, LS assessed using TE might be helpful for optimizing HCC surveillance strategies.

94. Poster (#SAT-434)
Non-Invasive markers of liver fibrosis
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

ALGORITHM TO RULE-OUT CLINICALLY SIGNIFICANT PORTAL HYPERTENSION COMBINING SHEAR-WAVE ELASTOGRAPHY OF LIVER AND SPLEEN: A PROSPECTIVE MULTI-CENTER STUDY

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Background and Aims: Clinically significant portal hypertension (CSPH) is associated with severe complications and decompensation. Shear-wave elastography (SWE) of the liver might be a promising tool to predict CSPH. Spleen stiffness by transient elastography (TE) is another tool to detect CSPH. However, the value of spleen-SWE (SSWE) is still uncertain.

Methods: 158 patients with pressure gradient measurements were included into this prospective multicenter study. Liver stiffness by SWE was obtained in 155 patients. Spleen stiffness by SWE was measured in 112 patients. Among these patients 109 received both measurements.

Results: SWE (L-SWE) and S-SWE correlated with clinical events and decompensation (Child, MELD Score, ascites). SWE of liver and spleen revealed strong correlations with the pressure gradient with a great ability to distinguish between patients with and without CSPH (AUC = 0.861 for L-SWE and AUC = 0.837 for S-SWE), as well as for pressure gradients >5 mmHg and >12 mmHg. The best cut-off values regarding sensitivity and specificity were 24.6 kPa for L-SWE and 26.3 kPa for S-SWE. L-SWE < 16.0 kPa and S-SWE <26.6 kPa were able to rule-out CSPH. Cut-off values of L-SWE >29.5 kPa and S-SWE >35.6 kPa were able to rule-in CSPH. Furthermore, in patients with LSWE <16.0 kPa, S-SWE was useful to identify CSPH and by sequential use, sensitivity was raised up to 98.6%.

Conclusions: SWE accurately identified patients with clinical decompensation of liver cirrhosis. Moreover, spleen stiffness by SWE is also useful to predict CSPH. Importantly, this study offers an easy algorithm to rule-out CSPH by using sequential L- and S-SWE.

Figure: Algorithm to diagnose CSPH.
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95. Poster (#SAT-435)
Non-Invasive markers of liver fibrosis
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

TRANSIENT ELASTOGRAPHY AND COMBINATION OF FIBROTEST® AND TRANSIENT ELASTOGRAPHY FOR DIAGNOSIS OF ADVANCED FIBROSIS AND CIRRHOSIS IN PATIENTS WITH ALCOHOLIC LIVER DISEASE: A PROSPECTIVE MULTICENTER COHORT STUDY


Background and Aims: Utility of transient elastography (TE) to assess liver fibrosis is insufficiently proved in alcoholic liver disease. Therefore, liver biopsy (LB) remains the gold standard for evaluation of hepatic fibrosis in these patients. The goal of our study is to validate the diagnostic utility of TE for advanced fibrosis and cirrhosis in patients with alcohol liver disease, and evaluate whether Fibrotest® add diagnostic value in comparison or in combination with TE.

Methods: We conducted a multicentre prospective cohort study including a total of 217 patients with heavy alcohol consumption (>80 g/day over a period ≥5 years) and indication for LB examination (high serum aminotransferase levels or suspected cirrhosis) admitted to alcoholism and alcoholic liver disease. The exclusion criteria were: concomitant liver disease, contraindication or refusal of LB, severe associated disease and body mass index ≥30 Kg/m2. All patients underwent ultrasound-guided LB, TE and Fibrotest®. The overall diagnostic performance was evaluated by the area under the receiver operating characteristic (ROC) curves. The Obuchowski measures were also assessed taking into account the distribution of fibrosis stages in the cohort.

Results: Twenty-four patients were excluded due to unsuitable LB (specimen length <10 mm and number of portal spaces <10) or unreliable TE. A total of 193 patientswere considered for the analysis. Distribution of patients according to liver fibrosis stage was homogenous: F0: 24%, F1: 16%, F2: 20%, F3: 25% and F4: 15%. Liver stiffness measurement was correlated to fibrosis stage (r = 0.73; p < 0.0001), presence of alcoholic hepatitis (r = 0.61; p < 0.0001) and steatosis stage (r = 0.19; p < 0.01). In multivariate analysis, fibrosis stage and presence of alcoholic hepatitis were the only parameters correlated with liver stiffness. For diagnosis of advanced fibrosis (F ≥ 3), the areas under the ROC curve were 0.90, 0.85 and 0.91 for TE, Fibrotest® and association TE Fibrotest® respectively. For diagnosis of cirrhosis, the areas under the ROC curve were 0.93, 0.88 and 0.94 respectively. The Obuchowski measures for diagnosis of fibrosis were 0.94, 0.92 and 0.94 respectively. Performances of Fibrotest® and combination TE Fibrotest® were not significantly different from those of TE.

Conclusions: TE has an excellent diagnostic value for cirrhosis and advanced fibrosis in patients with alcoholic liver disease. The combined use of TE and Fibrotest® does not improve the performance of TE.

96. Poster (#SAT-436)
Non-Invasive markers of liver fibrosis
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

LIVER STIFFNESS MEASURED BY ACOUSTIC RADIATION FORCE IMPULSE QUANTIFICATION IN PRIMARY SCLEROSING CHOLANGITIS: A COMPARISON WITH TRANSIENT ELASTOGRAPHY PERFORMED BY FIBROSCAN® AND OTHER NON-INVASIVE TESTS

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Background and Aims: Stratifiers of disease severity and prognosis in PSC are required. Recent data highlight the utility of non-invasive assessments of liver fibrosis by F-TE for staging and prognostication in PSC. Thus far there has been no direct comparison of acoustic radiation force impulse quantification (ARFI) and Fibroscan® (F-TE) in Primary sclerosing cholangitis (PSC). Our aim was to evaluate ARFI performance in a cohort of UK patients affected by PSC and its correlations with F-TE and the currently available clinical scores of fibrosis.

Methods: Demographics, biochemistry, clinical and ultrasonographic data were prospectively collected in 66 PSC patients [39(59%) male, 7 (10.6%) small duct, 15(23%) autoimmune overlap, 18(27%) cirrhotic] consecutively attending our clinic (Nov 2014-2015). F-TE (Fibroscan®), Echosens (10 valid measurements, IQR <30%, SR<60%) and ARFI (Affinity 70G Philips, median kPa of 10 measurements) were performed on the day of the visit, after 3 hrs fasting. The most commonly used clinical scores of disease/fibrosis severity were obtained on the day of assessment. Correlations of F-TE and ARFI with scores and clinical variables were investigated. Since histology was not available for the majority of patients, liver stiffness (LS) measured by Fibroscan was used as a surrogate of liver fibrosis, using the cut-offs recently validated in PSC (7.4, 8.6, 9.6 and 14.4 kPa for fibrosis stages F1, F2, F3, and F4, respectively). ROC curve analysis was performed in order to define optimal cutoff values for ARFI.

Results: F-TE and ARFI values were significantly correlated (p < 0.0001). LS obtained with both the techniques significantly correlated with portal hypertension, splenomegaly, presence of oesophageal varices, cholestasis and inflammation, Mayo risk and MELD score, APRI, FIB-4, Fibroindex, Goteborg University Cirrhosis Index (GUCI) and King’s score (p < 0.0001), FibroQ and Lok index (p < 0.01) but not with AST/ALT ratio. Areas under curves (95%CI) for ARFI were 0.91(0.84-0.99), 0.95(0.89-1), 0.99(0.97-1) and 0.97(0.94-1) for fibrosis stage ≥1, 2, 3 and ≥4, respectively. Optimal cutoff values for F ≥ 1, F ≥ 2, F ≥ 3, F ≥ 4 were 7 (89% sens, 82% spec), 8 (96% sens, 87% spec), 10.6 (100% sens, 93% spec) and 14.5 kPa (93% sens, 94% spec), respectively.

Conclusions: ARFI correlated well with Fibroscan and other noninvasive assessments of liver fibrosis/disease stage in this cohort of PSC patients. This novel preliminary data suggests a role for ARFI in staging and monitoring progression in PSC and identifies an optimal sensitivity and specificity in detecting significant fibrosis (F ≥ 3) with a cut off of 10.6 kPa.
Non-Invasive markers of liver fibrosis

Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

RAPID AND SUSTAINED IMPROVEMENTS OF LIVER STIFFNESS VALUES IN HCV-INFECTED PATIENTS TREATED WITH DIRECT ANTIVIRAL DRUGS


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Background and Aims: The use of interferon-free antiviral therapy in chronic HCV infected patients is associated with high rate of sustained virological response (SVR). The aim of this study was to evaluate changes of liver stiffness using Acoustic Radiation Force Impulse Imaging (ARFI) elastography and transient elastography (TE) during antiviral treatment and to evaluate its role in relation to SVR.

Methods: In total 337 chronic HCV patients (mean age 59 years, 42% females) were included in this prospective single center study. Genotype 1 accounted for 75%, 244 (72%) patients had liver cirrhosis (F4) at baseline. Patients received sofosbuvir/ledipasvir (n = 110), sofosbuvir/ribavirin (n = 104), ombitasvir/paritaprevir/ritonavir + Dasabuvir (n = 41), sofosbuvir/daclatasvir + ribavirin (n = 46), sofosbuvir/svir + ribavirin (n = 36), 254 patients (75%) reached follow up 24 (FU24). Duration of treatment varied between 8 and 24 weeks. All Patients received liver stiffness measurement by ARFI at baseline, W4, W12, W24, FU24 and FU48. TE was performed at baseline and FU24. Laboratory data including HCV RNA were performed at each timepoint, at which ARFI was done.

