The AASLD Liver Meeting 2016
November 11 – 15, Boston MA, USA

ORAL AND POSTER COMMUNICATIONS ON

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The intended use/indications for use for the FibroScan® are as follows:

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.

FibroMeter™

This test was developed and its performance characteristics determined by ARUP Laboratories. The U. S. Food and Drug Administration has not approved or cleared this test; however, FDA clearance or approval is not currently required for clinical use. The results are not intended to be used as the sole means for clinical diagnosis or patient management decisions.
FibroScan® Business Relevant Oral Presentations and Presidential posters of distinction

FibroScan® Oral Presentations

#42: Prospective Comparison to Liver Biopsy of VCTE/CAP, MRE, PDFF, and Multiparametric MRI for Predicting Degree of Steatosis and Diagnosis of NASH
  Parallel 5: NAFLD: Diagnosis and Natural History
  Sunday, 13 November 2016 – 2:30-2:45

#56: Factors associated with mortality, independently of sustained virological response (SVR), in HIV/HCV co-infected subjects - ANRS CO13 HEPAVIH cohort
  Parallel 8: HCV: Epidemiology and Natural History I
  Sunday, 13 November 2016 – 3:15-3:30

#58: Impact of all-oral antiviral therapy on portal pressure and hemodynamics on HCV-infected cirrhotic patients
  Parallel 8: HCV: Epidemiology and Natural History I
  Sunday, 13 November 2016 – 3:45-4:00

#85: Validating and refining non-invasive Baveno criteria for ruling out high-risk varices
  Parallel 13: Predictors of Outcomes in Cirrhosis
  Sunday, 13 November 2016 – 3:00-3:15

#104: Dynamic risk prediction of hepatocellular carcinoma development using risk prediction models in patients with chronic hepatitis B
  Parallel 16: Hepatitis B: Diagnostics and Natural History
  Sunday, 13 November 2016 – 5:00-5:15

#256: Paired Liver biopsy, Fibrotest and FibroScan® before and after treatment with DAA in liver transplanted recipients with recurrent hepatitis C: diagnostic accuracy and concordance
  Viral Hepatitis Plenary
  Tuesday, 15 November 2016 – 10:15-10:30

FibroScan® Presidential posters of distinction

#1051: Prospective Prevalence of Non-alcoholic Fatty Liver Disease (NAFLD) and Non-alcoholic Steatohepatitis (NASH) Among a Largely Middle-Aged Population Utilizing FibroScan®, Liver MultiScan (LMS), Magnetic Resonance Elastography (MRE), and Liver Biopsy: Interim Analysis
  Hall C
  Saturday, 12 November 2016 – 2:00-7:30

#1772: Transient Elastography in Assessment of Liver Fibrosis in Children with Chronic Hepatitis B: PEG-B-ACTIVE Liver Elasticity Substudy
  Hall C
  Monday, 14 November 2016 – 8:00-5:30
# Content

**#41:** Hepatic Steatosis and Fibrosis Diagnosed by Transient Elastography with Controlled Attenuation Parameter in Canadians Living with HIV Receiving Antiretroviral Therapy: Results of a Screening Program of 1033 Patients ................................................................. 1

**#42:** Prospective Comparison to Liver Biopsy of VCTE/CAP, MRE, PDFF, and Multiparametric MRI for Predicting Degree of Steatosis and Diagnosis of NASH ........................................................................... 1

**#56:** Factors associated with mortality, independently of sustained virological response (SVR), in HIV/HCV co-infected subjects ANRS CO13 HEPAVIH cohort ................................................................. 1

**#58:** Impact of all-oral antiviral therapy on portal pressure and hemodynamics on HCV-infected cirrhotic patients .......................................................... 2

**#74:** C-ISLE: Grazoprevir/Elbasvir plus Sofosbuvir in Treatment-naive and Treatment-experienced HCV GT3 Cirrhotic Patients Treated for 8, 12 or 16 weeks ........................................................................... 2

**#85:** Validating and refining non-invasive Baveno criteria for ruling out high-risk varices ........................................................................................................... 3

**#104:** Dynamic risk prediction of hepatocellular carcinoma development using risk prediction models in patients with chronic hepatitis B ................... 3

**#111:** RG-101 in Combination with 4 Weeks of Oral Direct Acting Antiviral Therapy Achieves High SVR Rates in Treatment Naive Genotype 1 and 4 Chronic Hepatitis C Patients ................................................................................ 4

**#114:** ENDURANCE-4: Efficacy and Safety of ABT-493/ABT530 Treatment in Patients with Chronic HCV Genotype 4, 5, or 6 Infection ......................... 4

**#176:** Liver-related morbidity and mortality in patients with Chronic Hepatitis C and cirrhosis with and without sustained virologic response 5

**#177:** 4AGP – A novel algorithm using indirect biomarkers out-performs established scores for detecting patients with elevated liver stiffness .... 5

**#209:** Long-Term Effect of Obeticholic Acid on Transient Elastography and AST to Platelet Ratio Index in Patients with PBC ............................................. 6

**#213:** Efficacy and safety treating the recurrent hepatitis C post-liver transplantation with Simeprevir and Sofosbuvir: The Spanish experience (SETH) ........................................................................................ 6

**#214:** Probiotic supplementation after Very Low Calorie Diet does not aid improvement of the metabolic syndrome or maintenance of weight loss post Liver Transplant. A randomised double-blind placebo controlled trial ........................................................................................................... 7

**#230:** A Phase 2 Study Of Titrating-Dose Lonafarnib Plus Ritonavir In Patients With Chronic Hepatitis D: Interim Results From The Lonafarnib With Ritonavir In HDV-4 (LOWR HDV-4) Study ............................................. 7

**#256:** Paired Liver biopsy, Fibrotest and FibroScan® before and after treatment with DAA in liver transplanted recipients with recurrent hepatitis C: diagnostic accuracy and concordance .......................................................... 8

**#258:** A Randomized Phase 3 Trial of Sofosbuvir/Velpatasvir/Voxilaprevir for 8 Weeks and Sofosbuvir/Velpatasvir for 12 Weeks for Patients with Genotype 3 HCV Infection and Cirrhosis: The POLARIS-3 Study .......................................................... 8

**#379:** Relationships between biochemical response to UDCA and progression of liver stiffness as determined by Fibroscan in patients with PBC 9

**#406:** A 48-gene Signature in Formalin-fixed Paraffin-embedded (FFPE) Liver Biopsies Enables Early Prediction of Adverse Outcomes in Patients with Autoimmune Hepatitis (AIH) ................................................................. 9

**#414:** Coffee & herbal tea consumption is protective of liver stiffness in the general population: The Rotterdam Study .................................................. 10

**#420:** Serum Wisteria floribunda Agglutinin-Positive Mac-2 binding protein level as a predictor of hepatic fibrosis in chronic HBV infection ..................... 10

**#557:** Controlled Attenuation Parameter (CAP), a presumed measure of hepatic steatosis in patients with Cystic Fibrosis (CF) ........................................... 10

**#573:** The real impact of fatigue in Haemochromatosis .......................................................................................................................... 11

**#596:** Hepatitis B (HBV) Reactivation During Anti-Hepatitis C (HCV) Therapy with Interferon (IFN)-Free Regimens: A Prospective Study .......................... 11

**#653:** Evolution of Cystic Fibrosis-Related Liver Disease Assessed By Elastometry ........................................................................................................... 12

**#655:** eLIFT, a new friendly user and ‘at-a-glance’ fibrosis test, combined with FibroMeterVCTE in a simple algorithm allows for the widespread detection of liver fibrosis in the large population of patients with chronic liver diseases ................................................................................ 12

**#656:** Early regression of liver fibrosis in HCV infected patients with or without HIV infection after treatment with DAAAs ............................................. 12

**#657:** Defining Liver Stiffness Measurement Cut-offs to Predict Mortality and Complications in Patients with Cirrhosis of Mixed Etiology .................... 13

**#661:** Diagnostic Value of Transient Elastography for Detection of Hepatic Fibrosis in Liver Transplant Recipients: A Systematic Review and Meta-Analysis ........................................................................................... 13

**#662:** The validity of two-dimensional shear wave ultrasound for assessing fibrosis stage in patients with chronic liver disease .......................... 14

**#664:** Point shear wave elastography has high diagnostic accuracy for staging of liver fibrosis in patients with chronic hepatitis B or C infection .................................................. 14

**#752:** Early decrease of liver stiffness after initiation of antiviral therapy in patients with chronic hepatitis C .......................................................... 14

**#776:** The prediction of hepatocellular carcinoma development and overall survival in chronic hepatitis C using liver stiffness measurement: a long-term outcome study .......................................................... 15

**#781:** Project iTTREAT (Integrated Community Based Test – Stage-Treat) HCV Service for People who Inject Drugs (PWID) .................................................. 15

**#784:** Divergency of liver and spleen stiffness dynamics 24 weeks after end of interferon-free treatment in patients with hepatitis C virus (HCV)-associated cirrhosis and sustained virologic response .................................................. 16

**#791:** Estimation of liver fibrosis by the use of non-commercial serum scores in comparison to transient elastography in HCV patients receiving direct acting antiviral treatment ........................................................................... 16

**#795:** Association between Liver stiffness measurement and serum Wisteria floribunda agglutinin-positive Mac-2 binding protein among Japanese patients with hepatitis B, C and NAFLD/NASH .................................................. 16

**#796:** Association of low-density lipoprotein cholesterol with spontaneous clearance in HCV-infected patients ........................................................ 17
Nonalcoholic Fatty Liver Disease: Epidemiological Study from General Mediterranean Population .................................................................32
#1147: Usefulness of the Controlled Attenuation Parameter (CAP) for detecting liver steatosis and metabolic syndrome in health check-up …33
#1148: The combination of Index of NASH score and liver stiffness improves the noninvasive diagnostic accuracy for severe liver fibrosis in patients with Non-Alcoholic Fatty Liver Disease ....................................33
#1151: Baseline patient characteristics and non-invasive image analysis in a Phase 2 therapeutic trial of GR-MD-02 in NASH patients with stage 3 fibrosis ..........................................................................................33
#1154: ALT as a non-invasive biomarker of histological response to pharmacotherapy in NASH patients: insights from the elafibranor GOLDENS05 trial ..................................................................................34
#1161: Improved Noninvasive prediction of Liver Fibrosis by Liver Stiffness Measurement in Patients with Nonalcoholic Fatty Liver Disease Accounting for Controlled Attenuation Parameter Values .........................................................34
#1167: Hepatic steatosis in Crohn’s disease – Non-invasive comparison between NASH and Crohn’s .........................................................................................................................34
#1168: A prospective study to evaluate the efficacy of a standardized low calorie diet according to PNPLA3 genotype in patients with Non Alcoholic Fatty Liver Disease (NAFLD) – week 2 data interim analysis. …35
#1178: Cytokeratin 18 and Transient Elastography with Controlled Attenuation Parameter as Screening Tools for Nonalcoholic Steatohepatitis in HIV Mono-infected Patients. ................................................................35
#1179: Controlling HIV using cART contributes to metabolic disorder and hepatic steatosis ..........................................................................................................................36
#1186: Comparison of non-invasive markers for assessing fibrosis in Asian patients with non-alcoholic fatty liver disease .................................................................36
#1429: How to define splenomegaly in the diagnosis of liver cirrhosis? : Significance of splenic volume measurement using ultrasonography ................................................36
#1441: The Impact of Nonselective Beta Blocker on the Liver Stiffness Measurement in Cirrhosis with Severe Portal Hypertension ..............................37
#1445: Availability of contrast-enhanced ultrasonography for the evaluation of partial splenic embolization in cirrhotic patients with hypersplenism .............................................................................37
#1449: LDV/SOF combination is associated with 100% SVR in patients with thalassemia major: a preliminary report from an Italian multicenter study ........................................................................38
#1475: HCV Cure: Increases Body Weight and Liver Fat Content .......38
#1635: 100% Virological response with 3D regimen and significant short-term liver stiffness improvement in patients with recurrent hepatitis C following liver transplantation ................................................................39
#1643: The Effect of a 12-month Weight Loss Program on Non-alcoholic Fatty Liver Disease in Obese Patients ..................................................................................39
#1684: Biological significance of connective tissue growth factor and its potential as a novel therapeutic target in hepatic fibrosis ................................................39
#1707: Screening of oesophagogastric varices in virus-related compensated advanced chronic liver disease: Baveno VI criteria and beyond ..........................................................................................40
#1709: Vibration-Controlled Transient Elastography (VCTE) is Useful in Identifying Clinically Significant Portal Hypertension in Patients with NASH Cirrhosis ..................................................................................40
#1732: The Northwell Health Real World Experience: A novel team approach is successful in overcoming barriers of access to obtaining HCV direct acting anti-viral therapies and obtaining SVR rates of 97% 40
#1743: Patient reported assessment of different diagnostic imaging tests for liver disease – visual representation and ownership of results improves understanding ........................................................................41
#1748: Community Approach Targeting Cirrhosis and Hepatocellular Carcinoma (CATCH) Community Cirrhosis Prevalence in Viral Hepatitis .................................................41
#1762: Lack of compliance to hepatocellular carcinoma (HCC) screening guidelines in hepatitis B (HBV) or C (HCV) virus co-infected HIV patients with cirrhosis .................................................................................42
#1772: Transient Elastography in Assessment of Liver Fibrosis in Children with Chronic Hepatitis B: PEG-B-ACTIVE Liver Elasticity Substudy ..........43
#1793: US Asian HBV Patients Have Liver Steatosis and Metabolic Syndrome at Lower BMI than non Asians .................................................................................43
#1808: Dynamic changes of liver stiffness predict histological reverse of liver fibrosis in chronic hepatitis B patients treated with entecavir ........................................................................43
#1820: Subcirrhotic liver stiffness by transient elastography correlates with lower risk of hepatocellular carcinoma in patients with HBV-related cirrhosis .................................................................................43
#1835: Validation of a diagnostic strategy combining the transient elastography liver stiffness value and enhanced liver fibrosis test to assess the fibrotic burden in patients with chronic hepatitis B .............................................................................................................44
#1836: Profile of viral, biochemical and non-invasive fibrosis markers in a cohort of inactive European hepatitis B (HBV) carriers: 3 years follow-up of a prospective longitudinal study (ALBATROS Study) ........................................................................44
#1839: Diagnostic performance of APRI, FIB-4 and Fibroscan for assessment of hepatic fibrosis in chronic hepatitis B patients receiving oral antiviral therapy; 7-year real lifedata ........................................................................45
#1854: The effects of non-alcoholic fatty liver disease on liverfibrosis in chronic hepatitis B patients on nucleosideanalogue therapy: results from a matched-case control study .................................................................................45
#1877: Silibinin treatment for hepatitis D: in vitro and in vivo ...........46
#1887: Post-treatment dynamic changes of liver stiffness to predict first 2-year outcomes in HBV compensated cirrhosis .................................................................................46
#1905: Liver stiffness and virologic outcomes after introducing tenofovir as part of antiretroviral therapy in lamivudine-experienced adults with HIV and hepatitis B virus (HVB) co-infection in Ghana: four-year follow up of the prospective HEPIK cohort ........................................................................46
#1911: Patients with HIGT 1/4 infection and compensated cirrhosis, without baseline NSSA RASs, could be treated with SOF + NSSA inhibitor for 12 weeks without RBV .........................................................47
#1923: Treatment of chronic HCV infection with direct antiviral agents (DAA) results in rapid regression of transient elastography (Fibroscan®) and validated fibrosis markers FIB-4 and APRI ................47
#1924: Favorable efficacy of combination therapy with direct-acting antivirals to elderly aged 70 and older with HCV genotype 1 ..........48

#1927: Efficacy and safety of sofosbuvir and daclatasvir for 8 weeks in treatment-naive non-cirrhotic patients with chronic HCV Genotype 3 Infection..................................................................................................................48

#1929: The efficacy and safety of sofosbuvir plus ribavirin with or without peg-interferon in treatment of naïve and experienced Vietnamese patients with chronic genotype 1 and 6 HCV infection ......48

#1977: Effects of interferon-free treatment on serum cholesterol levels are different between the two sofosbuvir-based regimens in chronic HCV-infected patients ..............................................................................................................49

#1981: Safety and efficacy of regimens including direct acting antivirals (DAAs) in chronic hepatitis C (CHC) patients over the age of 70 years ..........................................................................................................................49

#1992: Efficacy of All-Oral HCV Therapy in People Who Inject Drugs (PWID) ..........................................................................................................................50

#1995: Treatment of US Veterans with hepatitis C virus (HCV) genotype (GT) 1 infection: effectiveness of Ledipasvir/ Sofosbuvir (Harvoni®) and Ombitasvir/ Paritavir/ Ritonavir/ Dasabuvir (Viekira Pak®) regimens .................................................................................................................................50

#2009: Real-life Hepatitis C treatment: effectiveness of 8 or 12 week Sofosbuvir/Ledipasvir in Genotype 1 non-cirrhotic treatment-naïve mono or HIV-coinfected patients ........................................................................51

#2016: Treatment of chronic HCV infection with the new direct acting antivirals (DAAs): a Real World experience in Brazil .......................................................51

#2017: Effectiveness and security of 3D/2D treatment in HCV/ HIV coinfected cirrhotic patients ......................................................................................................................51

#2022: Changes in Liver Stiffness and Clinical Outcomes after SVR in Patients with Advanced Fibrosis or Cirrhosis from Hepatitis C Virus 52

#2057: Novel Serum Biomarkers Predict Outcome in Compensated Cirrhosis .........................................................................................................................52
1. Oral Presentation #41

Parallel 5: NAFLD: Diagnosis and Natural History
Sunday, 13 November 2016 – 2:15-2:30

#41: HEPATIC STEATOSIS AND FIBROSIS DIAGNOSED BY TRANSIENT ELASTOGRAPHY WITH CONTROLLED ATTENUATION PARAMETER IN CANADIANS LIVING WITH HIV RECEIVING ANTIRETROVIRAL THERAPY: RESULTS OF A SCREENING PROGRAM OF 1033 PATIENTS

Giada Sebastiani, Peter Ghali, Philip Wong, Lynda Lennox, Marc Deschenes, Marina B. Klein; Medicine, McGill University Health Centre, Montreal, QC, Canada

Background: Liver disease is emerging as a major health concern in HIV-infected patients. However, large-scale prospective data on hepatic steatosis and fibrosis are lacking.