Results: SVR was observed in 219/254 patients (86%). Mean ARFI values decreased significantly from baseline to FU48 (p = 0.042), with a gradually decrease from baseline to W4 (p = 0.001), from W4 to W12 (p = 0.004) and from FU24 to FU48 (p = 0.031). Median TE showed an overall decrease from baseline to FU24 (p < 0.001). ARFI values decreased at W48 from F4 to F3 in (17%), to F2 in (7%) and to <F2 (26%). Baseline values of ARFI (p < 0.001), TE (p < 0.001) and AST (p = 0.029) showed higher values in relapers than in patients with SVR. In the multivariable analysis, ARFI (p < 0.001), TE (p = 0.002), were predictors of response.

Conclusions: LSM by ARFI and TE decreased in almost all HCV-treated patients during the course of treatment. Importantly, about half of the patients with liver cirrhosis before therapy could be classified as non-cirrhotic one year after therapy. In addition, ARFI and TE might be used as predictors of response in HCV-infected patients treated with suboptimal DAA regimens.

Non-Invasive markers of liver fibrosis

Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

EUROPEAN MITOCHONDRIAL DNA HAPLOGROUPS IMPACT ON LIVER FIBROSIS PROGRESSION AMONG HCV AND HIV/HCV COINFECTED PATIENTS FROM NORTHWEST SPAIN

Non-Invasive markers of liver fibrosis

Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

EUROPEAN MITOCHONDRIAL DNA HAPLOGROUPS IMPACT ON LIVER FIBROSIS PROGRESSION AMONG HCV AND HIV/HCV COINFECTED PATIENTS FROM NORTHWEST SPAIN

Non-Invasive markers of liver fibrosis

Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

EUROPEAN MITOCHONDRIAL DNA HAPLOGROUPS IMPACT ON LIVER FIBROSIS PROGRESSION AMONG HCV AND HIV/HCV COINFECTED PATIENTS FROM NORTHWEST SPAIN
and 10 minutes at 200 Watts. Blood pressure was measured every 2 minutes using an inflatable (Riva-Rocci) cuff placed around the upper arm at roughly the same vertical height as the heart (GE healthcare systems, General Electric). LS was measured by transient elastography (Fibroscan) using the M (depth 25–65 mm, frequency 3.5 MHz) probe (Echosens, Paris, France). TE was performed on the right lobe of the liver in intercostal position. Before every set of LS measurements under exercise, the position of the liver was reevaluated by ultrasound in order to minimize measurement errors.

Results: Mean basal LS in all volunteers with valid measurements in a sitting position (n = 11) was 4.4 ± 1.8 kPa which did not significantly differ from baseline LS in a lying position (4.1 ± 1.0 kPa). Ten minutes exercise at 100W increased systolic pressure from 106 ± 8 mmHg to 135 ± 16 mmHg while heart rate increased from 79 ± 14 to 116 ± 20 bpm. Notably, LS increased significantly to 5.7 ± 1.4 kPa (p < 0.05).

Further increase of exercise to 200W led to an increase of LS to 6.7 ± 2.1 kPa aswell as systolic pressure and heart rate (146 ± 16 mmHgand 148 ± 18 beats per minutes). This increase in LS correlated highly significantly with systolic pressure (r = 0.527) followed by MAP and heart rate (r = 0.505 and r = 0.495), respectively. After a recovery phase of 10 minutes, blood pressure and heart rate returned to baseline values and LS also normalized (4.7 ± 0.9 kPa).

Conclusions: Elevated cardiac output and arterial pressure during physical exercise suffice to increase LS in healthy volunteers.

101. Poster (#SAT-443)
Non-Invasive markers of liver fibrosis

Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

PHARMACOLOGICAL VASODILATATION EFFICIENTLY DECREASES LIVER STIFFNESS IN RATS WITH TAA-INDUCED LIVER CIRRHOSIS

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Background and Aims: Liver stiffness (LS) as measured by transient elastography is increasingly used to non-invasively assess liver fibrosis. Several other conditions are known to increase LS irrespective of fibrosis, including congestion, cholestasis and food intake. We here study the role of vasodilatating drugs on hemodynamics and LS in a rodent model of TAA-induced cirrhosis.

Methods: Thirty male Wistar rats were allocated into groups (n = 6) and fibrosis was induced with i.p. thioacetamide (TAA) injections (200 mg/kg bodyweight twice weekly) for 8 weeks. Under isoflurane sedation, NO-releasing glyceroltrinitrate, the AT1 antagonist Losartan, the non-selective ß-blocker Propranolol or 1 mL 0.9% NaCl as control were administered intravenously. Arterial and portal pressures were invasively measured in real-time using the Powerlab device (AD Instruments, New Zealand) for 30 minutes after drug injection. LS was measured continuously using the µFibroscan device (Echosens, Paris).

Results: TAA treatment caused liver cirrhosis at a histological and macroscopic level which was accompanied by a significant increase of LS (19.7 vs 4.0 kPa). Portal pressure (PP) increased significantly (12.3 vs 8.6 mmHg) compared to untreated control animals while mean arterial pressure (MAP) and heart rate remained unchanged. PP correlated linearly with LS at LS values <12 kPa. At higher LS values, this linear association was lost most likely due to collateral formation. NO and Losartan both lowered MAP drastically from mean 86.5 to 61.8 mmHg. Concomitantly, PP and LS also decreased significantly from 12.3 to 8.7 mmHg and 19.3 to 13.9 kPa, respectively. Propranolol injection drastically reduced heart rate but MAP, PP and LS decreased only slightly without reaching levels of significance. No significant changes in LS were recorded in control animals following NaCl injection. Pearson correlation analysis showed a significant association between the decrease of LS and arterial pressure for NO (r = 0.476),
Losartan (r = 0.577) but not Propranolol (r = 0.121). Changes in PP were also best correlated with arterial pressure (r = 0.845).

Conclusions: Our data indicate that hepatic hemodynamics are a key component of liver stiffness in the diseased organ. In our experiments, a drastic reduction in mean arterial pressure led to a decrease in liver stiffness of about 25% accompanied by a significant reduction in portal pressure.

102. Poster (#SAT-445)
Non-Invasive markers of liver fibrosis
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00
ACCURACY OF THE LATEST RELEASE OF A POINT SHEARWAVE ELASTOGRAPHY METHOD FOR STAGING LIVER FIBROSIS IN PATIENTS WITH CHRONIC HEPATITIS C
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Background and Aims: This single center cross-sectional study was conducted to prospectively assess the performance of the latest release of a point shear wave elastography method by comparing the results to those obtained with transient elastography (TE).

Methods: Consecutive patients followed up for chronic hepatitis C and referred for abdominal ultrasound examination were enrolled. Liver stiffness measurements were performed with the latest release of the ElastPQ® method implemented in the Epiq7 ultrasound system (Philips Medical Systems, Bothell, WA, USA) and with the TE method of the FibroScan® device (Echosens, Paris, France). The two systems were used in a random order. For staging liver fibrosis we used the TE cutoffs of 7.0, 9.5 and 12.0 kiloPascal, respectively, for significant fibrosis (F ≥ 2), advanced fibrosis (F ≥ 3), and cirrhosis (F = 4). The diagnostic performance of ElastPQ® was assessed by calculating the area under the receiver operating characteristic (AUC) curve.

Results: 189 patients [110 males, 79 females; mean age, 58.7 (14.2) years] were studied. 80 individuals were in F0-F1 stage, 30 in F2 stage, 11 in F3 stage, and 67 in F4 stage. The optimal cutoff values of ElastPQ® for F ≥ 2, F ≥ 3, F = 4, respectively, were 6.8, 7.6 and 8.9 kilopascal. AUC calculations showed values of 0.95 (0.91–0.98) for F ≥ 2 [sensitivity, 91.5% (83.9–96.3); specificity, 96.2% (89.4–99.2); LR+, 24.4 (8.0–74.2); LR−, 0.09 (0.05–0.2)]; 0.98 (0.94–0.99) for F ≥ 3 [sensitivity, 95.6% (87.8–99.1); specificity, 90.5% (83.2–95.3); LR+, 10.0 (5.6–18.1); LR−, 0.05 (0.02–0.1)]; 0.96 (0.92–0.99) for F = 4 [sensitivity, 91.9% (82.2–97.3); specificity, 91.1% (84.2–95.6); LR+, 10.3 (5.7–18.7); LR−, 0.09 (0.04–0.2)].

Conclusions: These preliminary results showed that the latest release of ElastPQ® method is highly accurate for staging liver fibrosis in patients with chronic hepatitis C.

103. Poster (#SAT-448)
Non-invasive markers of liver fibrosis
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00
RISK ASSESSMENT OF HEPATOCELLULAR CARCINOMA USING WISTERIA FLORIBUNDA AGGLUTININ-POSITIVE HUMAN MAC-2 BINDING PROTEIN IN CHRONIC HEPATITIS B PATIENTS
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Background and Aims: Wisteria floribunda agglutinin-positive human Mac-2 binding protein (WFA+ M2BP) can assess the degree of liver fibrosis. We evaluated the accuracy of serum WFA+ M2BP to assess liver fibrosis and its prognostic value to predict the risk of hepatocellular carcinoma (HCC) development in chronic hepatitis B (CHB) patients.

Results: We evaluated 189 patients [110 males, 79 females; mean age, 58.7 (14.2) years] were studied. 80 individuals were in F0-F1 stage, 30 in F2 stage, 11 in F3 stage, and 67 in F4 stage. The optimal cutoff values of ElastPQ® for F ≥ 2, F ≥ 3, F = 4, respectively, were 6.8, 7.6 and 8.9 kilopascal. AUC calculations showed values of 0.95 (0.91–0.98) for F ≥ 2 [sensitivity, 91.5% (83.9–96.3); specificity, 96.2% (89.4–99.2); LR+, 24.4 (8.0–74.2); LR−, 0.09 (0.05–0.2)]; 0.98 (0.94–0.99) for F ≥ 3 [sensitivity, 95.6% (87.8–99.1); specificity, 90.5% (83.2–95.3); LR+, 10.0 (5.6–18.1); LR−, 0.05 (0.02–0.1)]; 0.96 (0.92–0.99) for F = 4 [sensitivity, 91.9% (82.2–97.3); specificity, 91.1% (84.2–95.6); LR+, 10.3 (5.7–18.7); LR−, 0.09 (0.04–0.2)].

Conclusions: These preliminary results showed that the latest release of ElastPQ® method is highly accurate for staging liver fibrosis in patients with chronic hepatitis C.

104. Poster (#SAT-449)
Non-Invasive markers of liver fibrosis
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00
DIRECT ANTIVIRAL AGENT TREATMENT OF CHRONIC HCV INFECTION RESULTS IN RAPID REGRESSION OF TRANSIENT ELASTOGRAPHY (FIBROSCAN®) AND VALIDATED FIBROSIS MARKERS FIB-4 AND APRI
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Background and Aims: Novel direct antiviral agents (DAA) for chronic hepatitis C have revolutionized the HCV treatment. Rates of SVR have improved drastically since introduction of DAA. Transient Elastography (TE) is the non-invasive technique to assess liver stiffness.
and TE values correlate with fibrosis stage. Indication for DAA treatment of HCV is often based on TE values. Histological regression of fibrosis has been well documented in long term studies. We here examined the changes in TE values within 12 months after successful DAA treatment of HCV.

**Methods:** 210 patients that received a DAA based treatment for chronic HCV were included. TE values recorded within 12 months prior to therapy and within 12 months after HCV therapy were evaluated. In addition, FIB-4 and APRI scores were calculated and histological results recorded if available.

**Results:** Median TE prior to DAA treatment was 14.35 kPa (IQR 8.42), median TE post treatment 10.3 kPa (IQR 7.15). This equals a TE regression of 28% within 12 months after successful HCV DAA treatment. Further subgroup analyses will be presented. Liver enzymes correspondingly showed significant reduction, often already during DAA treatment. Average FIB-4 and APRI prior to therapy were 3.86 and 2.06 respectively. Average post treatment FIB-4 was 2.47 while post treatment APRI was 0.64. This results in a decrease in FIB-4 of 1.39 and a regression in APRI of 1.42. Thus both values fall below the published cutoffs for significant liver fibrosis following successful DAA treatment of chronic HCV.

**Conclusions:** Patients with SVR after DAA therapy showed a rapid and significant regression of TE values within 12 months after end of treatment. Most patients displayed significant regression of liver stiffness within 3 months after end of treatment. Rapid decrease of TE is in concordance with regression of validated fibrosis scores FIB-4 and APRI. It remains to be examined whether this indicates a true regression of fibrosis or merely resolution of chronic liver inflammation with subsequent improvement of laboratory parameters. Further investigation into TE values and correlating liver histology after DAA treatment is warranted.

## 105. Poster (#SAT-450)

### Non-Invasive markers of liver fibrosis

**Date & Time:** Saturday, April 16, 2016 - 08:00 - 18:00

**THE BAVENO VI GUIDELINES: CAN WE CONFIDENTLY IDENTIFY LOW RISK CIRRHOTIC PATIENTS NOT REQUIRING ENDOSCOPIC SURVEILLANCE FOR VARICES?**


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**Background and Aims:** The Baveno VI guidelines propose that patients with a liver stiffness measurement (LSM) <20 kPa and a platelet count >150 x 103 cells/L can avoid screening endoscopy as their combination is highly specific for excluding clinically significant varices. The aim of the study was to validate these criteria.

**Methods:** Transient elastography (TE) data from 2008 to 2015 was collected from two institutions. Inclusion criteria were a LSM ≥10 kPa and an upper gastrointestinal endoscopy within 12 months. Exclusion criteria were portal-esmecenter-splenic vein thrombosis, previous transjugular intrahepatic portosystemic shunt and noncirrhotic portal hypertension. Varices were graded as insignificant (grade <2) or clinically significant (grade ≥2).

**Results:** Three hundred and ninety five patients where included in the study. Aetiology of liver disease was hepatitis C (n = 225 (57%)), alcoholic related liver disease (n = 55 (14%)), non-alcoholic fatty liver disease (n = 48 (12%)), hepatitis B+/− D (n = 25 (6%)) and other causes (n = 41 (11%)). Most patients were Child Pugh (CP) A (n = 313 (79%)) with 18% cases CP-B and 3% CP-C. One hundred and fifteen cases (29%) had varices, of which 35 (9%) were clinically significant. One hundred and eleven patients (28%) met the Baveno VI criteria. Of these cases, 12/111 (11%) had varices and 3/111 (3%) had clinically significant varices, representing 3/35 (9%) of all cases with clinically significant varices. Combining LSM and platelet count with the recommended cut-off values gave a sensitivity 0.91, specificity 0.30, positive predictive value (PPV) 0.11, negative predictive value (NPV) 0.97, positive likelihood ratio 1.31 and negative likelihood ratio 0.28. AUROC values for LSM, platelet count and the two variables combined were 0.693, 0.684 and 0.737 respectively. In a sub analysis by aetiology, the AUROC for these variables in viral hepatitis were 0.676, 0.733 and 0.745 and in NAFLD/NASH were 0.710, 0.635 and 0.706 respectively.

**Conclusions:** This data confirms a high NPV of 0.97 and a negative likelihood ratio 0.28 of the Baveno VI criteria. However we are concerned that 9% of clinically significant varices in our cohort were not identified by these criteria. Lowering the cut-off for LSM to 16.8 kPa would include all cases of large varices, at the cost of an additional 27 endoscopies (9% increase). We propose that further work with a prospective validation of these guidelines should be conducted before a change in practice can be recommended.

## 106. Poster (#SAT-452)

### Non-Invasive markers of liver fibrosis

**Date & Time:** Saturday, April 16, 2016 - 08:00 - 18:00

**OPPORTUNISTIC FIBROSCAN® TESTING IN A DUBLIN GENERAL PRACTICE (GP) MANAGING OPIATE SUBSTITUTION THERAPY: THE HEP CARE STUDY**

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3. Rotunda Hospital;
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5. Dublin North and North East, HSE, Dublin, Ireland

**Background and Aims:** In Ireland GPs provide long-term care for injecting drug users (IDUs), almost 80% infected with hepatitis C (HCV). Although multiple barriers exist the importance of continuity of care and linkages to screening and treatment interventions are highlighted. The HepCare study proposes a new service, supporting primary care/drug treatment centres in screening and clinical evaluation of community based HCV. Patients in Ireland are eligible for interferon free Direct Antiviral treatment (DAA) if they have transient elastography (TE) scores of >12 in mono-infected patients and >10 in HIV co-infected patients. TE is the current gateway for DAA treatment, offered only in selected specialist centres. Priority is given to advanced liver disease patients prior to decompensation.

**Methods:** Our study included development of GP liaison including: nurse liaison with primary care, screening for liver disease using TE (FibroScan®), evaluation by facilitating practice audit/feedback, and audit of healthcare records to identify reasons why patients were lost to follow-up.

**Results:** In this pilot, 58 known HCV positive patients were tested using portable FibroScan®. 15/58 patients, were found eligible for DAA treatment. 77% male, 33% female; with 53% followed in GP practice >10 years for methadone substitution therapy. 39/58 were previously referred to specialty service, Only 19 attended once and 3 had completed treatment with interferon/ribavirin but relapsed. The following reasons for not attendance included: chaotic drug and/ alcohol use, fear of biopsysand/or interferonside effects,mental health/psychiatric diagnoses. For those eligible for DAA's per Irish Guidelines, FibroScan®scores range: 10.8–63.9, mean 26. None had been identified in the GP practices as having significant clinical liver disease.

**Conclusions:** Previous attempts to engage these patients in hospital care were unsuccessful. Community Fibroscan identifies those with advanced liver disease, with urgent referral to hospital service for DAA treatment. Multiple barriers to engagement with secondary care were identified. Optimally a community based shared care partnership
between primary care and hospital services, with treatment being administered in the community, could be developed to ensure that this cohort of vulnerable patients has access to these new HCV interferon free DAA treatments.

107. Poster (#SAT-454)
Non-invasive markers of liver fibrosis
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

NON-INVASIVE EVALUATION OF CHRONIC HEPATITIS C PATIENTS WITH MODERATE FIBROSIS (F2) LONG-TERM IMPACT OF ANTIVIRAL TREATMENT

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Background and Aims: Studies evaluating the impact of antiviral therapy in patients with chronic hepatitis C (CHC) with moderate fibrosis (F = 2) are scarce and their follow-up period limited. The aim of our study was to evaluate with non-invasive techniques the impact of antiviral therapy on liver fibrosis in patients with CHC and F = 2.

Methods: Retrospective analysis of patients with CHC and F2 in liver biopsy (Metavir). Biopsies were reviewed by two pathologists (MG and JG). Patients were categorized into non-treated (NTs), nonresponders (NRs) and sustained viral responders (SVRs). During follow-up fibrosis was evaluated every 9 (±3) months with noninvasive techniques: indirect serological markers (APRI and HALT-C) and abdominal ultrasound. Since 2011 transient elastography (TE) has also been performed. We defined “incipient cirrhosis” (IC) when patients developed TE > 14.6 or APRI > 2 and HALT-C > 0.5, “established cirrhosis” (EC) when appeared a nodular liver surface with splenomegaly (abdominal ultrasound) or esophageal varices (upper endoscopy), and “decompensated cirrhosis” (DC) when developed decompensation or hepatocellular carcinoma. Patients were followed up to transplantation, missing or death.