Methods: We prospectively investigated prevalence and predictors of hepatic steatosis and fibrosis by transient elastography (TE) and associated controlled attenuation parameter (CAP) in a large series of unselected HIV-infected adults as part of a routine screening program. Hepatic steatosis (any grade involving>10% of hepatocytes) was defined as CAP 238 dB/m. Significant liver fibrosis and cirrhosis (stage 2 and 4 out of 4, respectively) were defined as TE measurement 7.1 and 13 kPa, respectively. Predictors of steatosis and significant liver fibrosis were determined by logistic regression analysis.

Results: 1033 consecutive HIV-infected patients (median age 51.6, IQR 43.8-57.5 years; 77.6% men; median CD4 count 565, IQR 373-780 cell/µL; 90% on antiretrovirals) were included in 2013-2016. Coinfection with HCV and HBV was found in 35% and 6% of cases, respectively. Hazard–us alcohol use was found in 8% of patients. HCV genotype 3 was present in 19% of HIV/HCV coinfected patients. Prevalence of hepatic steatosis, significant liver fibrosis and cirrhosis was as follows: 54%, 18% and 6% in HIV mono-infection; 39%, 40% and 18% in HIV/HCV coinfection, respectively. The results of a multivariable analysis are shown in the Table. Conclusion: Hepatic steatosis and fibrosis are major comorbidities in Canadians living with HIV. Hepatic steatosis is particularly frequent in HIV mono-infected patients, likely due to high prevalence of dysmetabolism. Liver fibrosis is associated with HIV coinfection, while steatosis is less prevalent, likely due to low proportion of HCV genotype 3 and to high prevalence of fibrosis/cirrhosis, resulting in burned out fatty liver. Non-invasive screening strategies can help early diagnosis and initiation of interventions, including weight loss, optimal HIV infection and glycemic control, treatment of dyslipidemia and antiviral therapy for HCV.

Table: Multivariable analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hepatic steatosis</th>
<th>Significant liver fibrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>aOR (55% CI)</td>
<td>p</td>
</tr>
<tr>
<td>Black ethnicity</td>
<td>0.99 (0.54-1.87)</td>
<td>0.99</td>
</tr>
<tr>
<td>Duration HIV infection (year)</td>
<td>1.01 (0.98-1.04)</td>
<td>0.37</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.81 (1.29-1.43)</td>
<td>0.008</td>
</tr>
<tr>
<td>BMI ≥25 kg/m2</td>
<td>2.54 (1.50-4.66)</td>
<td>0.001</td>
</tr>
<tr>
<td>HCV</td>
<td>0.66 (0.35-1.21)</td>
<td>0.001</td>
</tr>
<tr>
<td>HBV</td>
<td>0.85 (0.33-2.17)</td>
<td>0.73</td>
</tr>
<tr>
<td>Didanosine</td>
<td>1.01 (0.51-2.01)</td>
<td>0.98</td>
</tr>
<tr>
<td>ALT &gt; 40 U/L</td>
<td>1.26 (0.77-2.05)</td>
<td>0.36</td>
</tr>
<tr>
<td>CD4 &lt;200</td>
<td>0.50 (0.21-1.20)</td>
<td>0.12</td>
</tr>
<tr>
<td>LDL cholesterol (per unit)</td>
<td>0.36 (0.19-0.69)</td>
<td>0.002</td>
</tr>
<tr>
<td>Triglycerides (per unit)</td>
<td>1.28 (1.05-1.55)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

PREDICTING DEGREE OF STEATOSIS AND DIAGNOSIS OF NASH


1Gastroenterology, Brooke Army Medical Center, Fort Sam Houston, TX
2Radiology, Brooke Army Medical Center, Fort Sam Houston, TX
3Pathology, Brooke Army Medical Center, Fort Sam Houston, TX
4Biomedical Statistics, Institute for Surgical Research, Fort Sam Houston, TX

Background: Nonalcoholic fatty liver disease (NAFLD) is increasing in prevalence. 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. We report data from an ongoing NAFLD prevalence study in which we assess the ability of novel imaging techniques to predict the degree of hepatic steatosis and properly assess severity of disease.

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 (PDFD) using LMS. Similarly, the ability to diagnosis NASH non-invasively was compared among LMS using the LIIF score, FibroScan®, and MRE.

Results: To date, 400 participants have been enrolled; 270 had results available for interim analysis; 91 have completed biopsies14 had NASH. Mean PDFF of 4.38%, 8.64%, 17.04 and 26.17% for grade 0, 1, 2 and 3 steatosis, respectively. All five groups were significantly different (Kruskal-Wallis p<0.001). PDFF had an AUC of 0.896 for identification of steatosis (5%). Similarly, there was a mean CAP of 276.8 dB/m, 313.8 dB/m, 358.8 dB/m, and 350.3 dB/m, for grade 0, 1, 2 and 3 steatosis. The comparisons between groups, with the exception of grade 2 versus 3, were significant (Kruskal-Wallis, p<0.01). CAP values of <240 dB/m excluded steatosis (sens: 96%) and a CAP of >350 dB/m confirmed a diagnosis of NAFLD (spec:98%). The sens/spec/PPV/NPV for detecting or excluding NASH for LIIF > 2, Fibroscan® > 7 kPa, and MRE > 30 kPa are shown in Table 1.

Conclusions: Both CAP and PDFF are valid methods for predicting the grade of hepatic steatosis in NAFLD patients. This interim analysis shows that LIIF < 2 and Fibroscan® < 7 kPa demonstrate high NPV for excluding NASH while a MRE > 3 kPa has the highest PPV for NASH.

Imaging Modality Table

<table>
<thead>
<tr>
<th>Imaging Modality</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIIF score &gt; 2</td>
<td>0.90</td>
<td>0.32</td>
<td>0.25</td>
<td>0.95</td>
</tr>
<tr>
<td>Fibroscan® &gt; 7 kPa</td>
<td>0.69</td>
<td>0.80</td>
<td>0.48</td>
<td>0.91</td>
</tr>
<tr>
<td>MRE &gt; 3 kPa</td>
<td>0.73</td>
<td>0.98</td>
<td>0.83</td>
<td>0.85</td>
</tr>
</tbody>
</table>

2. Oral Presentation #42

Parallel 5: NAFLD: Diagnosis and Natural History
Sunday, 13 November 2016 – 2:30-2:45

#42: PROSPECTIVE COMPARISON TO LIVER BIOPSY OF VCETE/CAP, MRE, PDFF, AND MULTIPARAMETRIC MRI FOR
Piroth\(^5\), David Zucman\(^6\), Stephanie Dominguez\(^2\), François Raffi\(^7\), Laurent Alric\(^8\), Firouze Bani-Sadr\(^9\), Caroline Lascoux-Combe\(^3\), Daniel Garipuy\(^4\), Patrick Miallhes\(^4\), Daniel Vittecoq\(^4\), Olivier Lortholary\(^8\), Hugues Aumâtre\(^6\), Didier Neu\(^2\), Philippe Morlat\(^6\), François Dabis\(^1\), Dominique Salmon\(^2\)

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\(^5\) CHU Dijon, Dijon, France
\(^6\) CHU Strasbourg, Strasbourg, France
\(^7\) CHU Nantes, Nantes, France
\(^8\) CHU Toulouse, Toulouse, France
\(^9\) Hôpital Ducuing, Toulouse, France
\(^10\) CHU Lyon, Lyon, France
\(^11\) CH Perpignan, Perpignan, France
\(^12\) CHU Bordeaux, Bordeaux, France
\(^13\) UQED, Université de Bordeaux, Bordeaux, France

Methods: HIV/HCV co-infected patients from the French nation-wide, prospective, multicenter ANRS CO13 HEPAVIH cohort, with at least one liver stiffness measurement (LSM) by FibroScan\(^\text{®}\) (FS) meeting the validity criterion (IQFR/LSM<30%), a detectable HCV viral load when the first valid FS was performed, and at least one follow-up visit were included. The primary endpoint was all-cause mortality. The study started at the date of the first valid FS (t0) and ended at death or last follow-up visit. A Cox proportional hazards model with delayed entry was performed to determine factors associated with mortality. LSM and SVR as time-dependent covariates, sex, metabolic disorders (defined as presence of at least one of these conditions: diabetes, metabolic syndrome, insulin resistance, lipodystrophy), and alcohol use (past and current) were forced into the model. Factors significantly associated with mortality (with a 5% threshold) were metabolic syndrome, insulin resistance, lipodystrophy), and alcohol use determined with a backward stepwise selection procedure: 1/ fixed covariables determined at inclusion: tobacco use, drug use (past and current), mode of HIV transmission, AIDS stage, previous HCV treatment by pegylated interferon plus ribavirin, HCV genotype, HBs antigen; 2/ time-dependent covariables: HCV viral load, CD4+ level.

Results: 1062 patients were included: 69.8% of men, with a median age of 45.7 years (IQR: 42.4-49.1). 21.7% had a LSM>12.5 kPa at t0. Median follow-up was 4.9 years (IQR 3.2-6.1). 76 deaths were observed (26 liver-related, 10 HIV-related, 29 non liver non HIV related, 11 with undetermined cause). At 55 years, the mortality rate was 6.7% for patients with LSM<12.5 kPa compared to 20.2% for patients with LSM>12.5 kPa. Mortality rates were not significantly different between patients with LSM [7.1-9.5] and LSM [9.5-12.5] kPa compared to patients with LSM [2.5-7.1] kPa (hazard ratio (HR) [95% confidence interval]: 1.20 [0.57; 2.52] and 1.31 [0.56; 3.04] respectively). LSM>12.5 kPa patients had a significantly higher risk of all-cause mortality compared to LSM [2.5-7.1] kPa patients (HR=3.37 [2.00; 5.71], p=0.0001) in unvariable analysis. In adjusted analysis, LSM>12.5 kPa (adjusted HR (aHR)= 3.35 [2.06;5.45], p<0.0001), presence of previous HCV treatment (aHR=0.53 [0.32;0.90], p=0.01) and smoking (past versus never: aHR=5.69 [1.56;20.78]; current versus never: 3.22 [0.93;11.09], p=0.01) were significantly associated with all-cause mortality independently of SVR, age, sex, alcohol use and metabolic disorders.

Conclusions: Liver stiffness >12.5 kPa at any time was strongly associated with all-cause mortality independently of SVR. Close follow-up of these patients should remain a priority even after SVR.

4. Oral Presentation #58

Parallel 8: HCV: Epidemiology and Natural History I
Sunday, 13 November 2016 – 3:45-4:00
#58: IMPACT OF ALL-ORAL ANTIVIRAL THERAPY ON PORTAL PRESSURE AND HEMODYNAMICS ON HCV-INFECTED CIRRHOTIC PATIENTS

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Background: Data on the hemodynamic changes induced by sustained virological response (SVR) after all-oral therapy in patients with clinical significant portal hypertension (CSPH, HVPG≥10mmHg) are scarce. Previous data suggest that patients with CSPH, despite achieving SVR, remain at risk of liver decompensation (LD).

Methods: Multicenter prospective study of patients with HCV-related cirrhosis and CSPH before all-oral antiviral therapy (BL or baseline). By study protocol, patients underwent HVPG, right-heart catheterization and liver stiffness measurement (LSM) at BL and 24 weeks after end of treatment if SVR (FU or follow-up). Patients starting beta-blocker (BB) therapy between HVPG measures were excluded.

Results: 118 cirrhotic patients with CSPH were included. Most patients (92%) were CTP-A; 80% had esophageal varices (40% large) and 31% had at least one previous LD (14% variceal bleeding, 21% ascites). Overall, HVPG decreased from 16.44.5 to 14.54.6 mmHg after SVR (mean change -1.93; p<0.01). A clinically relevant decrease (10%) was observed in 65 (54%) patients (*p*<0.01). In multivariate analysis, the only variable associated with 10% decrease was BL-HVPG (OR 0.22 [0.07-0.66]; p<0.01). After achieving SVR, CSPH persisted in 86% of patients. Decrease in mean HVPG after antiviral therapy was similar in patients with (n=52) or without BB, however, due to higher BL-HVPG, CSPH persisted in 95% of patients with BB compared to 77% without BB (p<0.01). In 82 patients with paired BL, BS-LSM was 3115kPa with a mean reduction of -6 12kPa after SVR (p<0.05). Previously described cut-offs of 13.6 and 21kPa presented high NPV (92%) and PPV (97%) for the persistence of CSPH on follow-up, respectively. Paired right-heart catheterization (n= 82 patients) showed a significant rise in MAP due to increased systemic vascular resistance (+14% and +25%, p<0.05) with stable cardiac output. Interestingly, mPAP and pulmonary vascular resistance also rose after therapy (+15% and +21%, p<0.05). Indeed, pulmonary arterial hypertension (mPAP25mmHg) developed or exacerbated in 9 and 4 patients, respectively but only 2 presented increased pulmonary vascular resistance.

Conclusions: Despite achieving SVR, CSPH persists 24 weeks after therapy in most patients with HCV-related cirrhosis treated with all-oral antiviral therapy, indicating risk of decompensation. Previously described LSM cut-offs to rule-in or out CSPH are still useful after SVR. Interestingly, improvement of systemic hemodynamics after SVR was associated with pulmonary hypertension in some patients, indicating the need for continued careful monitoring on long-term follow-up.

5. Oral Presentation #74

Parallel 11: Hepatitis C: New and Existing Agents
Sunday, 13 November 2016 – 3:15-3:30
#74: C-ISE: GRAZOPREVIR/ELBASVIR PLUS SOFOSBUVIR IN TREATMENT-NAIVE AND TREATMENT-EXPERIENCED HCV GT3 CIRRHOTIC PATIENTS TREATED FOR 8, 12 OR 16 WEEKS
Background and Purpose: Current approved HCV GT3 therapies are limited in patients with cirrhosis demonstrating suboptimal responses (<90% Sustained Virologic Response) especially in treatment-experienced patients. In the UK, GT3 cirrhotic patients receive sofosbuvir (SOF)/peg-interferon (P)/ribavirin (RBV) or daclatasvir/SOF/RBV for 12-24 weeks. Supported by preliminary data showing high efficacy in GT3 patients treated with elbasvir (EBR)/grazoprevir (GZR) + SOF for 8-12 weeks, C-ISLE was developed as a regional study of HCV GT3 compensated cirrhotic patients treated for 8-16 weeks with EBR/GZR + SOF RBV.

Methods: 100 compensated cirrhotic HCV GT3 patients were randomized to 1 of 5 treatment arms in C-ISLE (PN083). 47 patients were treatment-naïve and randomized 1:1 to EBR/GZR + SOF + RBV for 8 weeks or EBR/GZR + SOF for 12 weeks. 53 patients were P/RBV treatment-experienced and randomized 1:1:1 to EBR/GZR + SOF for 12 weeks or EBR/GZR + SOF for 16 weeks. Presence of cirrhosis was confirmed by either liver biopsy F4 (16%) or FibroScan (84%; mean 25.44 range 12.6-69.1 kPa). The primary endpoint was the proportion of patients with HCV RNA <15 IU/mL 12 weeks after treatment (SVR12).

Results: Mean age of the patients was 53.4 years (range 32-70), 68% were male, and 29% were South Asians (predominantly Bangladeshi / Pakistani). At treatment week 4, the proportion of patients with HCV RNA <15 IU/mL ranged from 71 to 88%. At treatment week 8, 100% of patients in all arms had HCV RNA levels <15 IU/mL. Therapy was generally well tolerated. On-therapy serious adverse events (SAEs) included 5 patients (cellulitis; pneumonia; chest pain; opiate overdose; transient creatinine clearance decrease). Three patients on RBV had hemoglobin <10 g/dL. One patient discontinued due to an AE (cellulitis).

Conclusions: The pangenotypic, once-daily, direct-acting antiviral regimen of ABT-493/ABT-530 for 12 weeks in treatment-naïve or -experienced, non-cirrhotic patients with HCV GT2 infection is being compared to placebo for safety assessment, as well as the historic standard of care, SOF + RBV, to assess efficacy. The resulting data could influence the treatment of this patient population in the future.

Table:

<table>
<thead>
<tr>
<th>% Patients with HCV RNA &lt;15 IU/mL (All patients received EBR/GZR + SOF)</th>
<th>Treatment naive</th>
<th>Treatment-experienced</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ARM 1</strong></td>
<td><strong>ARM 2</strong></td>
<td><strong>ARM 3</strong></td>
</tr>
<tr>
<td>8 weeks + RBV</td>
<td>12 weeks + RBV</td>
<td>12 weeks No RBV</td>
</tr>
<tr>
<td>Treatment Week 4</td>
<td>87%</td>
<td>74%</td>
</tr>
<tr>
<td>Treatment Week 8</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
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6. Oral Presentation #85

Parallel 13: Predictors of Outcomes in Cirrhosis
Sunday, 13 November 2016 – 3:00-3:15

#85: VALIDATING AND REFINING NON-INVASIVE BAVENO CRITERIA FOR RULING OUT HIGH-RISK VARICES

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Background: Endoscopic variceal screening is recommended in patients with cirrhosis to identify high-risk varices (HRV) requiring primary prophylaxis. Per recent Baveno consensus, endoscopy can be avoided by using noninvasive criteria, specifically liver stiffness (LS) by transient elastography (TE) <20 kPa and platelets >150,000/mm3. 1) Validate Baveno criteria in two cohorts (U.S. and Italy); 2) investigate sensitivity and negative predictive value (NPV) including data from the literature and 3) refine Baveno criteria so that more endoscopies could be avoided.

Methods: Patients with compensated cirrhosis (never had ascites, encephalopathy or variceal hemorrhage) with a LS> 10 kPa who had endoscopy within 1 year of TE were included in the study. Sensitivity and NPV were assessed in the U.S and Italian cohorts and in combination with literature data. New cutoffs for LS/platelets were tested in the U.S cohort and validated in the Italian cohort.

Results: Of patients meeting Baveno criteria (61/205, 30%, in the U.S. cohort, 14/111, 13% in the Italian cohort), none had HRV (medium/large varices), thereby validating Baveno criteria. When adding data from 7 not fully published studies, 22% (530/2453) fulfilled Baveno criteria but nine (1.7%) patients with HRV would have been missed. Sensitivity was 94% [95% CI 89-97%]; NPV 97% [95-99%], indicating that up to 11% of patients with HRV could be misclassified. With modified criteria as depicted in the Figure (U.S. cohort) we could avoid 56% endoscopies. This strategy was validated in the Italian cohort (that had a higher prevalence of HRV) where 41% endoscopies could have been avoided, with a sensitivity 100% [81-100%], NPV 100% [90-100%].

Conclusions: Baveno criteria correctly identify patients without HRV with only 22% of endoscopies avoided. Refining criteria can allow the avoidance of up to 50% of endoscopies while maintaining a high sensitivity.

Figure:

7. Oral Presentation #104

Parallel 16: Hepatitis B: Diagnostics and Natural History
Sunday, 13 November 2016 – 5:00-5:15

#104: DYNAMIC RISK PREDICTION OF HEPATOCELLULAR CARCINOMA DEVELOPMENT USING RISK PREDICTION MODELS IN PATIENTS WITH CHRONIC HEPATITIS B

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Background: Several risk prediction models for the development of hepatocellular carcinoma (HCC) were recently proposed. We explored whether dynamic changes revealed by these risk prediction models applied at different time points are useful to assess changes in the risk of HCC development in patients with chronic hepatitis B (CHB).

Methods: In total, 1,397 patients with CHB who underwent liver stiffness (LS) measurements via transient elastography from 2006 to 2014 were recruited for retrospective analysis. All patients underwent follow-up LS measurements at intervals of >6 months. We evaluated the accuracy of various risk prediction models applied at both the first and second LS measurements.

Results: The median age of the study population (931 men and 466 women) was 482 years. At the time of the first LS measurement, 475 (34%) patients were being treated with ongoing antiviral therapy (AVT). The median CU-HCC, GAG-HCC, REACH-B, LSM-HCC, and mREACH-B scores at this time were 100, 854, 92, 115, and 83, respectively. The median LS values fell from 118 to 98 kPa between the 1st and 2nd LS measurements.During the follow-up period (median 68.0 months), 87 (6.1%) patients developed HCC. Upon multivariate analysis, all risk prediction models independently predicted HCC development at both the 1st LS measurement [hazard ratio (HR) 1.051-1.443 in the subgroup not on AVT, and 1.062-1.430 in the subgroup on AVT] and 2nd LS measurement (HR 1.049-1.448 in the subgroup not on AVT, and 1.062-1.280 in the subgroup on AVT), along with age, diabetes mellitus, and the LS values (all p<0.05). In contrast, neither the absolute nor percentage changes in the risk prediction values between the 1st and 2nd LS measurements predicted HCC development (all p>0.05). Of the risk prediction models, the GAG-HCC value at the time of the first LS measurement was significantly higher in the subgroup treated with AVT-characteristic (AUROC) than did the other models, and thus better predicted HCC development by 7 years for the subgroup on AVT (0.785 vs. 0.681-0.805; all p<0.005). At the same time point, the mREACH-B model had a significantly higher AUROC than did other models for the subgroup not on AVT (0.790 vs. 0.681-0.781, all p<0.05).

Conclusions: It was possible to predict HCC development by applying various risk prediction models at different time points to data from patients, with CHB, but change in the absolute or percentage values between two time-points were not useful in this regard. The GAG-HCC and mREACH-B models optimally predicted HCC development, and incorporation of these models into current surveillance strategies should be further investigated.

8. Oral Presentation #111

Parallel 17: Hepatitis C: Phase 2/3 Trials
Sunday, 13 November 2016 – 5:15-5:30

#111: RG-101 IN COMBINATION WITH 4 WEEKS OF ORAL DIRECT ACTING ANTIVIRAL THERAPY ACHIEVES HIGH SVR RATES IN TREATMENT NAÏVE GENOTYPE 1 AND 4 CHRONIC HEPATITIS C PATIENTS

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Background and aims: MicroRNA (miR)-122 is the most abundant miR in the liver and is essential for hepatitis C virus (HCV) replication. N- acetylgalactosamine (GalNAc) conjugation has been shown to significantly enhance delivery of oligonucleotides to hepatocytes. RG-101 is a potent hepatocyte targeted, GalNAc-conjugated, anti-miR-122 oligonucleotide with favorable tolerability and activity in healthy volunteers and HCV patients. Current HCV standard of care treatment consists of 8-12 weeks of direct acting antiviral (DAA) oral agents. The aim of this study was to assess the safety and efficacy of a 4-week combination treatment regimen of RG-101 plus oral DAAAs in HCV genotype (GT) 1 and 4 patients.

Methods: Treatment naïve, non-cirrhotic patients with chronic GT1 or 4 HCV infection were enrolled. Each patient received a single 2 mg/kg subcutaneous (SC) injection of RG-101 on Day 1, followed by 4 weeks of an oral DAA (either ledipasvir/sofosbuvir [LVD/ SOF], simprevir [SMV], or daclatasvir [DCV]), and a second 2 mg/kg SC injection of RG-101 on Day 29. Interim analysis was performed to assess sustained virologic response at week 12 post-treatment (SVR12). Response was defined as an HCV RNA level below the lower limit of quantification (LLOQ) using the Abbott RealTime HCV Assay (LLOQ=12 IU/mL).

Results: 79 patients were enrolled and received study therapy. Baseline disease characteristics were balanced across treatment arms. Mean age was 45.0 years, 54% were female, and mean baseline viral load was 5.805 (log10) IU/ml. 77% of patients had HCV GT1 (20% GT1a, 53% GT1b) and the majority (86%) had stage 0 fibrosis by Fibroscan®. Combination therapy was generally well tolerated. Most adverse events (AEs) were mild or moderate in intensity and there were no discontinuations due to AEs. SVR12 was achieved by 100% of patients (27/27) in the RG-101+LVD/SOF arm; 26/27 [96%] in the RG-101+SMV arm; and 22/24 [92%] in the RG-101+DCV arm. At the time of interim analysis, twenty-nine patients had 24 weeks of post-treatment follow-up. SVR24 was achieved by 100% (10/10) of patients in the RG-101+LVD/SOF arm; 80% (8/10) in the RG-101+SMV arm; and 89% (8/9) in the RG-101+DCV arm.

Conclusions: RG-101 in combination with a 4 week course of a DAA was well tolerated and resulted in high SVR12 and SVR24 rates. Long-term safety and efficacy through Week 48 of post-treatment follow-up is ongoing. These interim results indicate the potential for RG-101 plus DAA combination therapy to provide a curative HCV regimen with 4 weeks of treatment.

9. Oral Presentation #114

Parallel 17: Hepatitis C: Phase 2/3 Trials
Sunday, 13 November 2016 – 6:00-6:15

#114: ENDURANCE-4: EFFICACY AND SAFETY OF ABT-493/ABT530 TREATMENT IN PATIENTS WITH CHRONIC HCV GENOTYPE 4, 5, OR 6 INFECTION

Tarik Asselah1, Christophe Hezode2, Neddie Zadeikis3, Dr. Magdy Elkhashab4, Massimo Colombo5, Rui T. Marinho6, Kosh Agarwal7, Frederik Nevens8, Ran Lu9, Teresa Ng10, Federico Mensa11

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3 Hospital S. Maria, Medical School of Lisbon, Lisbon, Portugal
4 Institute of Liver Studies, Kings College Hospital, London, United Kingdom
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6 AbbVie, Inc., North Chicago, IL
Background: An estimated 26 million people are infected with hepatitis C virus (HCV) genotype (GT) 4, 5, or 6. ABT-493 is a NS3/4A protease inhibitor; ABT-530 is a NSSA inhibitor. Both are panenotypic and demonstrate a high barrier to resistance, potent activity against common NS5A and NSSA variants, and high rates of sustained virologic response (SVR). The phase 2b study SURVEYOR-I yielded 100% efficacy in 34 patients with GT4, 5, or 6 infection without cirrhosis following treatment with ABT-493 and ABT-530. The objective of this study is to confirm the results of SURVEYOR-I in a large, phase 3 trial investigating the safety and efficacy of a 12-week treatment of once-daily, co-formulated ABT-493/ABT-530 in patients with HCV GT 4, 5, or 6 infection without cirrhosis.

Methods: ENDURANCE-4 (NCT02636595) is an ongoing phase 3, multicenter, open label, single arm study that enrolled patients without cirrhosis who were either HCV treatment-naïve or treatment-experienced (interferon [IFN] or pegylated IFN ribavirin [RBV], or sofosbuvir + RBV with or without pegIFN). Patients were over 18 years of age with chronic HCV GT 4, 5, or 6 infection. Key exclusion criteria included presence of cirrhosis, as determined by either a liver biopsy (METAVIR score6), a FibroScan score <125 kPa, or a FibroTest score of 6. An additional exclusion criterion was co-infection with HIV or HBV, or infection with more than one HCV GT. Enrolled patients received ABT-493/ABT-530 300mg/120mg once daily for 12 weeks. Efficacy is calculated using a two-sided 95% confidence interval as the percent of patients achieving SVR at post-treatment week 12 (SVR12). Additional endpoints include patients experiencing on-treatment virologic failure or relapse. Adverse events and clinical laboratory abnormalities are monitored to assess safety and tolerability. Analysis of baseline resistance-associated variants will be conducted; if a patient does not achieve SVR12, additional analysis of post-baseline variants relative to baseline will be performed.

Results: ENDURANCE-4 (NCT02636595) enrolled 121 patients at 32 sites across 8 countries in Europe, North America, and Africa; 76 patients were infected with GT4, 26 with GT5, and 19 with GT6. At baseline, the mean HCV RNA was 6.13 log10 IU/mL, 31% of patients were treatment-experienced, 14% had fibrosis stage of F2-F3, and most (75%) had non-CC IL28B genotype.

Conclusions: The safety and efficacy of 12-week, RBV-free ABT493/ABT530 treatment for chronic HCV GT4, 5 or 6 infection in patients without cirrhosis is being investigated. Baseline characteristics, safety and SVR12 results will be available for presentation at the meeting.

10. Oral Presentation #176

Parallel 27: HCV: Epidemiology and Natural History II
Monday, 14 November 2016 – 10:15-10:30

#176: LIVER-RELATED MORBIDITY AND MORTALITY IN PATIENTS WITH CHRONIC HEPATITIS C AND CIRRHOSIS WITH AND WITHOUT SUSTAINED VIROLOGIC RESPONSE

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7 Internal Medicine, Kolding Sygehus, Kolding, Denmark
8 Hepatology, Herlev Hospital, Copenhagen, Denmark

11. Oral Presentation #177

Parallel 27: HCV: Epidemiology and Natural History II
Monday, 14 November 2016 – 10:30-10:45

#177: 4AGP – A NOVEL ALGORITHM USING INDIRECT BIOMARKERS OUT-PERFORMS ESTABLISHED SCORES FOR DETECTING PATIENTS WITH ELEVATED LIVER STIFFNESS
Stephen D. Bloom1,2, Diana Lewis1,2, Catherine Smith4, William W. Kemp2, John Lubel1,2
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2 Eastern Health Clinical School, Monash University, Melbourne, VIC, Australia
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4 Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia

Introduction: Transient elastography (TE) is a validated non-invasive tool with prognostic and therapeutic significance in chronic hepatitis C (CHC). In many clinical trials a cut-off of 125 kPa is used to define cirrhosis. Despite this, indirect biomarkers (such as APRI & FIB4) remain an attractive alternative due to their widespread applicability and availability. We aimed to determine the accuracy of indirect biochemical markers in patients awaiting DAA therapy for CHC and construct an optimized algorithm consisting of routinely measured and readily available laboratory data.

Methods: Liver stiffness measurement (LSM) and biochemical assessment were performed prospectively in patients with CHC. Data were analyzed using bootstrap analyses (1000 replicates followed by stepwise logistic regression) to determine clinical and biochemical variables most strongly associated with LSM 125 kPa. Variables included in at least 80% of models were used to derive a new predictive model that was then compared to APRI, FIB4 and FORNS using area under receiver operator curve (AUROC) for accuracy.

Results: There were 676 patients with CHC included in this analysis. The prevalence of LSM 12.5 kPa was 16.8% (N = 114). APRI 1.0 occurred in 23.8% (N = 161). APRI and LSM agreed in 83.8% and were moderately correlated (Pearson’s 0.587 p < 0.005). FIB4 1.45 was observed in 36.8% (N = 249) and agreed with LSM in 75.8% (Pearson’s 0.612 p < 0.005). The AUROC for APRI, FIB4 and FORNS were not statistically different (0.86, 0.89, 0.88, p = 0.13). Logistic regression modelling identified 6 variables strongly associated with LSM 12.5 kPa: Age, Albumin, AFP, AST Gender and Platelet count (4AGP). This new algorithm agreed with LSM in 82.2% (Pearson’s 0.579 p < 0.005), demonstrating a higher sensitivity (91.2%) and negative predictive value (97.8%) than the other scores (APRI 72.8%/93.9%; FIB4 85.1%/96.1%; FORNS 57.9%/91.6%). The AUROC for 4AGP (0.9211) was superior to FIB4, APRI and FORNS (p < 0.001). 4AGP correctly classified 104 patients of the 114 with an LSM 12.5 kPa (FP = 16.1%, FN = 1.5%).