Results: From January 1990 to September 2012, 300 patients with CHC and F2 were evaluated. Non-concordant biopsies (n = 45) and patients with <1 year of follow-up (n = 38) were excluded. The mean age was 45, 65% were male, 21% HIV, 37.3% NTs, 36% NRs and 104 (47.9%) SVRs. We identified 61 (28%) patients with IC, 55 (25%) with EC and 36 (16.6%) with DC during a median follow-up of 10.3 years. Time to diagnosis of IC, EC and DC was 5.6, 7.4 and 8.7 years, respectively (p < 0.001). Only 1 (1.6%) SVR developed IC, without progression to EC or DC during the follow-up (p < 0.001). Mortality rate by liver disease in SVRs, NTs and NRs was 0%, 17.6% and 20.3% (p < 0.001). The variables independently associated (OR, 95% CI, p) to mortality were age (1.16; 1.09–1.23; p < 0.001) and IC (OR: 1.01; 1.001–1.01; p = 0.003) or alcohol intake (0.09; 0.01 to 0.55; p = 0.01) during follow-up.

Conclusions: In patients with CHC and moderate fibrosis noninvasive evaluation identify early cirrhosis, SVR prevents the development of cirrhosis, hepatic decompensation and death. The antiviral treatment seems essential in old patients and those with non-invasive markers of fibrosis increaseamens or persistent alcohol intake.

108. Poster (#SAT-456)
Non-Invasive markers of liver fibrosis
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

AN ONTARIO BASED DIAGNOSTIC REFERRAL PROGRAM USING TRANSIENT ELASTOGRAPHY – A RETROSPECTIVE ANALYSIS

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Background and Aims: In 2010, The Toronto liver centre (TLC) created the first FibroScan® referral program in Ontario, and has since been serving the community. The aim of this analysis was to understand how Ontario physicians utilize fibroscan testing alongside current guidelines in the management and follow-up of chronic liver disease.

Methods: 5,438 patients were referred to TLC from June 17, 2010 to October 28, 2014 for fibroscan testing & stratification of liver fibrosis/steatosis. Referrals were assessed for: referring physician specialty & ethnicity, catchment area, patient demographics, disease etiology, fibrosis stage at referral & time between serial fibroscans.

Results: Physicians: 262 physicians referred patients for fibroscans; 63% were General Practitioners, 29% Gastroenterologist/Hepatologists, 3% Infectious Disease, & 5% Others. Of the 262 physicians, 67% were Chinese, 13% South Asian & 20% Unknown. Patient demographics: Results from fibroscan tests were reported for 5,437 patients, 58% men vs. 42% women. Median age was 53 years; women referred being older with a median age of 54 years vs. 52 years for men. Majority of patients were diagnosed with HBV or HCV (3,399, 866) respectively. Other liver conditions accounted for 21.8% (1,186) of patients with fatty liver condition being more prevalent. Catchment area extended to 25 cities within Ontario & 1 city outside of Canada. Fibrosis Stage: Approximately 67.8% of patients were F0 or F1. A fibrosis stage of F3 was reported for 6.4%, while F4 or cirrhosis was reported for 10.3% of patients. Serial fibroscans: Preliminary analysis of the available data for serial fibroscans shows no additional benefit in routine measurements of liver stiffness in a period less than 12 to 14 months.

Conclusions: Referrals from general practitioners comprised 63% of our database; where 16.7% of patients had liver fibrosis of F2 to F4, thereby qualifying those patients for treatment reimbursement. Furthermore, considering the large catchment area for this analysis (despite the lack of health insurance coverage) proves that fibroscan testing is widely accepted by patients and physicians within the community. Moreover, seeing that only 4.8% of patients underwent serial fibroscans, there’s a need for regulation of the frequency by which patients should be referred for fibroscan testing. We plan to assess this factor in the near future. Jean Palmer-statistical analysis.
The study had more than 90% evidence of fibrosis (≥6.5 kPa). In the Alcohol Treatment Clinic (ATC), to evaluate steatosis in patients with at least six hours, only values with 10 validated measurements were considered reliable. Data were expressed as mean and standard deviation (SD), or median and interquartile range (IQR) as appropriate. Students t-test was used to compare the group differences; an equivalence analysis was performed to investigate the clinical significance of 0.5 kPa.

**Results:** One hundred and fifteen HIV-monoinfected subjects [74 males and 41 females; mean age, 46.4 (SD:10.3) yrs; mean BMI, 24.0 (3.8) kg/m2; mean CD4 count, 649 (279) cells/mL; median length of antiretroviral medications, 54 (IQR:16–108) months] and 247 blood donors [155 males and 92 females; mean age, 41.9 (12.5) yrs; mean BMI, 23.7 (3.3) kg/m2] were studied. In HIV-monoinfected subjects the values of ALT, AST and GGT, respectively, were 21 (15–29) IU/L, 24.6 (15.4) IU/L and 30 (20–54) IU/L, and these values were not statistically different from those obtained in the blood donors. One failure in TE measurements was observed in the cohort of blood donors. All TE measurements were reliable. TE showed a value of 4.65 (1.06) kPa in HIV-monoinfected subjects and 4.27 (1.01) kPa in blood donors (p = 0.001); on the other hand the study had more than 90% power to detect an equivalence of 0.5 kPa between the two groups. CAP values were 235 (46) decibel/meter in HIV-monoinfected subjects and 233 (53) decibel/meter in blood donors (p = 0.72).

**Conclusions:** These preliminary results showed that HIV-monoinfected patients not immunosuppressed have significantly higher stiffness values than controls, however this difference is not clinically important. No significant difference in the degree of liver steatosis between patients and controls was observed.

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**109. Poster (#SAT-458)**

**Non-Invasive markers of liver fibrosis**

**Date & Time:** Saturday, April 16, 2016 - 08:00 - 18:00

**NONINVASIVE ASSESSMENT OF LIVER FIBROSIS AND STEATOSIS IN HIV-MONOINFECTED SUBJECTS**

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**Background and Aims:** It has been reported that HIV-infected patients are at risk of liver fibrosis due to antiretroviral medications and immunosuppression. The aim of this study was to assess liver stiffness by transient elastography (TE) and liver steatosis by means of controlled attenuation parameter (CAP) in a cohort of HIV-monoinfected subjects and to compare the results to those obtained in a large cohort of healthy volunteers who were blood donors.

**Methods:** HIV-infected subjects, negative for hepatitis B surface antigen and hepatitis C antibody, and a control group of blood donors were consecutively enrolled. TE and CAP measurements were carried out by using the FibroScan device (Echosens, Paris, France) following a fast of at least six hours. Only values with 10 validated measurements and an interquartile range/mean <30% for values higher than 7.1 kilopascal (kPa) were considered reliable. Data were expressed as mean and standard deviation (SD), or median and interquartile range (IQR) as appropriate. Students t-test was used to compare the group
<11 kPa) and 84 (40.5%) showed F3/F4 fibrosis (≥11 kPa) meeting criteria for referral to hepatology.

Conclusions: Nurse-led ATC setting is a valuable and effective setting for the early detection of ALD utilising fibroelastography. The programme is quick and patients value the addition of an objective measure for comparisons over time. Most important is that significant fibrosis was detected in over one third of patients who might not otherwise have been identified until much later in the natural history of liver damage and failure.

111. Poster (#SAT-460)
Non-Invasive markers of liver fibrosis
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00
LIVERTRAILCOM: A SMARTPHONE APP TO PREDICT PRESENCE OF LIVER FIBROSIS IN PATIENTS WITH ALCOHOL OVERUSE
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Background and Aims: Up to 50% of patients with a chronic alcohol overuse develop liver fibrosis. We aimed to design a smartphone app in collaboration with the app developer Manatee APS, to evaluate significant alcoholic fibrosis in alcohol overusing patients.

Methods: We developed a multivariable diagnostic tool available on the LiverTRAIL.com app, considering four scenarios: Only anamnestic and basic clinical data available, added blood tests, added ultrasound and added elastography. We modelled 36 algorithms that included all relevant combinations of diagnostic predictors, based on data from a large biopsy-controlled study of asymptomatic patients with alcoholic liver disease. The user can enter whatever information is available, with a possibility for subsequent improvement of the diagnostic accuracy after further investigations. Thus, the app calculates a patient’s risk of having significant alcoholic fibrosis and the accuracy of the risk prediction (certainty = 2(AUC-0.5)). Results are given together with two color-coded traffic lights for risk (red ≥50%, yellow 10–49% or green <10%) and accuracy of risk prediction (red <60%, yellow 60–79% and green ≥80%).

Results: The diagnostic study included 241 patients, of whom 41% had significant alcoholic fibrosis (F2–4, 38/174/44). Twelve predictors were independently associated with presence of F2 fibrosis. From these, we coded the LiverTRAIL app with 36 diagnostic algorithms from multivariable logistic regressions according to the four scenarios. Eleven algorithms covered the scenario of only anamnestic and clinical data, 24 algorithms covered the added biochemistry, 9 algorithms covered the added ultrasound and three algorithms covered the scenario of added elastography. Except for transient elastography (AUC for F2 fibrosis = 0.93), no single predictor had a certainty above 60%. Combining age, years of alcohol abuse, heart rate and mid-upper-arm circumference (MUAC) resulted in an AUC of 0.72. Adding biochemical data, the best performing algorithm combined Forns index, INR, bilirubin, alkaline phosphatase, years of alcohol abuse and MUAC (AUC 0.80). The diagnostic accuracy increased further when spleen length was added (AUC 0.91). The best performing algorithm included transient elastography, years of alcohol abuse and MUAC (AUC 0.94).