Conclusion: Using a large real-world cohort of patients with CHC we describe an optimised algorithm for the prediction LSM 12.5 kPa. The 4AGP demonstrates sufficient accuracy to identify patients with CHC at high risk of cirrhosis with a high sensitivity and negative predictive value. 4AGP performed better than established indirect biomarkers APRI, FIB4 and FORNS in predicting LSM12.5kPa and therefore may have utility in the initial assessment of patients with CHC in whom TE is not available. The 4AGP algorithm warrants further validation in CHC and non-CHC cohorts.

12. Oral Presentation #209

Parallel 31: PBC/PSC and Other Cholestatic Disease
Monday, 14 November 2016 – 4:00-4:15

#209: LONG-TERM EFFECT OF OBETICHOIC ACID ON TRANSIENT ELASTOGRAPHY AND AST TO PLATELET RATIO INDEX IN PATIENTS WITH PBC
Gideon M. Hirschfield1, Annarosa Floreani2, Palak J. Trivedi2, Richard Pencek2, Alexander Liberman3, Tonya Marmon3, Leigh MacConell4
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2 Università di Padova, Padova, Italy
3 Intercept Pharmaceuticals, Inc., San Diego, CA

Background: The AST to Platelet ratio (APRI) and transient elastography (TE) have both been identified as being predictive of adverse outcomes in primary biliary cholangitis (PBC). Obeticholic acid (OCA) is a farnesoid X receptor (FXR) agonist indicated for the treatment of PBC in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA. Using the randomized, double-blind (DB), placebo (PBO)-controlled Phase 3 study investigating OCA in patients with PBC, along with data from the ongoing open-label extension (OLE) we sought to investigate the effects of OCA on established non-invasive measures of liver fibrosis and outcomes in PBC.

Methods: Were-evaluated patients randomized and dosed in OCA 10 mg (n=73), OCA 5-10 mg (n=70, 33 patients titrated from 5 to 10 mg at Month 6), or PBO (n=73) groups during DB treatment. In the OLE, all patients were initially treated with 5 mg OCA with the option to increase to 10 mg (or later decrease) based on response and tolerability every 3 months. Non-invasive measures of liver fibrosis that were assessed were APRI and liver stiffness measurements (LSM) by transient elastography.

Results: APRI was significantly reduced from baseline to DB Month 12 in both OCA-treated groups compared to PBO (p < 0.001). PBO patients who initiated OCA during the OLE phase and patients randomized to OCA 5-10 mg had significant reductions from baseline to OLE Month 12 in mean APRI score (p < 0.05). The mean APRI score in OCA 10 mg was reduced, but not significant at OLE Month 12 compared to baseline. During DB and OLE phases, while not significant, the OCA 10 mg group had mean reductions in LSM, while both OCA 5-10 mg and PBO groups had mean increases in LSM (Table).

Conclusions: Both LSM and APRI, as non-invasive measures of liver fibrosis, have been found to be effective in predicting outcome in patients with PBC. DB and OLE treatment with OCA resulted in a mean reduction in liver stiffness and significant improvements in APRI suggesting that with long-term use, OCA has the potential to improve long-term outcomes for patients.

Table:

| Table 1. Mean Baseline and Change Values in Transient Elastography and APRI with OCA Treatment |
|-----------------|-----------------|-----------------|-----------------|
|                  | Mean [SD]       | Placebo [SD]    | OCA 5-10mg [SD] |
| Mean ([kPa])     | (OCA 10mg)      | (OCA 10mg)      | (OCA 10mg)      |
| Baseline         | 12.5 ± 5.7      | 12.5 ± 5.7      | 12.5 ± 5.7      |
| Change           | -0.5 ± 3.2      | -0.5 ± 3.2      | -0.5 ± 3.2      |

13. Oral Presentation #213

Parallel 27: HCV: Epidemiology and Natural History II
Monday, 14 November 2016 – 10:15-10:30

#213: EFFICACY AND SAFETY TESTING THE RECURRENT HEPATITIS C POST-LIVER TRANSPLANTATION WITH SIMEPREVR AND SOFSOBUVIR: THE SPANISH EXPERIENCE (SETH)
Gloria Sanchez-Antolin1,2, Milagros Testillano3, Martin Prieto2, Inmaculada Fernandez4, Xavier Xio6, Maria-Carola Londoño2, Luís Castells7, Juan Manuel Pascasio3, María Luisa Gonzalez Dieguez10, Alejandra Otero2, Magdalena Salcedo11, Isidoro Narvaez12, Jose A Pons13, Ignacio Herrero14, Sonia Pascual15, Jose Luis Montero2, Ana Arencibia16, Sara Lorente17, Esther Molina18, Jose Ramon Fernandez2, Valentin Cuervas-Mons19
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7 Hospital Universitario 12 de Octubre, Madrid, Spain
8 Hospital Universitario 12 de Octubre, Madrid, Spain
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18 Hospital Universitario 12 de Octubre, Madrid, Spain
19 Hospital Universitario 12 de Octubre, Madrid, Spain

Background: The challenge of recurrent hepatitis C (HCV) post-liver transplantation (LT) is well-known. Various antivirals have been used, but with limited success. We report our experience with Simeprevir and Sofosbuvir in the treatment of recurrent HCV post-LT in Spain.
Background: The treatments of hepatitis C until now had low efficacy and many adverse effects. The new direct acting antivirals have significantly increased the efficacy and safety of treatment in liver transplant hepatitis C patients. Simprevir (SIM) and sofosbuvir (SOF) is an effective combination in patients with genotype 1 and 4. Objectives:  To determine the efficacy and safety in real life of the combination SOF+SIM/RBV in a group of liver transplant patients genotype 1 and 4 in 21 liver transplant centers.

Results: In genotype 1 patients 737 were male and the average age was 61.4939. The 63.1% were ile 288 CT. The genotype 1a rate was 15.02%, and the 59.05% had been previously treated, the most part with interferon based therapy, but 108% with IP and the 43% with Sofosbuvir. The 511.4% were null responders. There was a 53.8% of patients with fibrosis 4. The average MELD was 8.862.87 with a range 6-24. In the 60.34% of the patients RBV was included in the treatment. Viral Response at week 4 was 97.28% and 93.75% at the week 12. The post-treatment mortality was 1.3% and no related with the treatment. In the genotype 4 patients all the patients were male. The 50% were ile 288 CT. The 4642% of the patients were pretreated and 76.9% of them were null responders. All the patients had been treated with interferon and ribavirin. The 39.3% of patients had fibrosis 3 and 38.7% fibrosis 4 respectively. The average value of FibroScan was 1240. The average MELD was 101.9. In the 75% of patients Ribavirin was associated with the treatment and in all cases the duration was 12 weeks. The viral response at the end of treatment was 100% and the Viral Response in the week 4 and 12 was 9583% and 9523%. The mortality rate post-treatment was 7.8%. All deceased patients were cirrhotic patient with an average MELD of 20.

Conclusions: The treatment of liver transplant patients with hepatitis C genotype 1 and 4 with Simprevir and sofosbuvir combination is a high effective and safe option in real life. There were no drug-related mortality, and overall mortality was very low in liver transplant patients.

15. Oral Presentation #230

Parallel 35: Hepatitis B: Novel Therapies
Monday, 14 November 2016 – 5:00-5:15

#230: A PHASE 2 STUDY OF TITRATING-DOSE LONAFARNIB PLUS RITONAVIR IN PATIENTS WITH CHRONIC HEPATITIS D: INTERIM RESULTS FROM THE LONAFARNIB WITH RITONAVIR IN HDV-4 (LOWR HDV-4) STUDY

Heiner Wedemeyer1, Kerstin Porti1, Katja Deterding1, Anika Wranke1, Janina Kirschner2, Eduardo B. Martins2, Jeffrey Glenn3, Markus Cornberg1, Michael P. Manns2

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2 Eiger Biopharmaceuticals, Palo Alto, CA
3 Division of Gastroenterology and Hepatology, Stanford University School of Medicine, Palo Alto, CA

Background: Globally 15-20 million people are coinfected with the hepatitis delta (HDV) and hepatitis B (HBV) viruses. Lonafarnib (LNF) is an oral prenylation inhibitor that has been shown to reduce levels of HDV RNA in short-term studies in a dose-dependent manner. Prenylation inhibitors are associated with gastrointestinal (GI) adverse effects (AE) at higher doses (anorexia, nausea, diarrhea, weight loss), but step-wise increase in dose has been shown to be well-tolerated in a pediatric population. Previous data in HDV patients demonstrated that co-administering LNF + ritonavir (RTV), a CYP3A4 inhibitor,
increases the post-absorption levels of LNF with lower GI exposure. LOWR HDV-4 is an open-label, phase 2 dose-titration study of LNF+RTV in patients with HDV to investigate if rapid step-wise increases in LNF dose can allow more patients to achieve higher doses.

**Methods:** Key inclusion criteria: positive HDV RNA by qPCR, ALT <10xULN, compensated liver disease, platelet counts >90,000/μL. All patients were started on LNF/RTV (50mg/100mg bid). If well tolerated, LNF could be increased to 75mg bid after a minimum of 4 weeks, and next to 100mg bid after a minimum of 2 weeks since the last dose escalation. RTV was kept at 100mg bid regardless of the LNF dose. Safety, HDV RNA, HBV DNA, HBsAg and ALT were assessed at each visit. Here we present the interim data at Week 8 of treatment.

**Results:** 15 patients (11 male) were enrolled. At baseline (BL), mean HDV RNA was 6.53 log10IU/ mL (range 4.43-8.31 log10IU/mL); mean ALT 111 IU/mL (range 53-362 IU/mL), mean Fibroscan 14.4 kPa (range 6.324.5 kPa). Two patients were cirrhotic on biopsy. By Week 8, 10/15 (66%) patients were able to be dose-escalated to LNF 100mg bid + RTV, 6 of which still remain at this dose. All patients had HDV RNA declines with a mean decline from BL to Week 8 of 1.87 log10IU/mL (range 0.88-3.13 log10IU/ mL). Three patients had HBV DNA rebound associated with HDV RNA decline, two of which were started on tenofovir. 11 patients were on a nucleos(t)ide (NUC) at BL. AE were mostly grade 1-2 intermittent diarrhea; 3 patients had grade 3 AE (2 diarrhea; 1 asthenia), all transient and non-recurring; none had grade 4 AE.

**Conclusion:** Dose-escalation of LNF+RTV was feasible, and led to early decline in HDV RNA in all patients. HDV RNA decline was associated with a rebound of HBV DNA in patients not receiving a NUC, suggesting a suppressive effect of HDV on HBV replication. These interim data support longer durations of therapy. The Week 24 end of treatment data will be presented.

### 16. Oral Presentation #256

**Viral Hepatitis Plenary**

**Tuesday, 15 November 2016 – 10:15-10:30**

**#256: PAIRED LIVER BIOPSY, FIBROTEST AND FIBROSCAN® BEFORE AND AFTER TREATMENT WITH DAA IN LIVER TRANSPLANTED RECIPIENTS WITH RECURRENT HCV: DIAGNOSTIC ACCURACY AND CORRELATION**

**Maria F. Donato**, **Cristina Rigamonti**, **Federica Invernizzi**, **Giuseppe Colucci**, **Mirella Fraggelli**, **Marco Maggoni**, **Barbara B. Antonelli**, **Sara Monico**, **Giorgio Rossi**, **Massimo Colomba**

1 Division of Gastroenterology and Hepatology, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, University of Milan, Italy
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3 Division of Gastroenterology and Endoscopy, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, University of Milan, Italy
4 Division of Pathology, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, University of Milan, Italy
5 Division of Surgery and Liver Transplant, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy
6 Department of Gastroenterology and Hepatology, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, University of Milan, Italy
7 Division of Pathology, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, University of Milan, Italy
8 Division of Surgery and Liver Transplant, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy
9 Division of Pathology, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy
10 Division of Pathology, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy

**Background:** Non-invasive tools have been shown to reliably predict liver graft fibrosis and have been included in the management of hepatitis C virus (HCV) liver transplanted (LT) recipients Aims: To evaluate the diagnostic performance of Fibrotest (FT) and transient elastography (TE, FibroScan®) in detecting liver fibrosis as well as additional histological features before and after DAA and the role of DAA on graft fibrosis reversibility.

**Methods:** This retrospective study included consecutive HCV-LT recipients who underwent DAA at Maggiore Hospital Policlinico, Milan (Jan 2013 July 2015), with paired liver biopsy (LB), FT and TE before and 6-12 months after DAA. Activity (A) and stage of fibrosis (F) were scored (METAVIR), presence of sinusoidal fibrosis (SF) and steatosis (S) were also recorded. The published 79 and 12 kPa TE cut-off and 048 and 0.74 FT cut-off were applied for F2 and F4 diagnosis, respectively. Changes were categorized as follows: 1 point F increase/decrease; 0.2 increase/decrease of FT value; 30% increase/decrease TE value.

**Results:** 31 patients were included (26 males, median age 56 yr, 65% CyA). SVR was 97%. LB length was 4 cm (range 2-7). Histological features, diagnostic performance of FT and TE before and after DAA treatment are shown in the Table. After DAA treatment A2, F2, F4, S did not change, whereas SF significantly decreased (p=0.0003). F increased in 10%, decreased in 23% and was stable in 68% of patients; TE increased in 13%, decreased in 45%, was stable in 42%. Of patients with a TE decrease, 79% showed decrease/ disappearance of SF at LB vs.29% with stable or increased TE (p=0.001).

**Conclusions:** DAA significantly decreased the extent of sinusoidal fibrosis in LT recipients with recurrent hepatitis.

**Table:** TE showed overall better concordance with histology while both TE and FT properly assessed SF and its changes.

<table>
<thead>
<tr>
<th></th>
<th>Before DAA</th>
<th>After DAA</th>
<th>P.e.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A2</td>
<td>20(74%)</td>
<td>10(39%)</td>
<td>0.05</td>
</tr>
<tr>
<td>F2</td>
<td>12(74%)</td>
<td>20(66%)</td>
<td>0.35</td>
</tr>
<tr>
<td>F4</td>
<td>2(20%)</td>
<td>0(0%)</td>
<td>1</td>
</tr>
<tr>
<td>Sinusoidal F</td>
<td>13(71%)</td>
<td>0(0%)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

**17. Oral Presentation #258**

**Viral Hepatitis Plenary**

**Tuesday, 15 November 2016 – 10:45-11:00**

**#258: A RANDOMIZED PHASE 3 TRIAL OF SOFOBUVIR/VELPATASVIR/ VOXILAPREVIR FOR 8 WEEKS AND SOFOBUVIR/VELPATASVIR FOR 12 WEEKS FOR PATIENTS WITH GENOTYPE 3 HCV INFECTION AND CIRRHOSIS: THE POLARIS-3 STUDY**


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13 Alfred Hospital, Melbourne, VIC, Australia

**Introduction:** Patients with HCV genotype 3 infection, particularly those with cirrhosis, have emerged in the current era of DAA regimens as a more difficult to cure population. Voxilaprevir (VOX, GS-9857) is a pangenotypic inhibitor of the HCV protease. We hypothesized that the addition of VOX to create a fixed dose combination (FDC) targeting 3 distinct viral proteins would allow treatment to be shortened to 8 weeks while maintaining high rates of SVR12. This Phase 3 study evaluates treatment with SOF/VEL/VOX FDC for 8 weeks and SOF/VEL FDC for 12 weeks in patients with genotype 3 HCV infection and
Methods: Patients were randomized 1:1 to receive open-label SOF/VEL (400 mg/100 mg daily) FDC for 12 weeks or SOF/VEL/VOX (400 mg/100 mg/100 mg daily) FDC for 8 weeks. Patients were stratified according to their prior treatment with an interferon-based regimen. Patients had cirrhosis defined by liver biopsy, Fibroscan >12.5 kPa, or combined Fibrotest >0.74 and APRI >2.0. HCV RNA was measured with the CAP/CTM HCV 2.0 assay with LLOQ=15 IU/mL. The primary endpoint compares the sustained virologic response 12 weeks after treatment (SVR12) of each treatment, to a pre-specified historic control rate of 83%. Secondary endpoints included safety and tolerability, viral resistance, and additional efficacy outcomes.