Conclusions: We developed an app to identify patients with significant alcoholic liver fibrosis. The app may support clinical decision making for patients with alcohol overuse. It is available for free in AppStore and GooglePlay.

112. Poster (#SAT-461)
Non-Invasive markers of liver fibrosis
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00
A LIVER SCORE THAT COMBINES DIRECT MARKERS OF EXTRACELLULAR MATRIX FORMATION WITH PLATELET COUNT, INR AND AGE ACCURATELY DIAGNOSE LIVER FIBROSIS AND CIRRHOSIS IN PATIENTS WITH ALCOHOL OVERUSE
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Background and Aims: To improve early diagnosis of patients with alcoholic liver disease, serological fibrosis markers are needed. Indirect markers of chronic liver disease such as indices combining common liver blood tests have suboptimal diagnostic accuracy, especially for significant fibrosis. Therefore, novel direct markers of extracellular matrix formation should be investigated. We aimed to develop a diagnostic liver score combining indirect markers of chronic alcoholic liver damage with direct markers of total and crosslinked type III collagen formation (ProC3 and ProC3X).

Methods: In a prospective study, 189 patients with various degree of alcoholic liver disease (METAIVIR fibrosis grades F0–4 = 12/98/33/13/33) underwent same-day liver blood tests, measurement of ProC3 and ProC3X, transient elastography and liver biopsy. We fitted a multivariable logistic model to provide maximal discrimination and calibration for both significant fibrosis (≥F2) and cirrhosis (≥F4). The model was developed by selecting the strongest predictors of nine predefined liver blood tests, age, ProC3 and ProC3X. Internal validation was performed with the leave-one-out method.

Results: The best fitting model included the product of ProC3 and ProC3X with platelet count, International Normalized Ratio (INR) and age in the following algorithm: 1 + 0.0018*ProC3*ProC3X + 2.5 (if platelet count < 150) + 2 (if INR > 1.3) – 2 (if age < 30 years) or – 1 (if age 30–50 years). The Figure shows risk prediction plots for significant fibrosis (light grey) and cirrhosis (dark grey). The liver score yielded an AUC of 0.92 for the diagnosis of significant fibrosis (95% CI 0.87–0.96; sensitivity 81%, specificity 90%, PPV 85%, NPV 87%, optimism-corrected AUC 0.85). And for cirrhosis, an AUC of 0.89 (0.84–0.95; sensitivity 85%, specificity 83%, PPV 52%, NPV 96%). The score outperformed the age-platelet- and Forns index for fibrosis (AUCs 0.79 and 0.83, p = 0.002), but not cirrhosis (AUCs 0.83 and 0.82, p = 0.091). And the combination of direct and indirect fibrosis markers was better than the direct markers alone (ProC3 AUC 0.83, ProC3X 0.84, p < 0.001). While transient elastography was not superior to the diagnostic score for fibrosis (AUC 0.94, p = 0.110), it was for cirrhosis (AUC 0.94, p = 0.045).

Conclusions: Combining direct markers of extracellular matrix formation and collagen crosslinking with age, platelet count and INR
results in a liver score with high diagnostic accuracy for both significant alcoholic fibrosis and alcoholic cirrhosis.

P. T175A allele (78%) had been scheduled for liver biopsy. This variant was however not associated with histological fibrosis stages, ALT (p = 0.63), GGT (p = 0.57), or AP activities (p = 0.13). Of note, none of the carriers of the p.T175A had signs of chronic cholestatic disease. Presence of the ABCB4 c.711 variant was in turn not associated with liver stiffness, results of liver biopsy, or liver function tests (all p > 0.05).

Conclusions: Carriers of the ABCB4 p.A175T risk allele who suffer from chronic liver disease might be at increased risk of progressive liver injury and fibrosis. This effect appears to be less pronounced in NAFLD patients. Our observation points to a sensitizing role of procholostatic mutations and underscores the value of elastography for integrated assessment of pathogenic pathways in chronic liver disease.

114. Poster (#SAT-464)

Non-Invasive markers of liver fibrosis

Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00

BAVENO VI RECOMMENDATION ON AVOIDANCE OF SCREENING ENDOSCOPY IN CIRRHOTIC PATIENTS BASED ON LIVER ELASTOGRAPHY AND PLATELET COUNT – ARE WE THERE YET?

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Background and Aims: Recent studies have assessed the predictive value of liver transient elastography (LE) (combined or not with platelet count) for the presence of esophageal varices (EV) in patients with liver cirrhosis, and multiple cut-offs have been proposed. The Baveno VI consensus states that patients with a liver stiffness <20 kPa and a platelet count >150,000 have a very low risk of having varices requiring treatment, and therefore can avoid screening endoscopy. We aimed to validate this newBaveno recommendation in a cohort of cirrhotic patients.

Methods: Retrospective evaluation of all patients with a liver stiffness (FibroScan®) compatible with liver cirrhosis (>12.5 kPa) between September 2009 and October 2015, as well as upper endoscopy and blood tests within 12 months from elastography at our centre. Patients on propranolol ≥80 mg/day or carvedilol ≥12.5 mg/day, as well as those with previous EV bleeding or treatments for EV were excluded. EV requiring treatment were defined according to Baveno VI. We analyzed patient characteristics, evaluated the accuracy of the new recommendation in this cohort, and explored optimized cut-offs for the Baveno VI proposal.

Results: One hundred and twelve patients met eligibility criteria, 76.8% (n = 86) males, median age at LE 54 (20;78) years. In 89 (79.5%) patients, LE was performed for staging of chronic hepatitis C, in 8 for alcoholic liver disease, and in 15 for other causes. Ninety-seven patients were Child-Pugh (CP) A; 14 CP B, and 1 CP class C. Fifty-four patients had EV (35 small varices without red signs, 2 small varices with red signs, and 17 large varices). Median liver stiffness was 25.9 kPa [13.2;75.0]. According to Baveno VI, among those patients without indication for screening endoscopy (n = 12,10.7%), none had EV requiring treatment (2 patients had small EV without red signs and CP A or B). Among those patients inwhom screening endoscopypwas indicated (n = 100), 52 had EV, 20 of them requiring treatment. None of the patients with liver elastography ≤30 kPa and platelet count ≤120,000 (n = 33, 29.5%) had EV requiring treatment (30 without EV; 3 had small EV without red signs and CP A or B).

Conclusions: The new Baveno VI recommendation correctly identified patients in which screening endoscopy did not impact on management, but only avoided endoscopies in a small proportion of patients. Alternative cut-offs may be explored to safely avoid
endoscopies in larger subgroups patients with low risk of EV requiring treatment.

115. Poster (#SAT-465)

Non-Invasive markers of liver fibrosis
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00
SUSTAINED VIROLOGICAL RESPONSE RESULTS IN REGRESSION OF LIVER STIFFNESS IN PATIENTS WITH CHRONIC HEPATITIS C VIRUS INFECTION
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Background and Aims: The prognosis in patients with chronic hepatitis C virus (HCV) infection is determined by the degree of liver fibrosis. Currently, noninvasive methods like transient elastography, are being used to assess severity of liver disease. Little is known about the impact of sustained virological response (SVR) on regression of liver fibrosis on the long term. The aim of this study was to assess the influence of SVR on liver stiffness (LS).

Methods: In this retrospective cohort study, patients with chronic HCV mono-infection with at least two reliable LS measurements between 2005 and 2015 were enrolled. LS was measured by FibroScan (Echosens, Paris) and expressed in kilo Pascal (kPa). The data obtained included treatment status, alcohol consumption, body mass index and the presence of diabetes mellitus (DM). Fibrosis-4 (FIB-4) score was calculated with laboratory parameters obtained within one month of LS measurement. A mixed linear model including FIB-4 score was used to predict LS. In the model we adjusted for follow up duration, time interval between LS measurements and LS values at previous visits. Multivariable logistic regression was used to identify factors associated with accelerated liver fibrosis progression (above median of 1.03 kPa/year).

Results: In total 371 patients were included, predominantly males (67%) and the majority of patients was treatment naive (61%). The median number of LS measurements per patient was 2 (range: 2–8). Median follow-up duration was 4.7 years (range: 0–9 years). Patients in whom treatment status changed from naive to SVR had significantly lower mean LS (Estimated marginal mean (EMM): 7.1 kPa) compared to those who remained naive or failed to achieve SVR (EMM = 10.6 kPa; p < .001 and EMM= 10.0 kPa; p < .001 respectively). In addition, achieving SVR resulted in a significant regression of LS compared to patients who remained treatment naive (EMM = −1.5 kPa, EMM=+1.0 kPa respectively, p < 0.001). Multivariable logistic regression analysis showed that age and DM were both significantly associated with progression of LS (OR = 1.04; p = .032 and OR = 2.57; p = .029, respectively). Gender showed a borderline significant association with LS progression (OR = 1.80; p = .07).

Conclusions: Achievement of SVR causes regression of LS, whereas maintaining treatment naive results in progression of LS over time. Age and DM were associated with progression of LS.

116. Poster (#SAT-466)

Non-Invasive markers of liver fibrosis
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00
ARE NON INVASIVE TEST GOOD ENOUGH TO PREDICT GASTROESOPHAGEAL VARICES IN PATIENTS WITH COMPENSATED ADVANCED CHRONIC LIVER DISEASE?
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Background and Aims: It is necessary to predict non invasively the presence of gastroesophageal varices (GEV) in compensated advanced chronic liver disease (cACLD) (Transient elastography (TE) 10–15 KPa suggestive; ≥15 KPa very suggestive). The aim of our study was to validate non invasive methods and recommendations of Baveno VI to predict the presence of GEV in a cohort of patients with suspected cACLD.

Methods: We retrospectively reviewed clinical and radiological data collected prospectively of consecutive patients with suspected cACLD measured by Fibroscan® and a gastroscopy performed for screening of GEV in a Hepatology Unit of a University Hospital. We evaluated platelets, spleen diameter (SD), TE, LSPS (TE×SD/platelets), variceal risk index (VRI) and the strategy of Baveno or the sequential algorithm previously proposed.

Results: From September 2013 to September 2014, 442 patients (281 excluded) were reviewed. Finally 161 patients were included (39.8% with cACLD suggestive, and 60.2% very suggestive), mean age 57(SD10), male 104(64.6%) and HCV etiology 137(85.1%). Baseline laboratory test: creatinine 0.7 mg/dL (SD0.2), bilirubin 0.9 mg/dL (SD0.5), ALT 78 U/L (SD59), AST 68 U/L (SD45), platelets 144 × 103 (SD62), albumin 4.2 g/L (SD0.4), INR 1.1(SD 0.3). Mean MELD was 8 (SD2). Mean SD and TE were 11.8 cm (SD2) and 20.4 KPa (SD11.4). Patients with GEV showed statistically significant differences in platelets (117SD51.1 vs 149SD62.3; p = 0.02), SD (12.8SD2 vs 11.6SD2; p = 0.01) and TE (27.6SD15.5 vs 19.1SD10.1; p = 0.001). Logistic regression analysis confirmed, discreetly, TE OR 1.04 (1.02 to 1.1; p = 0.03). Non invasive methods previously proposed were analized. A TE ≥ 20 KPa, LSPS ≥ 21, VRI=0.4 and Baveno VI strategy diagnosed correctly rates of 71.4%, 77.7%, 78.3% and 77.5% with S and E (TE 76% and 71%; LSPS 39.1% and 85%, VRI 32% and 88%, and VI Baveno strategy 68% and 79.3%). Despite high number of patients diagnosed
correctly, there is an appreciable number of patients with GEV undiagnosed: TE 24%, Baveno 32%, LSPS 56%, VRI 60%. In our cohort, platelets, SD or sequential algorithm previously proposed, demonstrated correct diagnosis rate in 50% of patients.

Conclusions: Although non invasive methods classify correctly a large number of patients and avoid performing unnecessary gastroscopies, there are a significant percentage of patients with GEV undiagnosed. TE is the best non invasive single method and the Baveno strategy the best combined method.

117. Poster (#SAT-467)
Non-Invasive markers of liver fibrosis
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00
PRECORE AND BASAL CORE PROMOTER MUTANTS IMPROVE THE DIAGNOSTIC PERFORMANCE OF FIBROSCAN® OR FIBROTEST® TO PREDICT SIGNIFICANT FIBROSIS IN CHRONIC HEPATITIS B PATIENTS
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Background and Aims: Predicting significant fibrosis (METAVIR F ≥ 2) is crucial for both the prognosis and the decision to treat patients with chronic hepatitis B (CHB). We aimed to investigate the potential of HBV precore (PC, G1896A) and basal core promoter (BCP) mutants (A1762T/G1764A) to improve the performance of non-invasive alternatives FibroScan® (FS) and Fibrotest® (FT) to predict significant fibrosis in a large cohort of unselected CHB patients.

Methods: Two hundred and eighty-six treatment-naïve patients with an available liver biopsy (65 HBeAg-positive and 221 HBeAg-negative) infected with genotypes A to E were included. Training cohort (TC) included 186 patients, validation cohort (VC) included 100 patients. Clinical and biochemical data, PC and BCP mutations, HBV-DNA, qHBsAg, FT and FS were determined within 6 months from biopsy. Diagnostic accuracy was assessed by c-index and its 95% confidence interval.

Results: HBV genotypes A, B, C, D, E were observed in 22%, 10%, 11%, 26% and 31% of the 286 patients. FS was available for 226 patients and FT for 215 patients. Thirty-eight percent (71/186) and 22% (22/100) of the patients had fibrosis METAVIR F ≥ 2 in TC and VC, respectively. In TC, prevalence of BCP mutants was 19% and 37% in F0-1 and F ≥ 2 patients, respectively, combined BCP/PC mutants were detected in 31% and 37% of F0-1 and F ≥ 2 patients, respectively. The age (p = 0.008), ALT (p = 0.03), AST (p = 0.002) and HBV-DNA levels (p = 0.02) and the presence of HBV mutants (p = 0.005) were independently associated with fibrosis F ≥ 2. The diagnostic accuracy of the combination of age, ALT, AST, HBV-DNA and HBV mutants in predicting fibrosis F ≥ 2 was evidenced by a c-index of 0.80 [CI95% 0.74–0.86]. This result was confirmed in VC [0.78 [CI95% 0.68–0.89]].

HBV mutants status associated with FS showed a better c-index than FS alone to predict fibrosis F ≥ 2 (n = 226; 0.84 [CI95% 0.78–0.90] vs 0.81 [CI95% 0.74–0.87], respectively). HBV mutants associated with FT showed a better c-index than FT alone to predict fibrosis F ≥ 2 (n = 215; 0.76 [CI 95% 0.70–0.83] vs 0.73 [CI95% 0.66–0.80], respectively).

Conclusions: In this well-characterized cohort, patients with BCP mutants were more at risk of fibrosis F ≥ 2 (37% [26/71] vs 19% [22/115]). The combination of FS or FT with HBV mutants improves the accuracy to discriminate patients with fibrosis F ≥ 2. These results strongly suggest that the detection of HBV mutants is relevant to assess the severity of HBV-related liver disease.

118. Poster (#SAT-468)
Non-Invasive markers of liver fibrosis
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00
UTILITY OF MAC-2 BINDING PROTEIN GLYCOSYLATION ISOMER (M2BPGI) FOR ADVANCED FIBROSIS AND HEPATOCELLULAR CARCINOMA IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE
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Background and Aims: the serum M2BPGI value using a glycan-based immunoassay may provide an accurate and reliable method for assessing the liver fibrosis stage in chronic hepatitis C patients. The aim of this study was to assess the diagnostic performances of M2BPGI comparison with liver stiffness and Fib4-index for the diagnosis of advanced liver fibrosis and HCC in patients with NAFLD.

Methods: A total of 540 consecutive patients with NAFLD who underwent ultrasonography were prospectively enrolled in this study. M2BPGI (COI), Fib-4 index, FibroScan (kPa), and VTQ (m/s) were measured on the same day. Advanced fibrosis group was determined by cut of level in each marker from previous reports. (M2BPGI > 1.46 COI, Fib4 > 2.67, FibroScan > 9.8 kPa, and VTQ > 1.77 m/s) Liver stiffness measurement (LSM) failure was defined as zero valid shots; unreliable examination was defined as <10 valid shots, an interquartile range (IQR)/LSM ≥ 30%, or a success rate <60%. LSM failure or unreliable examination was deemed "inadequate."

Results: One hundred sixteen seven patients (31%) and 175 patients (32%) were inadequate FibroScan and VTQ, respectively. Skin capsule distance (SCD) had the strongest association with inadequate LSM rates. In 252 patients with adequate by LSM, the number of patients with advanced fibrosis by Fib-4 (n = 34, 13%) decreased with use of VTQ, FibroScan, and M2BPGI (5%, 9%, and 9%, respectively). In multiple analyses, M2BPGI and LSM could select advanced fibrosis in NAFLD patients whose platelet count was maintained, compared with Fib4; however, M2BPGI value reduced male patients. M2BPG value in all non-cirrhotic patients (n = 40) who underwent liver biopsy showed less than the cut off level of M2BPGI for advanced fibrosis. (mean [SD]:0.81[0.5]); however, among 30 patients with HCC, only 12 patients (40%) increased more than the cut of level.

Conclusions: Serum M2BPGI is an efficient marker for the evaluation of advanced liver fibrosis in NAFLD patients, although M2BPGI value interacts with gender and is insufficient for HCC monitoring. For accurate evaluation of liver fibrosis, it is necessary to combine different modalities with a consideration of their advantages and disadvantages.

119. Poster (#SAT-470)
Non-Invasive markers of liver fibrosis
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00
A SEROLOGICAL MARKER OF COLLAGEN TYPE III CROSSLINKING CORRELATES STRONGLY WITH SEVERITY OF LIVER DISEASE
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Background and Aims: Enzymatic collagen crosslinking by lysyl oxidase-like enzymes (LOXs) and processing of pro-collagens are keys for tissue maturation and stability. In patients with organ fibrosis, collagens become highly crosslinked thus are less prone to fibrosis resolution. LOXL2 is a main driver in pathophysiological collagen crosslinking in fibrotic tissue and novel LOXL2 antagonists are undergoing clinical trials. We aimed to explore the utility of a serum assay for crosslinked type III collagen (Pro-C3X) to describe disease severity in patients with alcoholic liver disease compared to the non-crosslinked type III collagen formation marker Pro-C3.

Methods: Serum Pro-C3 and Pro-C3X was measured using specific ELISAs in 200 patients with biopsy-proven alcoholic liver disease. Fibrosis was assessed by META VIR fibrosis grade F0-4 and collagen proportionate area (CPA%). All blood tests, liver biopsy, and elastography were performed on the same day.