Results: Of 219 patients randomized and treated, 72% were male, 89% were white, 42% had the IL28B CC genotype, and 30% had previously failed treatment with an interferon-based regimen. Patients from the US (44%) and other regions (56%) were well represented. Most (90%) patients with treatment experience had received a Peg-IFN+RBV regimen. All patients had cirrhosis; the median platelet count was 139×10^3 cells/μL with 24% of patients having a platelet count of <100×10^3 cells/μL. Treatment was well tolerated; at the time of abstract submission, one patient had discontinued therapy due to an unrelated adverse event. No serious adverse events attributed to either study medication had been reported. Complete safety and SVR12 data for all patients will be presented.

Conclusions: The single tablet regimen of SOF/VEL/VOX for 8 weeks has the potential to be a safe, well-tolerated and effective treatment option for genotype 3 patients with cirrhosis.

2. Poster Presentation #406

#406: A 48-GENE SIGNATURE IN FORMALIN-FIXED PARAFFIN-EMBEDDED (FFPE) LIVER BIOPSIES ENABLES EARLY PREDICTION OF ADVERSE OUTCOMES IN PATIENTS WITH AUTOIMMUNE HEPATITIS (AIH)
Mu Hao Hsu, Ellina Lytvyak, Jeffrey Tompkins, Aldo J. Montano-Laza, Banu Sis

Background: Patients with AIH might develop cirrhosis despite adequate immune suppression treatment. Clinical and histological variables in AIH cannot reliably predict the risk of cirrhosis development. We recently defined and validated a 48-gene signature for advanced liver fibrosis in microarrays of 140 human livers (96% accuracy). We tested if the 48-multigene signature in FFPE liver biopsies can accurately predict development of cirrhosis in AIH patients.

Methods: FFPE liver needle biopsies from 55 patients with AIH were profiled for expression of 48-genes by NanoString platform. Development of cirrhosis was defined by follow-up biopsies or Fibroscan-value>17.6kPa. Adverse outcome was defined as liver decompensation, requirement of liver transplantation, and/or liver-related death.

Results: Of 55 patients, 18% had cirrhosis at presentation, 22% developed cirrhosis, 35% did not develop cirrhosis, 25% no follow-up biopsy or Fibroscan, and 18% had adverse outcomes. Levels of 48-gene signature were correlated with increased histological Metavir-fibrosis stages (r=0.352, p=0.008), IgG levels (r=0.379, p=0.011), bilirubin (r=0.323, p=0.025), and low albumin (r=-0.311, p=0.045) and platelet counts (r=-0.310, p=0.034). Level of 48-gene signature in biopsies was higher in patients who developed cirrhosis, but histological stages were not different (Figure 1A). The 48-gene signature for predicting development of cirrhosis showed an area under the curve (AUC) of 0.78 (p=0.01), whereas discriminative ability of histology for development of cirrhosis was poor (AUC=0.46, p=0.72). A high 48-gene signature in biopsies was related with increased adverse outcomes (Figure 1B). The 48-fibrosis gene signature significantly improved the accuracy for predicting adverse outcomes from 40% to 80% (Figure 1C).

Conclusions: The 48-gene score in FFPE liver biopsies enables early prediction of development of cirrhosis and provides a personalized risk score for adverse clinical outcomes in patients with AIH.

Table:
Tea and coffee are the most consumed beverages worldwide and share common substances, such as polyphenols and caffeine. Both substances have been proposed to exhibit beneficial effects on liver health. Several studies suggest that coffee prevents liver cirrhosis, but it is unknown if this is also true for fibrosis development in the general population. Therefore, our aim is to study the effect of coffee and tea consumption on liver fibrosis, assessed by transient elastography (TE), in a large well-characterized population study. The Rotterdam Study is an ongoing prospective population-based cohort study, involving healthy inhabitants of a suburb in Rotterdam, the Netherlands. From 2009 onwards, all participants aged 45 underwent TE and completed a validated 389-item food frequency questionnaire. Linear and logistic regression analyses were used to study the association between coffee and tea consumption and liver stiffness measurements (LSM). Clinically relevant fibrosis was defined as LSM > 8.0 kPa and secondary causes of increased LSM were excluded. Coffee and tea consumption were categorized into no, low (<32), or high (>3) intake in cups/day. Tea was further specified into subtypes of green, black and herbal tea (categorized as no or any). Data were available for 2424 participants (age 66.57 ± 4.33% male) of whom 125 had LSM > 8.0 kPa (5.2%). Overall, 93.2% and 84.7% of the individuals consumed coffee and tea, respectively. Proportion of LSM > 8.0 kPa decreased with increasing coffee intake (7.8%, 6.9% and 4.1% for no, low and high coffee consumption resp.; P trend = 0.006). This inverse relation between coffee intake and LSM > 8.0 kPa was confirmed in regression analyses even after adjustment for total energy, age, sex, BMI, insulin resistance, ALT, steatosis, smoking, alcohol, milk and sugar use (ORlow = 0.76 CI 0.37-1.54; ORhigh = 0.40 CI 0.20-0.81; P trend = 0.003). Overall tea consumption was not associated with LSM. Herbal tea consumers (36.3%) had lower liver stiffness in multivariate linear regression (β tea = -0.042 CI -0.069; 0.015, P = 0.003) and less frequently LSM > 8kPa (5.9% vs. 3.9%, no and any consumers resp.; P = 0.035). High coffee consumption appears protective of liver stiffness even in individuals with no known liver disease. Interestingly, in this first study to correlate herbal tea and liver health, herbal tea is independently associated with lower LSM. Unlike coffee, herbal tea does not contain caffeine, which leaves room for thought whether the anti-fibrotic effects can be ascribed to polyphenols. Studies enlightening underlying mechanisms between coffee, herbal tea and LSM are needed to develop preventative and therapeutic strategies for a healthy liver.

4. Poster Presentation #420

420: SERUM WISTERIA FLORIBUNDA AGGLUTININ-POSITIVE MAC-2BINDING PROTEIN LEVEL AS A PREDICTOR OF HEPATIC FIBROSIS IN CHRONIC HBV INFECTION

Pil Soo Sung1, Dong Wook Jekarl2, Jeong Won Jang3, Si Hyun Bae1, Jong Young Choi1, Yanggoo Kim2, Seung Kew Yoon3

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2 Incheon St. Mary's Hospital, Incheon, Korea (the Republic of)
3 Department of Laboratory Medicine, Catholic General Hospital, Seoul St. Mary Hospital, Seoul, Korea (the Republic of)

Background: The Wisteria floribunda agglutinin-positive Mac-2-binding protein (WFA*-M2BP) was recently identified as a hepatic fibrosis biomarker in patients with chronic hepatitis C (CHC) infection, and it has also been shown as a predictive marker in patients with CHC-related hepatocellular carcinoma. In the present study, we investigated the association between WFA*-M2BP levels and liver histological findings for patients with chronic hepatitis B virus (HBV) infection, comparing with transient elastography (FibroScan) measurements or the Enhanced Liver Fibrosis (ELF) score.

Methods: Biopsy proven, 106 chronic hepatitis B (CHB) patients with alanine aminotransferase (ALT) less than 150 were analyzed. We examined the effect of WFA*-M2BP level on severity of liver fibrosis, comparing with transient elastography (FibroScan) measurements and the Enhanced Liver Fibrosis (ELF) score, a serum ECM marker set consisting of tissue inhibitor of metalloproteinases 1 (TIMP-1), aminoterminal propeptide of type III procollagen (PIIINP) and hyaluronic acid (HA). Receiver operating characteristic curve (ROC) analysis was performed for calculating the area under the ROC (AUROC).

Results: The WFA*-M2BP value ranged from 0.2 to 24.2 COI (median value, 0.55 COI). The median values in each Knodell fibrosis stage were: 0.22 COI in A, 0.38 COI in B, 0.62 COI in C, and 0.82 COI in D (P = 0.004). For predicting liver cirrhosis (Knodell fibrosis stage D), WFA*-M2BP level had the AUROC of 0.753. By correlation analysis, serum M2BG level significantly correlated with ELF score (r = 0.176, P = 0.0001) and FibroScan measurements (r = 0.232, P < 0.0001). In the validation cohort, serum WFA*-M2BP levels were significantly higher in chronic hepatitis patients without cirrhosis and even higher in patients with liver cirrhosis than normal controls (P < 0.0001).

Conclusion: Our data suggest that serum WFA*-M2BP value can be useful for predicting liver cirrhosis in patients with chronic hepatitis B infection.

Table:

5. Poster Presentation #557

557: CONTROLLED ATTENUATION PARAMETER (CAP), A PRESUMED MEASURE OF HEPATIC STEATOSIS IN PATIENTS WITH CYSTIC FIBROSIS (CF)

Razan Bader1, Maureen M. Jonas1, Paul D. Mitchell2, Shanna M. Wiggins1, Christine K. Lee2

1 Division of Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital, Boston, MA
2 Clinical Research Center, Boston Children's Hospital, Boston, MA

Background: Hepatic steatosis is a common finding in patients with CF.
and thought to be the earliest manifestation of Cystic Fibrosis related liver disease (CFLD). CAP obtained during transient elastography (TE) has been used to detect and quantify liver steatosis.

**Aim:** To obtain CAP measurements in patients with CF. 2. To examine the relationship between CAP and CFLD. 3. To examine the correlation of CAP with ALT, GGT, BMI, pancreatic insufficiency, use of feeding tubes, presence of CF related diabetes and liver stiffness measurements (LSM).

**Study design:** This is a prospective longitudinal cohort study of patients with CF seen for routine outpatient care at Boston Children’s Hospital enrolled between January 1 and December 30, 2013. CAP measurements were obtained during TE done for another study of CFLD. CAP was obtained at enrollment then yearly for 2 more years. Biochemical and clinical data were obtained from medical records. CFLD was determined based on published criteria.

**Results:** 124 patients (mean age 194 years; 56% male) underwent baseline CAP. 100 (81%) had a second CAP 123 months later. 58 patients (47%) had CFLD. The mean CAP (dB/m) at enrollment was normal and similar in patients with and without CF liver disease (2198 vs 2065, P=0.17). There was no change in mean CAP in the cohort from baseline to first follow up (14 dB/m, P=0.79). CAP did not correlate with any of the examined clinical and biochemical parameters (Table). Ultrasound (US) was obtained in 74/124 subjects; 49 were normal, 12 had abnormal liver echogenicity and 13 demonstrated cirrhosis and portal hypertension (PHN). The mean CAP was higher in patients with abnormal liver echogenicity compared to patients with normal liver US (25659 vs 21244; P=0.005) and patients with cirrhosis and PHN (25659 vs 19642; P=0.007).

**Conclusion:** In patients with CF, CAP were normal and did not correlate with standard clinical and biochemical markers of liver disease. Patients with abnormal echogenicity on US suggestive of steatosis had higher CAP values in this study. CAP may be more useful than blood tests or other clinical parameters to detect early CFLD as manifested by steatosis.

**Table:** Association of CAP scores with patient and clinical factors 230 dB/m is the optimal cut-off value to detect steatosis.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N</th>
<th>CAP&lt;230 dB/m</th>
<th>CAP ≥230 dB/m</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (Age &lt;20y, median IQR)</td>
<td>72</td>
<td>0.09 (-0.13, 0.15)</td>
<td>0.13 (+0.07, 0.12)</td>
<td>0.18</td>
</tr>
<tr>
<td>Crude, n (%)</td>
<td>122</td>
<td>91(11%)</td>
<td>7(17%)</td>
<td>0.36</td>
</tr>
<tr>
<td>GGT (U/L, median IQR)</td>
<td>71</td>
<td>16(11, 29)</td>
<td>12(13, 31)</td>
<td>0.07</td>
</tr>
<tr>
<td>ALT (U/L, median IQR)</td>
<td>124</td>
<td>13(14, 28)</td>
<td>16(15, 33)</td>
<td>0.07</td>
</tr>
<tr>
<td>Pancreatic insufficiency, n (%)</td>
<td>124</td>
<td>57(33%)</td>
<td>61(100%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>134</td>
<td>51(38%)</td>
<td>73(54%)</td>
<td>0.09</td>
</tr>
<tr>
<td>LSM1Pa, median (IQR)</td>
<td>120</td>
<td>5.5 (3.0, 6.7)</td>
<td>5.14 (4.1, 6.6)</td>
<td>0.18</td>
</tr>
</tbody>
</table>

6. Poster Presentation #573

**#573: THE REAL IMPACT OF FATIGUE IN HAEMOCROMATOSIS**

**Aisling Murphy; University Hospital Galway, Galway, Ireland; Department of Hepatology, University Hospital Galway, Galway, Ireland**

**Introduction:** Haemochromatosis is one of the commonest genetically inheritable conditions in Irish people. Fatigue is a common complaint and presenting symptom. Despite this, the level of fatigue experienced by patients with haemochromatosis has never been adequately quantified. Anecdotal experience would suggest that fatigue responds to treatment i.e. venesection.

**Aim:** Our aim was to formally assess the impact of fatigue on patients with Haemochromatosis, by quantifying the severity and where possible identifying contributing factors. Method We performed a prospective observation based cohort study on patients with Haemochromatosis. Baseline demographics were obtained along with laboratory assessment of iron storage in patients attending a dedicated haemochromatosis clinic. Patients were asked to fill in a questionnaire regarding levels of fatigue, physical activity and co-existent symptomatology using widely validated scoring systems.

**Results:** We recruited 169 patients (39% female) attending our outpatient venesection programme and undergoing treatment as per standard protocol, median ferritin values were 83 (range 11-4900). Median Transferrin saturations (TF sats) were 50% (range 11-97%), and median ALT was 22 (range 4-138). Median Fibroscan value was 5.1kPa. The majority of patients complained of fatigue when asked (67.9%). Joint pain was also commonly reported (57.3%). When asked a series of questions to quantify level of fatigue 38.4% of patients had a fatigue severity score >36. Ferritin (r=0.05), TF Sats (r= -0.22) or level of physical activity (r=0.073) showed no correlation with severity of fatigue levels. Concomitant pathology associated with haemochromatosis was generally rare in our cohort; Diabetes was reported in 3.4%, Heart disease in 5.4%. Interestingly 22% of responders described anxiety/depression and 34.2% of patients described memory loss/impairment. Activity levels were surprisingly high with only 28.9% of patients reporting low levels according to their IPAQ score.

**Conclusion:** Fatigue is extraordinarily common in patients with haemochromatosis (over two thirds), even in patients whom have been adequately de-ironed. More surprisingly the severity of fatigue in patients with haemochromatosis was severe in almost 40% comparable to end stage neurological illness such as MS and Parkinsons (i.e. FSS>36). Ferritin or TF sats levels do not appear to correlate with fatigue severity. Alternative aetiologies to fatigue should be considered in these patients; in particular co-existent psychiatric illness/depression.

7. Poster Presentation #596

**#596: HEPATITIS B (HBV) REACTIVATION DURING ANTI-HEPATITIS C (HCV) THERAPY WITH INTERFERON (IFN)-FREE REGIMENS: A PROSPECTIVE STUDY**

**Maria-Carolita Londoño1-2, Sabela Lens1, Zoe Mariño1, Martin S. Bonacci1, Anna Pla2, Concepció Bartres1, Xavier Ariza1, Maria-Vittoria Adriani2, Xavier Forns1-2**

1Liver Unit, Hospital Clinic, Barcelona, Spain
2IDIBAPS, Barcelona, Spain

**Background:** Five cases of HBV reactivation during anti-HCV therapy with IFN-free regimens have been recently reported. However, the magnitude of this problem is currently unknown.

**Aim:** To determine the incidence of HBV reactivation during anti-HCV therapy with IFN-free regimens.

**Methods:** All patients who started IFN-free antiviral therapy against HCV between September 2015 and May 2016 were enrolled in this single center, prospective and observational study. Before therapy, HBsAg and anti-HBc were determined. In patients with positivity of any of these markers, HBV-DNA and ALT were monitored at baseline, week 4 of therapy, end of treatment (EOT) and 12 weeks after treatment discontinuation (FU12). Virological HBV reactivation was defined as an increase of 1log10 in HBV-DNA. Clinical HBV reactivation was defined as an increase in ALT levels 3 times compared to baseline.