Results: The cohort included 200 patients, META VIR F0-4 = 12/103/35/14/36/52 male/female, age = 55 ± 11 years, BMI 27 ± 5, median CPA 4.0% (IQR 4.5). Pro-C3 increased in a step-wise manner from F0-1 (median 12.4 ± 6.4 ng/mL) to F2 (20.8 ± 24), F3 (27.2 ± 35.9) and F4 (47.4 ± 39.7), p < 0.001 as well as correlated with collagen proportionate area (correlation coefficient 2.09, p < 0.001) and so did Pro-C3X (correlation coefficient 0.72, p < 0.001). In patients with cirrhosis, Pro-C3 did not correlate with MELD score (p = 0.527), but Pro-C3X strongly correlated (corr coefficient 3.34, p < 0.001). Both markers correlated with Child-Pugh score (Pro-C3 = 13.37, p = 0.008; Pro-C3X = 5.41, p < 0.001). Pro-C3X explained 43% of the variance in MELD score and 34% of the variance in Child-score among cirrhotics. Pro-C3 differences only explained 16% of the variance in Child-score and none of the MELD score variance. Of the standard liver function tests, Pro-C3 only correlated negatively with albumine, while Pro-C3X correlated with albumine, bilirubine and GGT. Both markers correlated strongly with transient elastography. In the subgroup of patients with cirrhosis or severe fibrosis (≥F3), Pro-C3X was stronger associated with MELD score than both Pro-C3 and transient elastography.

Conclusions: Collagen crosslinking measured by Pro-C3X is stronger associated with severity of liver disease than transient elastography in patients with compensated advanced chronic liver disease of alcoholic etiology.

120. Poster (#SAT-471)
Non-Invasive markers of liver fibrosis
Date & Time: Saturday, April 16, 2016 - 08:00 - 18:00
CIRCULATING MICRORNAs AS BIOMARKERS FOR DISEASE PROGRESSION IN CHRONIC HEPATITIS C VIRUS INFECTION
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Background and Aims: Disease progression in chronic hepatitis C virus (HCV) infection is variable and poorly understood, although premature ageing of the immune system may contribute. Data are emerging to suggest that delaying treatment results in increased risk of liver-related death and reduced treatment effectiveness. There is an unmet clinical need for non-invasive biomarkers to characterize subjects at high risk of developing end-stage liver disease during HCV infection who should be prioritised for treatment. To correlate circulating microRNA (miRNA) expression with markers of immune ageing to identify prognostic biomarkers for patients at high risk of disease progression.

Methods: Matched peripheral blood mononuclear cell (PBMC) and serum samples were obtained from an existing cohort of HCV genotype 1 and 3 infected patients attending Glasgow hospitals. Samples from 16 non-cirrhotic patients (liver stiffness <7.1 kPa) and 9 cirrhotic patients (liver stiffness >12.5 kPa) were selected. 8 healthy age and sex matched controls were identified. The non-cirrhotic patients were subdivided into “high bio-age” and “low bio-age” based on PBMC mRNA expression of the biomarker of ageing CDKN2A compared to healthy controls (i.e. individuals with a high relative expression of CDKN2A were characterised as having a “high bio-age”). Total RNA was extracted from 500 μL serum and mRNA profiling was performed using the Taqman® Array Human MicroRNA A&B Cards v3.0. Significant findings were validated using Taqman® Advanced MicroRNA Assays; data were normalised to MiR-574-3p.

Results: 22 miRNAs were significantly upregulated in the sera of HCV infected patients compared to healthy controls, and 5 miRNAs were significantly downregulated (fold change >2; p < 0.05). Expression of mir-885-5p and mir-21-5p correlated significantly with mRNA expression of CDKN2A; MiR-122-5p was negatively correlated (Figure 1). Additionally, mir-885-5p expression was significantly correlated with liver stiffness (R = 0.753; p < 0.001). Expression patterns were similar between genotypes.

Conclusions: We observe distinct miRNA profiles in the sera of patients with chronic HCV infection when stratified by fibrosis stage and biomarkers of ageing. We have identified two miRNAs that are upregulated in both cirrhotic patients and non-cirrhotic patients with elevated markers of immune senescence. We propose these miRNAs may act as novel diagnostic biomarkers to identify non-cirrhotic individuals at high risk of disease progression.
**Results:** Fifty patients were included in this preliminary analysis (64% were males, mean age was 66.8 ± 10.2 ys., 76% were cirrhotics and 54% had body mass index ≥25 kg/m²). Our patients received: simprevir/sofosbuvir ± ribavirin [n = 35], sofosbuvir + ribavirin [n = 7], paritaprevir/ritonavir/ombitasvir/dasabuvir ± ribavirin [n = 7], ledipasvir/sofosbuvir [n = 1]. Overall, LS declined from 21.6 ± 10.1 kPa (range 10.5–48.8) to 15.6 ± 9.9 kPa (range 4.7–63.9) after treatment with mean absolute and relative changes in LS of −6.0 kPa and −20.8%, respectively (p < 0.001). In patients with F3 fibrosis, LS decreased from 11.5 ± 0.8 kPa to 8.0 ± 2.6 kPa with mean absolute and relative changes in LS of −3.5 kPa and −31.2%, respectively (p < 0.001). Likewise, in F4 patients it decreased from 24.7 ± 9.6 kPa to 18.0 ± 10.1 kPa with mean absolute and relative changes in LS of −6.7 kPa and −27.1% (p < 0.001). In the univariate analysis, only APRI (AST/Platelet Ratio Index), albumin and platelets at baseline were associated with improvement in LS (p = 0.003, <0.001 and 0.036, respectively). Only albumin was associated with LS improvement in multivariate analysis (p < 0.001).

**Conclusions:** Our preliminary data suggest that CHC patients with advanced fibrosis/cirrhosis who successfully treated with DAAAs can achieve a significant improvement in liver stiffness within 12 weeks after treatment cessation and irrespective of HCV genotype, type of treatment, BMI or liver enzymes. Presumably, this rapid decrease of stiffness is the result of a decreased inflammation rather than an actual change of fibrosis stage.

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**122. Poster (#SAT-476)**

**Non-Invasive markers of liver fibrosis**

**Date & Time:** Saturday, April 16, 2016 - 08:00 - 18:00

**THE UTILITY OF FIBROSCAN AND PLATELET COUNT TO IDENTIFY PATIENTS WHO CAN OMIT VARICEAL SURVEILLANCE ENDOSCOPY: VALIDATION OF THE BAVENO GUIDELINES IN A SCOTTISH COHORT**


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**Background and Aims:** Recent Baveno guidelines on portal hypertension suggest patients with a liver stiffness measurement (LSM) <20 kPa and a platelet count >150/mm³ are at low risk of clinically significant varices (CSV), and can safely omit upper GI endoscopy. These cut offs are derived from cohorts where viral hepatitis is the predominant liver disease. We sought to examine the utility of these cut offs in a Scottish cohort.

**Methods:** Patients undergoing Fibroscan between October 2008 and August 2014 at Glasgow Royal Infirmary were identified from electronic records. Those with LSM >10.0 underwent case note review to identify those with an endoscopy and full blood count between 12 and 3 months respectively of their Fibroscan. In the cases of DI, measurements of DI were compared to diagnostic accuracy of the index finger. We sought to examine the utility of these cut offs in a Scottish cohort.

**Results:** Of 1,290 patients with a LSM >10, 542 had undergone upper GI endoscopy within 12 months of whom 478 had a platelet count available. Mean age was 54 (±12) years. Median follow up was 33 months (IQR 25.4). The most common liver disease aetiologies were ALD (174, 36.4%), Hepatitis C (158, 33%) and NAFLD (101, 21.1%). 52 (10.9%) of patients had CSV (49 oesophageal, 3 gastric) at index endoscopy. Sensitivity, specificity, positive and negative predictive values for the screening test are shown in Table 1. 86 (18%) of patients died, 76/367 (20.7%) of those with a positive screening test, and 10/111 (9.0%) of those with negative screening test (p = 0.004). 17/367 (4.6%) of those with positive tests and 0/111 of those negative, experienced variceal bleeding (p = 0.01). Negative predictive values were high in both viral (100%) and non viral (96.2%) liver disease.

**Conclusions:** In a cohort with a high prevalence of ALD and NAFLD, using a platelet count of >150 and LSM <20 kPa would prevent around 1 in 4 endoscopies, with a high negative predictive value for the presence of CSV. Patients with negative screening tests had lower all cause mortality and none experienced variceal bleeding on followup.

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**123. Poster (#SAT-476)**

**Non-Invasive markers of liver fibrosis**

**Date & Time:** Saturday, April 16, 2016 - 08:00 - 18:00

**LIVER SURFACE DEFORMABILITY: A NOVEL ULTRASOUND TECHNIQUE IN THE NON-INVASIVE ASSESSMENT OF HEPATIC FIBROSIS**


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**Background and Aims:** Liver surface deformability (LSD) is a novel ultrasound technique measuring liver stiffness that can be performed with ordinary ultrasound machines.

**Methods:** With the patient in deep inspiration several thrusts are applied by the index finger to the right hypochondrium, perpendicularly and close to the probe, until maximum indentation of the liver surface is achieved. A clip is recorded and the depth of indentation (DI) of the liver surface in mm is measured by means of calipers. A shadow is produced by the thrust of the index finger.

**Results:** 196 patients with chronic liver disease and 25 healthy controls underwent the examination. Decompensated cirrhosis were excluded. A successful measurement of DI could be obtained in 79% of cases (22 controls and 153 patients: 19.6% HBV, 57.5% HCV, Alcohol 9%, NASH 4.5%, others 9.1%). Failure was due to increased thickness or contraction of the abdominal wall in 17% and bowel interposition in 4% of cases. Measurements of DI were compared to transient elastography (TE) in 85%, liver biopsy in 10.4%, both performed in the preceding 18 months, or clinical diagnosis of cirrhosis in 4.6% of the cases. 45% had Metavir F0-F1 fibrosis, 11% significant fibrosis (F2), 32% advanced fibrosis (F3) and 32% cirrhosis (F4). AUROC for significant fibrosis, advanced fibrosis and cirrhosis were 0.89, 0.92 and 0.92 respectively. At a cut-off >6.7 mm DI (60 patients) negative predictive value for F3-F4 fibrosis was 97%, while at a cut-off <4.6 mm (60 patients) positive predictive value for F3-F4 fibrosis was 95%. The remaining 55 patients (31%) had DI measurements between 4.6 and 6.7 and could not be correctly classified.

**Conclusions:** LSD can reliably diagnose advanced fibrosis/cirrhosis in roughly two thirds of the patients and could be used in resource poor countries to prioritize access to treatment or to select patients to be studied with other more expensive non-invasive methods.
Non-Invasive markers of liver fibrosis  
**Date & Time:** Saturday, April 16, 2016 - 08:00 - 18:00

**LIVER FIBROSIS DIAGNOSIS BY BLOOD TEST AND ELASTOGRAPHY: AGREEMENT OR COMBINATION?**

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3. Liver-Gastroenterology, University Hospital, Bordeaux, France

**Background and Aims:** The EASL-ALEH guidelines recommend to compare transient elastography (TE) with a blood test (BT) in chronic hepatitis C (CHC) and to accept the fibrosis staging if both agree. They stated that the combination was superior only for significant fibrosis in CHC but not for cirrhosis. The AASLD-ISDA guidelines also recommend the combination in CHC. We aimed to clarify these rules and to improve them with a test simultaneously combining BT and TE (BTE) in several etiologies.

**Methods:** 1,083 patients with CHC or chronic hepatitis B (CHB) or NAFLD, liver biopsy, TE, and a patented BT were included. The primary outcome was severe fibrosis (Metavir F ≥ 3) in 679 CHC. Diagnostic cut-off was either the Youden index or that provided by a fibrosis classification (6 classes).

**Results:** Accuracy (% well classified patients) using the Youden cutoff: all patients: BT: 75.7%, TE: 79.1%, BTE: 79.4% (p = 0.066); discordant (28.4% of patients) vs concordant (71.6%) tests, respectively: BT: 44.0 vs 88.3% (p < 0.001), TE: 56.0% vs 88.3% (p < 0.001), BTE: 61.5% vs 86.5% (p < 0.001). EASL-ALEH rule is thus validated. Accuracy by fibrosis classifications: all patients: BT: 84.1%, TE: 88.2%, BTE: 91.7% (p < 0.001); discordant (26.8%) vs concordant (73.2%) tests, respectively: BT: 68.1% vs 89.9% (p < 0.001), TE: 79.1 vs 91.5% (p < 0.001), BTE: 89.0 vs 92.7% (p = 0.118). EASL-ALEH rule is thus improved by BTE classification since its accuracy is not dependent on test concordance. The same significant improvement by BET classification was observed for significant fibrosis in CHC. BTE classification significantly improved cirrhosis diagnosis in CHC but this was more marked in discordant tests. The same significant improvements by BTE classification was observed in CHB and partially in NAFLD. The combined test BTE had significantly higher accuracy (by AUROC for significant or severe fibrosis or cirrhosis or Obuchowski index) than its composite tests in all these diagnostic targets in CHC, CHB and NAFLD.

**Conclusions:** The EASL-ALEH concordance rule is validated. A combined test classification improves this rule by avoiding any biopsy requirement. BTE outperformed other single tests validating and extending the 2015 EASL-ALEH and AASLD-ISDA guidelines. Thus, non-invasive fibrosis evaluation can be simplified in the main etiologies of chronic liver diseases by using a unique test combining simultaneously blood markers and liver elastography.
Background and Aims: The prevalence of cirrhosis in the community is unknown and there is an urgent need to detect those in the community at risk of liver related morbidity and mortality. Fibroscan is a suitable screening tool with predetermined cut-offs validated in chronic hepatitis B (CHB) and C (CHC). The aim of this study was to determine the feasibility of community screening and estimate the prevalence of significant fibrosis and cirrhosis as assessed by liver stiffness measurement (LSM) in at-risk populations.

Methods: Participants were recruited from 18 primary care practices throughout Melbourne, Australia. Inclusion criteria included age 18–80 years, with CHB or CHC (duration >6 months), absence of prior or recent (<18 months) specialist input and no current or prior HCC. Clinical assessment, transient elastography (TE) (Fibroscan® 402) and blood analysis were performed at their place of primary care. Scans were accepted if the success rate was >60% and IQR/median stiffness <0.3. LSMs of 8 kPa and 13 kPa were taken as cut-offs to represent significant fibrosis (F2F3) and cirrhosis (F4). Individuals meeting these cut-offs were referred for ongoing management.

Results: From October 2014 to November 2015, 727 participants were invited to participate. Failure to attend rate was 37.9% and LSM failure occurred in one patient (0.18%). In total 526 were assessed (M/XL probe S10/16). Of these, 346 were CHC (Male 75.2%, mean age 42.3 y) and 261 CHB (Male 45.9%, mean age 44.5 y). CHC cohort in comparison to CHB had a higher prevalence of at risk alcohol consumption (>140 g/wk) (45.4% vs 6.6% p < 0.001), higher BMI (26.5 vs 23.6 p < 0.001), various LSM circumference (93.45 cm vs 82.1 cm p < 0.001) and ALT (79.3 vs 29.4 IU/L p < 0.001). Mean LSM was 10.3 kPa in CHC and 4.9 kPa in CHB (p < 0.001). LSM > 8 kPa was seen in 29.8% of participants (CHC 42.5% v CHB 6% p < 0.001. LSM > 13 kPa was seen in 10.2%, all were CHC (15.6% of CHC cohort). Three CHB participants were diagnosed as cirrhotic on a radiological basis, all had LSM >11 kPa. Three malignancies were detected, one of each; colorectal, lung and hepatocellular carcinoma (BCLC Stage A).

Conclusions: Study demonstrates that screening at-risk patients in the community is feasible and a practical addition to current management. Furthermore, this study highlights the applicability of TE, with a high success rate of assessments in an unselected cohort. The estimated prevalence rates of cirrhosis (15.6%) and significant fibrosis (42.5%) in the CHC population has profound implications for health policy.
**Results:** Baseline characteristics such as underlying liver disease (B/C/nonB, nonC/Alcohol), bilirubin, INR, Child-Pugh Class (A/B) of training set and validation set were different (p < 0.05). In training set, based on univariate analysis, recurrence was associated with BMI, clinical liver cirrhosis, platelet count, spleen diameter and LSM. However, in multivariate analysis, only LSM was selected as independent predictors of recurrence (hazard ratio = 1.038, p < 0.001; 95% confidence interval, 1.025–1.051). We develop a predictive model for HCC recurrence using parameters including platelet count, spleen diameter and tumor number, which showed borderline statistical significance, as well as LSM. LSM-spleen diameter to platelet ratio score (LSPS) and LSM-spleen diameter-tumor number to platelet ratio score (LSNPS) were calculated in terms of prediction of HCC recurrence. LSMalone (area under the receiver operating characteristic curve (AUROC) = 0.710) was not superior compare to LSPS and LSNPS (AUROC = 0.691 and 0.702). When the patients were divided into two groups using the optimal cutoff value (12.5 kPa) that maximized the sum of sensitivity (75.0%) and specificity (53.0%) from time-dependent receiver operating characteristic curves, patients with LSM values >12.5 kPa were at a higher risk for recurrence compared with those with LSM values <12.5 kPa (HR = 3.881, p < 0.001; 95% CI, 2.216–6.796). Moreover, patients with LSM values >12.5 kPa had more de novo recurrence and shorter disease free survival in the training set. In validation set, using a cutoff value of LSM 12.5 kPa, the recurrence rate was also significantly greater at LSM values >12.5 kPa patient group. (HR = 4.433, p = 0.002; 95% CI, 1.727–11.378).

**Conclusions:** HCC recurrence after RFA have a substantial influence on long term prognosis. This work suggests that LSM can be a useful predictor of recurrence after radiofrequency ablation of HCC.
The FibroScan® system is intended to provide 50Hz shear wave speed measurements and estimates of tissue stiffness as well as 3.5 MHz ultrasound coefficient of attenuation (CAP: Controlled Attenuation Parameter) in internal structures of the body. FibroScan® is indicated for noninvasive measurement in the liver of 50 Hz shear wave speed and estimates of stiffness as well as 3.5 MHz ultrasound coefficient of attenuation (CAP: Controlled Attenuation Parameter). The shear wave speed and stiffness, and CAP may be used as an aid to clinical management of adult patients with liver disease. Shear wave speed and stiffness may be used as an aid to clinical management of pediatric patients with liver disease.

European Union: FibroScan™ is a class Ila medical device according to Directive EC/93/42 and is manufactured by Echosens. Assessment of its conformity with the essential requirements of the Directive EC/93/42 is established by the LNE-G-MED (n°0459) - France -. FibroScan™ is indicated for the non-invasive measurement of liver stiffness (E) and controlled attenuation parameter (CAP) in humans. It is expressly recommended to carefully read the guidance within the users’ guide and labeling of the device. FibroScan™ examination must only be performed by operators certified by the manufacturer or its accredited local representative. The values obtained with FibroScan™ must be interpreted by a physician experienced in dealing with liver disease, taking into account the complete medical record of the patient. In France, liver stiffness measurement by FibroScan™ is reimbursed by national Social Security medical insurance, in some circumstances and under certain conditions: see terms on the ameli.fr website.