**Results:** 35 patients were enrolled, 53% were male with a mean age of 60 years (20-84). Most of the patients were infected with genotype 1b (70%), 1.5% were on dialysis, and 6.5% and 2.5% had a previous liver or kidney transplant, respectively. Mean liver stiffness measurement at baseline was 155 kPa (3-75); 44% of the patients had cirrhosis. Most of the patients received antiviral treatment with 3D/2D regimen (n=173, 49%) or Sofosbuvir/Ledipasvir (n=143, 41%). At baseline, 5 (1%) and 65 (19%) patients were HBsAg or anti-HBc positive, respectively. Three HBsAg positive patients (60%) and one (15%) anti-
HBc positive patient presented virological reactivation at week 4 of therapy but no HBV clinical reactivations were observed throughout the duration of therapy. HBV-DNA levels spontaneously decreased 1 log10 at the end of therapy in all but one HBsAg positive patients and returned to baseline in 2 patients (Table 1).

**Conclusion:** HBV virological reactivation is common in HBsAg positive patients receiving anti-HCV therapy with an IFN-free regimen, but unlikely in those whose only marker is anti-HBc. HBV-DNA should be frequently monitored in HBsAg positive patients.

**Table:** Characteristics of patients with HBV virological reactivation

<table>
<thead>
<tr>
<th>Positive HBV reactivation</th>
<th>HBV status</th>
<th>Borderline HBV-DNA (IU/mL)</th>
<th>Week 4 HBV-DNA (IU/mL)</th>
<th>E0P HBV-DNA (IU/mL)</th>
<th>ALT and HBV reactivation (IU/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 HBSAg</td>
<td>Non reactive</td>
<td>335</td>
<td>19790</td>
<td>345</td>
<td>51</td>
</tr>
<tr>
<td>2 HBSAg</td>
<td>Undetectable</td>
<td>3640</td>
<td>2726</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>3 HBSAg</td>
<td>Undetectable</td>
<td>74</td>
<td>669</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>4 Anti-HBc</td>
<td>Undetectable</td>
<td>&lt;15</td>
<td>669</td>
<td>31</td>
<td></td>
</tr>
</tbody>
</table>

8. Poster Presentation #653

**#653: EVOLUTIONARY CYSTIC FIBROSIS-RELATED LIVER DISEASE ASSESSED BY ELASTOMETRY**

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**Objectives and Study:** Cystic Fibrosis Related Liver Disease (CFRLD) slowly progress to fibrosis and cirrhosis in about 10 to 15% of patients. Liver biopsy cannot be repeated, and data from non-invasive markers of this evolution are lacking. The aim of this study is to evaluate CFRLD progression with repeated elastometry.

**Methods:** We studied 86 CF children, 49 boys and 37 girls, median age 69 years, with at least 2 elastometry measurements with Fibroscan® at a minimum of 2-year interval. CFRLD was diagnosed according to classical criteria (hepatomegaly, increased ALT, hyperechoenecity on US examination).

**Results:** Median initial elastometry value was 3.7 kPa (IQR: 1.3) and final elastometry value was 4.8 kPa (IQR: 2.23). Mean increase of elastometry was 0.24 kPa/year (7%/year). Children developed CFRLD during the study period. Increased initial ALT value was the only factor found to be predictive of developing CFRLD (p=0.0001). Increased initial ALT value was correlated with the evolution slope of elastometry (r=0.38; p=0.0005). Percentage of increase of elastometry was higher in children developing CFRLD compared to who remained without CFRLD (94% vs 23%; p=0.002). Genotype, pancreatic insufficiency, severity of lung disease had no influence on evolution of elastometry.

**Conclusion:** Elastometry measured by Fibroscan® slowly worsens in CF children. An elevated ALT value and a rapid increase of elastometry value are predictive of a progression to CFRLD.

9. Poster Presentation #655

**#655: ELIFT, A NEW FRIENDLY-USER AND ‘AT-A-GLANCE’ FIBROSIS TEST, COMBINED WITH FIBROMETRELCVE IN A SIMPLE ALGORITHM ALLOWS FOR THE WIDESPREAD DETECTION OF LIVER FIBROSIS IN THE LARGE POPULATION OF PATIENTS WITH CHRONIC LIVER DISEASES**

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**Introduction:** Chronic liver diseases (CLD) are highly frequent but silent for a long time. Thus, most of the patients with CLD are not referred to hepatologists but managed by non-specialized physicians who have no access to liver elastometry or best blood fibrosis tests. We aimed to develop and validate a simple stepwise algorithm for the detection of liver fibrosis in all patients with CLD.

**Methods:** Data from 9 studies about non-invasive tests of liver fibrosis were pooled in a cross-sectional population. A longitudinal cohort retrospectively included all patients with compensated liver disease (bilirubin <30 μmol/l and prothrombin time 70%) who had a non-invasive evaluation of liver fibrosis in Angers centre between 01/2005 and 12/2009.

**Results:** 3754 patients with liver biopsy were included in the cross-sectional population and 2:1 randomly divided into derivation and validation sets. First-line ‘simple’ test: FIB4 was significantly more accurate than APRI but impaired by 82% false positive result for significant fibrosis in patients 60 years old. The Easy Liver Fibrosis Test (eLIFT), a new user-friendly test including age, sex, gammaGT, AST, platelets and prothrombin time was developed in the derivation set. eLIFT is the sum of points attributed to its composite variables (example: 4 points if prothrombin time <84%). In the validation set, there was no significant difference in accuracy between eLIFT and FIB4 but, importantly, eLIFT was not influenced by age. Second line ‘diagnostic’ test: blood fibrosis tests, Fibroscan, and FibroMeter®Cte (FMsc) were all available in 1946 patients. FMsc was the most among the 8 fibrosis tests evaluated.eLIFT (first-line) and FMsc (second-line if positive eLIFT) were combined in a stepwise algorithm which categorized patients in 4 subgroups: ‘no/mild fibrosis’, ‘undetermined diagnosis’, ‘significant fibrosis’, ‘cirrhosis’. Using this algorithm in the validation set, the diagnosis was ‘no/mild fibrosis in 46.4% of patients with thus no need for a referral to a specialised hepatologist. Finally, 79.7% patients were well classified, sensitivity was good for significant fibrosis (76.1%) and excellent for cirrhosis (92.1%). The longitudinal cohort included 1275 patients. Liver-related survival was excellent in patients diagnosed as ‘no/mild fibrosis by the algorithm, with significant difference compared to the 3 other subgroups.

**Conclusions:** The new user-friendly and ‘at-a-glance’ eLIFT helps to extend the diagnosis of liver fibrosis to all patients with CLD. Used with the FibroMeter®Cte in a stepwise algorithm, it will allow to regulate the flow of patients between primary care and specialized centers.

10. Poster Presentation #656

**#656: EARLY REGRESSION OF LIVER FIBROSIS IN HCV INFECTED PATIENTS WITH OR WITHOUT HIV INFECTION AFTER TREATMENT WITH DAAS**

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2 Scientific Direction, Clinical Epidemiology Unit, IRCCSSanMatteoFoundation, Pavia, Italy, Pavia, Italy

**Introduction:** A sustained virological response (SVR) in HCV infected patients is associated with an improvement of liver-related morbidity and mortality. Moreover, several studies suggested a progressive regression in liver fibrosis (LF) over time after HCV eradication. In a group of HCV infected patients treated with direct antiviral agents (DAAs)
we evaluated changes in liver fibrosis at SVR24 to assess if an early LF improvement could be evidenced. Patients with or without early regression of LF were compared.

Methods: All patients treated with DAAs in our Center and achieving SVR, with at least 24 weeks of follow-up after completion of treatment, were included. Clinical, virological and biochemical data were collected. LF was determined by means of surrogate biomarkers (FIB-4 and APRI) and by liver stiffness (LS) performed at baseline and at SVR24. Patients were divided into two groups: early regressors (ER) and non regressors (NR). ER were considered all subjects who achieved an improvement 30% in LS compared with baseline.

Results: 84 subjects were eligible for the analysis, 31 (36.9%) HIV-HCV co-infected patients and 53 (63.1%) HCV mono-infected. Cirrhosis was found in 65 patients (77.3%), 44 (83%) HCV and 21 (67.7%) HIV-HCV positive patients, respectively. All cirrhotic patients had a compensated liver disease. 30 HIV-HCV patients were on antiretroviral therapy (ART) and had an undetectable HIV viral load. An overall improvement of LS (median baseline LS 15.5 kPa vs 10.8 kPa at SVR24; p=0.0002), Fib-4 (median baseline Fib-4 3.02 vs 191 at SVR24; p<0.0001) and APRI (median baseline APRI 125 vs 0.41 at SVR24; p<0.0001) were observed as shown in the following figure. An early regression was found in 40 (47.6%) subjects. ER and NR were compared. HIV-HCV patients were more likely to be non regressors (p=0.09) compared to HCV monoinfected patients. ER showed an higher liver stiffness at baseline compared with NR (p=0.02). No other clinical differences between the two groups were observed.

Conclusion: An early improvement of APRI, Fib-4 and LS were observed at SVR24. The greater improvement of LS in patients with higher baseline fibrosis could be explained as a result of a rapid reduction of liver inflammation. HIV-HCV patients seem to be more likely NR.

Figure:

11. Poster Presentation #657

#657: DEFINING LIVER STIFFNESS MEASUREMENT CUT-OFFS TO PREDICT MORTALITY AND COMPLICATIONS IN PATIENTS WITH CIRRHOSIS OF MIXED ETIOLOGY

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Background Liver stiffness measurement (LSM) using transient elastography can predict hepatic complications, including decompensation and HCC. Most studies to date have been performed in viral hepatitis at all stages. Limited data exist in relation to predicting mortality in patients with cirrhosis of mixed etiologies.

Aim To determine the utility of LSM to predict mortality and complications in patients with compensated cirrhosis of mixed etiologies.

Methods 408 patients were identified with a baseline LSM 12 kPa between 2008 and 2014, without hepatic decompensation at a large UK teaching hospital. Retrospective analysis of the case notes, radiology and endoscopy reports was undertaken. Survival analysis was performed with Cox regression to ascertain the association between LSM and death and a composite endpoint including the development of ascites, variceal bleeding, hepatic encephalopathy, liver transplantation and death. A binary regression analysis was used to generate a model to predict outcomes.

Results 408 patients (63% male, median age 53.5 years) had advanced fibrosis or cirrhosis due to alcohol (ALD) (24%), fatty liver disease (18%), HBV (11%), HCV (37%), and other/unknown diagnoses (11%). The median follow up was 26 months (max 83.6) and the overall proportion who died within 1, 2 and 3 years was 3%, 6% and 10% respectively. 3 year mortality (3YM) was significantly higher in those with ALD compared to other diagnoses (24% v 3.7%, p<0.001). Median LSM was higher in those that died (27 v 20 kPa, p<0.001). Mortality increased with increasing LSM cut-offs. At 3 years the proportion of patients who died was 3%, 15%, 17% and 22% patients with baseline LSM <20 kPa, 20 kPa, 30 kPa and 40 kPa respectively (p<0.004). LSM and ALD were independent predictors of mortality. At 3 years, adjusted hazard ratios were 2.87 (95% CI 1.24–6.62) for ALD v non-ALD and 3.62 (95% CI 1.27–9.81) for LSM 20 kPa v <20 kPa. A regression model including LSM and diagnosis (ALD vs non ALD) predicted 3YM (AUROC 0.74). LSM 20 kPa had a sensitivity of 83% and positive predictive value of 11% for 3YM, increasing to 20% in ALD patients. Age and LSM predicted the composite endpoint at 3 years (AUROC 0.76), for which LSM <20 kPa had a negative predictive value of 99%. ALD was not an independent predictor of this endpoint.

Conclusions LSM and ALD were independent predictors of mortality in this large cohort of patients with cirrhosis. We propose 20 kPa as a clinically useful cut-off as patients with LSM 20 kPa are at risk of death at 3 years and could be candidates for enhanced surveillance/intervention, whereas LSM <20 kPa is associated with a low risk of complications and death.

12. Poster Presentation #661

#661: DIAGNOSTIC VALUE OF TRANSIENT ELASTOGRAPHY FOR DETECTION OF HEPATIC FIBROSIS IN LIVER TRANSPLANT RECIPIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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2 Gastroenterology/Hepatology, University of Tennessee Health Science Center, Memphis, TN
3 Transplant Hepatology, University of Miami Miller School of Medicine, Miami, FL
4 Surgery, Methodist University Hospital Transplant Institute, Memphis, TN
5 Surgery, University Of Tennessee Health Sciences Center, Memphis, TN

Background Several studies have reported diagnostic accuracy of TE to assess fibrosis in orthotopic liver transplant (OLT) recipients. We conducted a systematic review and meta-analysis to evaluate the cumulative accuracy of TE in comparison to liver biopsy for detection of hepatic fibrosis in OLT recipients.

Methods We searched Medline, Embase, Cochrane databases, ISI Web of Science and Scopus from inception to 10/25/15 to identify studies assessing the diagnostic performance of TE to detect fibrosis after OLT. Fibrosis was defined as stage F2 (METAVIR and Scheuer scoring systems) and stage S3 ( Ishak scoring system). Sensitivity, specificity, positive predictive (PPV) and negative predictive values (NPV) of TE were pooled using random effects model. Meta-regression analysis was done to explore heterogeneity. Publication bias was assessed by Egger’s test.

Results A total of 9 studies with 853 patients were included in the analysis. Two studies provided separate data for diagnostic performance of TE in non-hepatitis C (HCV) related fibrosis in OLT recipients. Therefore, a total of 11 studies were pooled in the meta-analysis. The pooled sensitivity with 95% CI was 82% (77%, 87%) (I2=68%). Publication bias was detected by Egger’s test (P=0.05). The trim and fill test recalculated the sensitivity as 80% (74%, 85%). On metaregression
analysis, TE had better sensitivity for recurrent HCV fibrosis (P=0.03). Different cut-off values for liver stiffness in studies also accounted for significant heterogeneity (P=0.003). The pooled specificity was 84% (78%, 89%) (I2=73%), Egger’s test detected publication bias and the recalculated specificity was 83% (77%, 88%). The pooled PPV was 78% (69%, 85%) (I2=84%). No publication bias detected (P=0.006). Only Scheuer scoring system was associated with higher specificity and higher PPV (P=0.03). The pooled NPV was 85% (75%, 91%) (I2=88%). No publication bias was found (P=0.08). Only different cut-off value of liver stiffness accounted for heterogeneity (P=0.03).

Conclusion: TE appears to be a valuable first line, non-invasive modality for assessing fibrosis (Stage≥F2) in OLT recipients.

### Table:

<table>
<thead>
<tr>
<th>Stage</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
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<tr>
<td>F1</td>
<td>0.78</td>
<td>0.89</td>
<td>0.62</td>
<td>0.78</td>
</tr>
<tr>
<td>F2</td>
<td>0.91</td>
<td>0.86</td>
<td>0.73</td>
<td>0.91</td>
</tr>
<tr>
<td>F3</td>
<td>0.96</td>
<td>0.96</td>
<td>0.95</td>
<td>0.96</td>
</tr>
<tr>
<td>F4</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
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</tbody>
</table>

14. Poster Presentation #664

#664: POINT SHEAR WAVE ELASTOGRAPHY HAS HIGH DIAGNOSTIC ACCURACY FOR STAGING OF LIVER FIBROSIS IN PATIENTS WITH CHRONIC HEPATITIS B OR C INFECTION

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2 Gastroenterology and Hepatology, Victor Babes University Timisoara, Timisoara, Romania

Background and aim: Non-invasive evaluation of liver fibrosis is important in determination of prognosis and treatment strategy in patients with chronic hepatitis B (HBV) and C (HCV) virus infection. Vibration controlled transient elastography (TE) is a well-established method for assessment of liver stiffness (LS) and staging of liver fibrosis. Point shear wave elastography (pSWE) is a novel technique that measures the speed of an acoustic wave through the liver to determine LS. This method is integrated in an ultrasound device and could therefore result in more accurate assessment of liver fibrosis due to real time imaging. The aim of this study was to determine diagnostic performance of pSWE for staging of liver fibrosis in patients with chronic HBV and HCV infection.

Methods: In this international multicenter study, patients with chronic HBV and/or HCV infection underwent TE and pSWE LS measurement. TE was performed with Fibroscan® (Echosens, Paris, France) and pSWE was performed with ElastPQ®, which is implemented in the EPIQ 7 ultrasound system (Philips Medical Systems, Bothel, USA). Successful TE was defined as 10 successful measurements with an interquartile range of >30% of the median. A minimum of 10 successful pSWE measurements was required. TE cut off points for significant fibrosis (>F2), advanced fibrosis (>F3) and cirrhosis (>F4) were 7.0, 9.5 and 14.5 kiloPascal (kPa). Diagnostic accuracy of pSWE was assessed by calculating the area under the receiver operating characteristic curve (AUROC), using TE as a reference.

Results: For 265 patients both a successful TE and pSWE measurement were available. The majority was female (54%), mean age was 53 years and 67% of patients had chronic HCV infection. Median (IQR) LS assessed by TE and pSWE was 10.7 (5.6-21.2) kPa and 7.5 (4.6-17.3) kPa. There was a significant linear correlation (r: 0.86, P< 0.001) between TE and pSWE measurements and the linear regression of the Bland and Altman plot was non-significant (p=0.19), proving similar performance. The AUROC (95% confidence interval (CI)) was 0.94 (0.91-0.96) for >F2, 0.96 (0.94-0.98) for >F3 and 0.96 (0.94-0.98) for >F4. Sensitivity and specificity (95% CI) for pSWE were 90.1% (84.494.2) and 76.9% (67.6-84.6) for a cutoff point of 5.39 kPa for >F2, 93.6% (88.2-97) and 86.3% (79.9-118) for a cutoff point of 6.39 kPa for >F3, and 95.3% (89.3-98.5) and 85.5% (79.1-90.6) for a cutoff point of 8.63 kPa for >F4, respectively.

Conclusion: pSWE performed by the novel elastPQ® method has high diagnostic accuracy for staging of liver fibrosis in patients with chronic HBV and HCV infection.

15. Poster Presentation #752

#752: EARLY DECREASE OF LIVER STIFFNESS AFTER INITIATION OF ANTIVIRAL THERAPY IN PATIENTS WITH CHRONIC HEPATITIS C

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Liver elastography is widely used to assess liver fibrosis in patients with chronic hepatitis C and has also been recommended to monitor regression of liver fibrosis after successful antiviral therapy. We studied
early changes of liver stiffness after initiation of antiviral treatment. The study population comprised 53 patients with chronic hepatitis C (mean age SD: 49±10.7 years; METAVIR fibrosis stage F2, n=23; F3, n=12; F4, n=18; genotype (GT) 1, n=32; GT3, n=17; GT4, n=4; mean BMI SD: 25±3.8). All patients were treated with interferon-free all oral regimens. Prior to therapy and 1-6 weeks after initiation of antiviral treatment fibrosis stage was assessed by transient elastography using the Fibroscan® 502 Touch device with the M-probe (Echosens, Paris, France) and classified according to the METAVIR scoring system. Cut-off values for liver stiffness were defined as 7.1 kPa for F2, 9.5 kPa for F3 and 12.5 kPa for F4 [4]. Mean liver stiffness at baseline was 14.69±11.15 kPa and decreased to 12.41 983 kPa at follow-up Fibroscan® performed between week 1 and week 6 (p<0.006). When the same Fibroscan® cutoff values applied at baseline were applied after initiation of antiviral therapy the following results were obtained: Within 6 weeks after initiation of treatment fibrosis stage improved by at least one stage in 23/53 (43%) patients, remained stable in 28/53 (53%) and worsened in 2/53 (4%). From the 23 patients classified as F2 at baseline, 11 (48%) were classified as F0/F1 at week 1–6, 10 (43%) as F2, and 2 (9%) as F3. From the 12 patients classified as F3 at baseline, 3 (25%) were classified as F0/F1 at week 1–6, 4 (33%) as F2, and 5 (42%) as F3. From the 18 patients with F4 at baseline, 1 (6%) was classified as F0/F1 at week 1–6, 2 (11%) as F2, 2 (11%) as F3 and 13 (72%) as F4. Decrease of liver stiffness did not correlate with baseline AST (r=0.28) or ALT (r=0.04) levels. In our study a marked decrease of liver stiffness was observed within two weeks after initiation of antiviral therapy. From a pathophysiological point of view a clinically significant decrease of liver fibrosis within such a short period of time seems impossible. We therefore assume, that the decrease is caused by resolution of the inflammatory activity within the liver. Current cut-off values for assessment of fibrosis stage in patients with chronic hepatitis C by transient elastography were obtained in patients with fibrosis and active inflammation. Therefore, our data clearly indicate that lower cut-off values for liver stiffness are appropriate for monitoring liver fibrosis after initiation of antiviral therapy.

16. Poster Presentation #776

#776: THE PREDICTION OF HEPATOCELLULAR CARCINOMA DEVELOPMENT AND OVERALL SURVIVAL IN CHRONIC HEPATITIS C USING LIVER STIFFNESS MEASUREMENT: A LONG-TERM OUTCOME STUDY

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Background and Aims: To evaluate the utility of liver stiffness measurement for the prediction of hepatocellular carcinoma (HCC) development and survival in chronic hepatitis C patients.

Method: We enrolled 1,130 patients in whom liver stiffness was measured using FibroScan® at the authors’ hospital from December 2004 to December 2015. We excluded patients who had already achieved sustained virological response (SVR) at the initial liver stiffness measurement. We assessed HCC development and overall survival based on liver stiffness using Kaplan-Meier method.

Results: The patients consists of 493 males and 637 females with median age of 64. Liver stiffness at the enrollment was 5 kPa in 235, 5.1–10 kPa in 454, 10.1–15 kPa in 190, 15.1–20 kPa in 96, 20.1–25 kPa in 57, and >25 kPa in 98, respectively. During the mean follow-up period of 6.6 years, HCC developed in 191 patients. The cumulative incidence rates of HCC at 1, 2, 3, 5, 7, and 10 years were 1.9%, 4.9%, 7.4%, 12.1%, 17.3%, and 233%, respectively. Cumulative HCC incidence rates at 5 years were 1.7% in those with 5 kPa, 3.3% in 5.1–10 kPa, 16.4% in 10.1–15 kPa, 25.4% in 15.1–20 kPa, 38.4% in 20.1–25 kPa, and 43.2% in >25 kPa, respectively (P<0.001). During the study period, 101 patients died. The cause of death was liver cancer in 30, liver failure in 17, gastrointestinal bleeding in 7, and others in 47. Overall survival rates at 1, 2, 3, 5, 7, and 10 years were 99.9%, 99.5%, 98.8%, 96.8%, 93.0%, and 86.7%, respectively. Ten-year survival rates were 99.3% in those with <5 kPa, 95.7% in 5.1–10 kPa, 81.7% in 10.1–15 kPa, 80.9% in 15.1–20 kPa, 64.5% in 20.1–25 kPa, and 483% in >25 kPa, respectively (P<0.001). Conclusions: Liver stiffness can predict long-term outcomes over 5 years in chronic hepatitis C patients.

17. Poster Presentation #781

#781: PROJECT IITREAT (INTEGRATED COMMUNITY BASED TEST – STAGE-TREAT) HCV SERVICE FOR PEOPLE WHO INJECT DRUGS (PWID)

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Objective/Aims: Majority (90%) of HCV positive individuals in England are people who inject drugs (PWID) with poor engagement with health services. Our ongoing study assesses feasibility of non-invasive detection, staging and treatment of HCV.

Methods: Four-year prospective study (Dec 2013–Nov 2017) conducted at a large substance misuse service in SE England. Individuals offered dry blood spot testing (DBST), mobile transient elastography (TE), HCV treatment (including DAA) and qualitative interviews with recent addition of patient reported outcomes (SF-12v2, SFLDQOL) and health economics (EQ-5D-5L).

Results: To date, 391 individuals recruited, 81% males with mean age of 400 yrs (sd 98). There was high prevalence of injecting drug use (IDU) [274 (70%), alcohol use [336 (86%)] and psychiatric illness [174 (45%)].

Uptake of DBST was 49% (n=190); prior testing being the main reason for declining. Prevalence of positive serological markers/PCR were: HbAcAB 20% (n=71), HCV antibody 53% (n=200), HCV PCR 82% (163/200); genotypes 1=71 (44%) and 3= 79 (48%).

Onlogistic regression, independent predictors of a positive HCV serology were if ever injected (OR 85, 95% CI 42-174); positive HbAcAB (OR 35 95% CI 19-66) and a psychiatric diagnosis (OR 2.1, 95% CI 13-35). Of those with a positive HCV PCR (n=163), 132 (81%) underwent TE (mean LSM kPa 99 (sd 10.3), 59 (36%) having LSM > 7.5 kPa, 32 (20%) having cirrhosis (LSM >12 kPa). There was a significant association between a positive HCV serology and LSM >75 kPa: 72% of those with LSM>75 were positive compared to 98% with LSM > 7.5 (p<0.001). None had had prior HCV treatment. Forty-eight (29%) were not treatment candidates (chaotic lifestyle). Of the remaining (n=115), 50 commenced treatment.

Characteristics of treated cohort were: age 45 yrs (sd 102), 92% male, > 80% having substance/alcohol use, 86% undergoing TE; genotypes (1 = 41%, 3= (55%), treatment received: INF/ RBV 32%, INF+DAA=38% and DAA 30% and treatment outcomes were: 35 (70%) SVR/EOTR, nine (18%) on-going treatment, six (12%) NR (included four RR). Twentytwo had pre-treatment questionnaires done.

Conclusions: Prevalence of positive HCV serological markers remain high in PWID, which might explain the almost 40% prevalence of significant hepatic fibrosis. Compliance in this difficult to engage cohort was ~ 90% with HCV treatment outcomes comparable to secondary care. Our ongoing prospective study endorses the success of this novel, easy to replicate “one-stop” community based HCV treatment model with onsite mobile TE.
#784: DIVERGENCY OF LIVER AND SPLEEN STIFFNESS DYNAMICS 24 WEEKS AFTER END OF INTERFERON-FREE TREATMENT IN PATIENTS WITH HEPATITIS C VIRUS (HCV)-ASSOCIATED CIRRHOSIS AND SUSTAINED VIROLOGIC RESPONSE

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Background: Regression of cirrhosis and portal hypertension (PT) is a major goal in treatment of patients with hepatitis C virus (HCV) associated cirrhosis. Improvement of Child-PughTurcotte (CPT) and model of end stage liver disease (MELD) scores were consistently observed in current trials investigating direct antiviral agents (DAA)-based treatment in HCV associated cirrhosis. However, persistence of PT has been reported despite sustained virologic response (SVR) and improvement in CTP/MELD-scores. In the current study, we prospectively evaluated dynamics of liver and spleen stiffness in patients with HCV associated cirrhosis and SVR after DAA-based antiviral treatment.

Methods: A total of 54 patients (69% male) with HCV associated cirrhosis and SVR after DAA-based antiviral treatment were included. Liver and spleen stiffness was assessed at baseline (BL), end of treatment (EOT), and 24 weeks after EOT (FU24) by transient elastography of the liver (LTE) as well as acoustic radiation force impulse (ARFI) of the liver (L-ARFI) and spleen (S-ARFI). Biochemical, virological and clinical data were obtained in parallel.

Results: There was a significant reduction of liver stiffness between BL [median (range), 32.5 (91-75) kPa] and EOT [median (range), 213 (67-735) kPa; p<0.0001] as well as between BL and FU24 [median (range), 212 (54-70) kPa; p<0.0001] by LTE. Liver stiffness assessed by L-ARFI significantly decreased between BL [median (range), 2.7 (12-41) m/s] and FU24 [median (range), 2.4 (12-39) m/s; p=0.002], while spleen stiffness assessed by S-ARFI did not decrease significantly between BL, EOT and FU24. Improvement of liver stiffness was more pronounced between BL and EOT than between EOT and FU24. In addition, a significant improvement of MELD-score between BL [median (range), 9 (6-17)] and FU24 [median (range), 8 (6-18)] was observed (p=0.011).

Conclusion: Liver, but not spleen elastography improved significantly in patients with HCV associated cirrhosis and SVR after DAA-based antiviral therapy. As this effect was mainly associated with the first 12-24 weeks of treatment, it must be discussed to which amount improvement of liver stiffness was associated with decrease of hepatic necroinflammation or regression of fibrosis and portal hypertension. Studies investigating only dynamics of CTP and MELD-score or liver stiffness may overestimate the degree of putative regression of cirrhosis.

#791: ESTIMATION OF LIVER FIBROSIS BY THE USE OF NON-COMMERCIAL SERUM SCORES IN COMPARISON TO TRANSIENT ELASTOGRAPHY IN HCV PATIENTS RECEIVING DIRECT ACTING ANTIVIRAL TREATMENT

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Background: Liver stiffness measurement (LSM) using Fibroscan and serum Wisteria floribunda agglutinin-positive Mac-2 binding protein (M2BPGi) were novel, noninvasive, and reliable technique to assess the degree of liver fibrosis, transient and portal hypertension. Studies investigating only dynamics of CTP and MELD-score or liver stiffness may overestimate the degree of putative regression of cirrhosis.

#795: ASSOCIATION BETWEEN LIVER FIBROSIS MEASUREMENT AND SERUM WISTERIA FLORIBUNDA AGGLUTININ-POSITIVE MAC-2 BINDING PROTEIN AMONG JAPANESE PATIENTS WITH HEPATITIS B, C AND NAFLD/NASH

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Background: As optimal management of chronic liver disease depends on the degree of liver fibrosis, accurate, but non-invasive evaluation of liver fibrosis is of importance. Though liver stiffness measurement (LSM) using Fibroscan and serum Wisteria floribunda agglutinin-positive Mac-2 binding protein (M2BPGi) were novel, noninvasive, and reliable technique to assess the degree of liver fibrosis, trans- etiological comparison between two parameters has not yet been available in the literature. The aims of this study were to assess the correlation between LSM and serum M2BPGi levels among Japanese patients with hepatitis B, C and NAFLD.

Methods: A total of 1,347 patients who underwent LSM between...
21. Poster Presentation #796

#796: ASSOCIATION OF LOW-DENSITY LIPOPROTEIN CHOLESTEROL WITH SPONTANEOUS CLEARANCE IN HCV-INFECTED PATIENTS

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Background: Host, viral and environmental interactions play a major role in the clinical outcomes of HCV infection. Spontaneous clearance (SC) may be associated with immunological mechanisms, as well as genetic and metabolic factors related with serum lipids. Therefore, Apolipoprotein E (ApoE) isoforms interacting with low-density lipoprotein cholesterol (LDL-c) could alter the course of the disease.

Aim: To analyze the anthropometric, metabolic and lipid alterations of SC patients and the association of ApoE alleles and LDL-c with SC.

Methods: Totally, 299 treatment-naïve, anti-HCV positive patients were included. Patients were classified in chronic hepatitis (CH) (n=206) who had at least two detectable viral loads (VL), and SC (n=93) after two undetectable VL in the last 12 months. A clinical record was elaborated for all participants. Body mass index (BMI) was evaluated by electric bioimpedance (InBody 3D). Biochemical tests were accessed by dry chemistry assay. VL was determined by COBAS® TaqMan 48 HCV test. Liver damage was evaluated by transitional elastography, and ApoE genotypes were identified by TaqMan Real-Time PCR.

Results: No statistical differences were detected in age, gender, and risk factors for HCV infection between groups. However, BMI was higher in SC than CH, predominating more CH patients with normal weight than SC (366% vs. 195% p=0.007). Total cholesterol (CHol) and hypercholesterolemia (>200 mg/dL) was higher in SC than CH patients (184.1 43.3 mg/dL vs. 148.1 43.3 mg/dL, p<0.001 and 32.6% vs. 9.8% p<0.001, respectively). No significant differences were detected in insulin resistance and type 2 diabetes between CH and SC groups (55.4% vs. 43.5% p=0.072 14.1% vs. 7.8% p=0.183, respectively). Liver damage was detected (37.5%, 18/48) in SC patients despite the low levels of ALT and AST (below 50 IU/mL each). The ApoECom allele frequency was significantly higher in the SC patients compared to CH group (p=0.042). Also, in the e4 allele subgroup, total CHol and LDL-c values were higher in patients with SC compared to CH patients (193 42 mg/dL and 125.2 35 mg/dL vs. 160.5 45 mg/dL and 1019 42.4 mg/dL, respectively). LDL-c, e4 allele and BMI were associated with SC (OR=0.20, 95% CI 0.10-0.41, p<0.001 OR=0.55, 95% CI 0.31-0.987, p=0.042 OR=0.37, 95% CI 0.18-0.76, p=0.007), whereas ALT was associated as a risk factor for CH (OR=5.67, 95% CI 2.69-11.97, p<0.001).

Conclusions: LDL-c, e4 allele, and BMI were independent factors for SC. Cholesterol and LDL-c levels modulated by genetics or dietary factors may influence the natural history and long-term outcome of HCV infection.

22. Poster Presentation #803

#803: DIRECT ACTING ANTI-VIRAL (DAA) THERAPY FOR CHRONIC HEPATITIS C VIRUS (HCV) INFECTION IS ASSOCIATED WITH REGRESSION OF LIVER FIBROSIS, ASSESSED BY SERIAL TRANSIENT ELASTOGRAPHY (FIBROSCAN)

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Background: Liver fibrosis stage determines clinical outcomes from chronic HCV infection. Those who achieved sustained virologic response (SVR) with interferon-based therapies had regression of fibrosis over time. This study aimed to assess the effect of HCV DAA therapy on changes in liver fibrosis, using transient elastography (Fibroscan).

Methods: Patients being treated with DAA therapy for chronic HCV were enrolled in this prospective cohort study. We performed pretreatment-baseline Fibroscans, then repeat scans at end of treatment (EOT) and 12 months post-treatment. The primary outcome was significant improvement in liver fibrosis (>30% decrease in Fibroscan score 12 months after treatment), relative to baseline. Multivariable logistic regression analysis was used to control for confounding. Signed rank test was used to assess change in liver stiffness measurement (LSM) between time points.

Results: Of the 47 patients who have completed the protocol, 27 (57%) had significant baseline liver fibrosis (LSM >7.3 kPa), and 27 (57%) were treatment-experienced. SVR rate was 95.7%. The primary outcome of >30% improvement in LSM was met in 24 (51.1%) patients. The 2 relapsers did not reach this outcome. Of those with baseline Metavir stage F3 (LSM >8.5 kPa), 9/23 (39.1%) improved to <8 kPa (cutoffs from reference 1). Baseline LSM >7.3 kPa was associated with reaching the primary outcome, and remained significant after controlling for BMI and elevated ALT (OR=88.95% CI 1.9-372). In this subgroup (baseline LSM >7.3 kPa), median intra-patient change in LSM between pre-treatment and 12 months post-treatment was -4.5 kPa (IQR -7.1, -20 P<0.0001).

Conclusions: Treatment of chronic HCV with DAs leads to clinically relevant reduction in liver fibrosis over the first year post-treatment,
measured by Fibroscan, even after controlling for BMI and elevated ALT. This outcome was more likely in those with baseline significant liver fibrosis, with some experiencing improved Metavir fibrosis stage.

Figure:

### 23. Poster Presentation  #805

**#805: IS THERE ANY PLACE FOR NON-INVASIVE MARKERS OF FIBROSIS PREDICTING THE DEVELOPMENT OF COMPLICATIONS IN PATIENTS WITH CHILD-PUGH A POST HEPATITIS C CIRRHOSIS (ANRS CO12 CIRVIR PROSPECTIVE COHORT)?**

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There are no specific marker predicting the development of any complication in patients with Child-Pugh A post hepatitis C cirrhosis, sustained virological response excepted. The aim of the study was to analyze the place of surrogate markers of fibrosis in a French national multicenter prospective cohort of HCV-infected patients with biopsy-proven cirrhosis (ANRS CO12 CIRVIR) included in 35 centers in order to predict the development of complications especially HCC. This study was a case control study ratio (1/4), the main events were collected on a 36 month period and were HCC, ascites, digestive hemorrhage, Actitest-Fibrotest, Fibrometer 3G, performed independently in one lab, and fibroscan were analyzed every 6 months between months 0 to 36. Our multivariate analysis took into account confounding factors, matching and changes in markers with time (conditional logistic regression and mixed-effects model). We included 136 cases (74/136 had HCC) and 270 controls (cirrhotic patient without any liver related events). In all groups mean age was 58±10 years, 65% were males. The 2 groups were comparable for comorbidities (diabetes, kidney failure, HA, dyslipidemia) and all viral factors, except for SVR (66.8% vs 29.1%, p <0.001), and lab data (bilirubin, gammaGT, platelets, TP). Results were systematically adjusted on SVR. From D0 onwards, a significant difference between cases and controls was systematically found for the mean marker scores and persisted between D0 and M36: Fibrotest: 0.720.18 vs 0.840.10 Fibrometer 3G (fibrosis: 0.720.13 vs 0.940.06, 0.850.13 vs 0.940.06) and FibroScan: 17.011.2 vs 22.512.8 (p<0.0001).

This significant difference was found in SVR patients except for Fibroscan. The kinetics between D0 and M36 showed few clinically relevant changes, thus multivariate exploration of the predictive value of the tests was carried out for D0. After adjusting for SVR, all markers remained associated with the occurrence of a complication. To conclude, all surrogates markers of fibrosis are able to early predict the occurrence of complications especially HCC in patients with post hepatitis C cirrhosis. Markers kinetic do not give any additional information. We hereby propose to monitor more accurately patients with high initial values, threshold remaining to be determined.

### 24. Poster Presentation  #806

**#806: FLOW MEDIATED DILATION MAY BE AN INDIRECT MEASURE OF LIVER STIFFNESS IN HCV GENOTYPE 1 RELATED CHRONIC HEPATITIS**

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**Introduction:** Brachial Flow Mediated Dilation (FMD) is a well-known non-invasive method to assess endothelial function. In chronic liver disease, endothelial function was shown impaired suggesting a significant correlation among liver damage, sinusoidal endothelial function and liver stiffness.

**Aim and Methods:** To investigate the relationship between endothelial function and liver stiffness we performed a cross-sectional study including 100 consecutive HCV Genotype 1 patients who underwent a complete clinical and laboratory screening for HCV infection. Liver stiffness was assessed by transient-elastography (TE). FMD and Carotid Intima-Media Thickness (c-IMT) were evaluated by 2-d ultrasound. Mean age was 62±12.5 years and 41.8% were woman. Based on TE score and according to liver fibrosis (Metavir score) patients were grouped as follows: F0:14%; F1:19%; F2:10%; F3:20%; F4:37%.

**Results:** Results show a significant inverse linear correlation between FMD and TE until the value of 20kPa of stiffness (p<0.001). For TE higher than 20kPa the correlation shown not significant although the tendency of FMD enhancement was of note. In the whole population with Spearman test, FMD was inversely correlated with TE (p<0.001), age (p=0.002), male sex (p=0.002), GGT (p=0.035), low PLT (p=0.001), APRI (p<0.001), c-IMT (p=0.003) and directly with unconjugated bilirubin (p=0.014). At the multivariate regression analysis only TE (p<0.001), c-IMT (p=0.003) were inversely, and unconjugated bilirubin (p=0.031) directly, associated with FMD. Further sub analysis was conducted in patients with TE>20kPa (n=30) and <20kPa (n=70). In patients with TE=20 kPa at the multivariate analysis only unconjugated bilirubin (p=0.031) and low albumin (p=0.012) were directly correlated with FMD. While in the group with TE<20 kPa the only independent factors inversely associated with FMD were TE (p=0.017) and c-IMT (p=0.001).

**Conclusion:** In conclusion an impaired FMD is significantly associated to a worst TE in chronic HCV related hepatitis. In patients with sickest disease, the liver failure, surprisingly, seems to be associated with a reconstituted endothelial function.

### 25. Poster Presentation  #813

**#813: COMPARING APRI AND FIBROSCAN SCORE FOR PRE-TREATMENT ASSESSMENT OF HCV-RELATED LIVER DISEASE IN COMMUNITY SETTINGS**

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**Background** Fibrosis assessment prior to hepatitis C (HCV) treatment is recommended, however access to elastography is limited by resources in many settings, even in high-income countries. This study aims to assess whether routine blood tests can be used to triage need for non-invasive fibrosis assessment in a community-based cohort of people who inject drugs (PWID).

**Methods:** The HCV Treatment And Prevention (TAP) Study examines the feasibility of community-based HCV treatment for PWID using oral sofosbuvir/ledipasvir /ribavirin in Melbourne. Haematological, biochemical and fibrosis assessment using transient elastography (FibroScan™) were performed at screening. The AST:Platelet Ratio Index
(APRI) was calculated and compared with valid FibroScan scores (10 readings >60% success; <30% IQR/median) at screening. Cirrhosis (Ishak F4) was defined as FibroScan score ≥12.5 kPa. Negative (NPV) and positive predictive values (PPV) were calculated for predicting cirrhosis at high (2D) and low (1D) APRI.

Results: Of participants screened to date, APRI was calculable in 114/118, and valid FibroScan was available among 99/114. Participants were 67% male, median age 37 years (IQR 33−44 years), with median body mass index 23.1 (IQR 20.9−26.4). Median APRI was 0.54 (IQR 0.29−0.98). Median FibroScan score was 5.6 kPa (IQR 45−68 kPa); 7% and 12% had liver stiffness ≥12.5 kPa and ≥95 kPa, respectively. Two individuals had discrepant APRI<10 and FibroScan>125 kPa: either both were male, aged 32 and 35 years old, with BMI 27.5 and 22.5, and ALT 74 U/L and 70 U/L, respectively. Using an APRI cut-off of 10, NPV for cirrhosis was 96% (70;73; 95% CI 89−99%), and PPV was 19% (5;26%). Using an APRI cut off of 20, NPV for cirrhosis was 94% (88/94) and PPV was 40% (2/5).

Conclusions: A low APRI score (<1.0) may be an acceptable community screening test to exclude cirrhosis where FibroScan is unavailable. Use of APRI may facilitate treatment initiation in such settings. APRI thresholds >1.0 should not be used to diagnose cirrhosis.

26. Poster Presentation #815

#815: NON-INVASIVE ASSESSMENT OF LIVER FIBROSIS AND CIRRHOSIS REGRESSION IN CHRONIC HEPATITIS C PATIENTS TREATED WITH PAN-ORAL DIRECT-ACTING ANTIVIRALS

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Background and Aim: In the era of direct-acting antivirals (DAAs), sustained virological response (SVR) rates in patients with chronic hepatitis C (CHC) are remarkably increased. However, whether DAAs therapies can improve liver histology is still largely unknown. We aim to evaluate the impact of DAA therapies on liver fibrosis and cirrhosis non-invasively by liver stiffness measurement (LSM).

Methods: One hundred and seventy-five Chinese patients with genotype 1 CHC were included in this study, which were treated with pan-oral DAAs for 12 weeks (Group 1), including ledipasvir (90 mg)/sofosbuvir (400 mg) (n=123), daclatasvir (60 mg)/sofosbuvir (400 mg) (n=50) and paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) plus dasabuvir (250 mg) (n=2). Fifty-five age and gender matched patients treated with long-term pegylated interferon (PEG-IFN) based therapies (median treatment duration: 60 weeks) were enrolled as the control group (Group 2). The median follow-up duration for Group 1 and 2 were 44 weeks and 46 weeks respectively. LSM was measured at baseline, the end-of-treatment and the end of follow-up by transient elastography (TE). Advanced liver fibrosis or cirrhosis (F3) is defined by LSM>9.5 kPa.

Results: One hundred and seventy-two patients in Group 1 (172/175, 98.3%) achieved SVR at the end of follow-up, which was significantly higher than that of Group 2 (42/55, 76.4%) (p<0.001). Median LSM decreased significantly from baseline to the end-of-treatment in both groups (Group 1: 12.5 vs. 10.6 kPa, p<0.001, Group 2: 15.2 vs. 12.1 kPa, p<0.001). Median LSM also decreased significantly during the follow-up in Group 1 (10.6 vs. 8.7 kPa, p<0.001), but not in Group 2 (12.1 vs. 13.2 kPa, p=0.378). The median LSM reduction from the baseline to the end of follow-up in Group 1 was 1.8 kPa, which was equivalent to the median LSM reduction in Group 2 (2.4 kPa, p=0.08). In Group 1, there were 105 (60.0%) patients had advanced liver fibrosis or cirrhosis (F3) at baseline, which significantly reduced to 54.3% (95/175, p=0.001) at the end-of-treatment and further significantly reduced to 46.3% (81/175, p<0.001) at the end of follow-up. Similarly, patients with advanced fibrosis and cirrhosis at baseline in Group 2 (41/55, 74.5%) were also significantly reduced to 61.8% (34/55, p<0.001) after PEG-IFN treatment, but there is no significant change from the end-of-treatment to the end of follow-up (65.4%, p=0.378).

Conclusion: Liver fibrosis and cirrhosis significantly regressed during the treatment and follow-up of DAA therapies in genotype 1 CHC patients. The impacts of 12-week DAAs therapies on liver stiffness were equivalent to long-term PEG-IFN treatment.

27. Poster Presentation #816

#816: NEW BLOOD TEST MULTI-TARGETED FOR LIVER FIBROSIS OUTPERFORMS ALL OTHER BLOOD TESTS AND EVEN ELASTOGRAPHY IN CHRONIC LIVER DISEASES

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Fibrosis blood test construction is classically limited to a unique diagnostic target: significant fibrosis. Yet, these single-target tests are commonly used for other diagnostic targets like cirrhosis. Therefore, our aim was to improve the accuracy of non-invasive fibrosis staging by targeting biomarkers for all diagnostic targets using a new statistical method.

Methods: 2589 patients were included: 1012 with chronic hepatitis C (CHC) in a derivation population and 1577 in 5 validation populations of different etiologies (CHC, chronic hepatitis B, HIV/CHC, NAFLD, alcoholic liver disease) using Metavir fibrosis stages (F) by liver biopsy as reference. FibroMeter biomarkers were statistically combined against as many fibrosis targets as made possible by Metavir staging. Several statistical functions were successively used to provide a unique score ranging from 0 to 1 as in classical fibrosis scores. This new score was called multi-target FibroMeter (MFM) classification. Accuracy was evaluated primarily by the Obuchowski index discriminating all Metavir stages and secondarily by AUROC for binary diagnostic targets and by correct classification rates in fibrosis classifications (into 6 fibrosis classes from F0/1 to F4).

Results: In the derivation CHC population, the Obuchowski index (0.853) and AUROC for cirrhosis (0.929) of MFM were significantly superior to those of single-target (F2) FibroMeter (0.843 and 0.907, respectively, p<0.001). MFM classification was more accurate (29.3%) than FibroMeter classification (87.6%, p<0.001). In the CHC validation population (641 patients), the Obuchowski index and AUROC for cirrhosis of MFM were significantly superior to those of all other single-target classical blood tests: FibroMeter (0.863), CirrhosMeter (0.907), APRI, Fib4, Fibrotest, Hepascence and Zeng score. MFM was also globally superior to untargeted Fibroscan according to the Obuchowski index: 0.797 vs 0.766, respectively, but this was not significant (p=0.178).

Similarly, their AUROCs for cirrhosis were not significantly different, MFM: 0.880, Fibroscan: 0.897, p=0.090. MFM classification remained more accurate (88.0%) than FibroMeter classification (83.6%, p<0.001). Most of these results were confirmed in other etiologies.

Conclusion: Multi-targeting biomarkers improves the accuracy of non-invasive fibrosis staging in a highly significant manner compared to
classical single-target blood tests, matching liver elastography even for cirrhosis diagnosis.

28. Poster Presentation  #822

#822: REGRESSION OF LIVER FIBROSIS STAGE IN CHRONIC HEPATITIS C INFECTED PATIENTS AFTER ACHIEVING SUSTAINED ViroLOGIC RESPONSE USING DIRECT-ACTING ANTIvIRALS AS DEMONSTRATED BY ELASTOGRAPHY

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Background: Cirrhosis due to HCV infection has been associated with increased risk for hepatocellular carcinoma. The aim of our study was to assess changes in liver transient elastography (TE) and fibrosis-4 (FIB-4) score in patients with chronic hepatitis C (CHC) who achieved sustained virologic response (SVR).

Methods: Our retrospective prospective study included 60 patients with CHC and a baseline liver biopsy who achieved SVR after treatment with DAA regimens and had a pretreatment TE study and at least one follow-up TE measurement at 24 weeks or later post end of treatment response (EOTR). The estimated stage of liver fibrosis based on TE was categorized as F0-F2 (<9.4 Kpa), or F3 (9.5 – 12.4 Kpa), or F4/cirrhotics (TE >12.5 Kpa).

Results: Median age was 62 y/o, 56% were male, and the median BMI was 26.8 kg/m2. The median baseline TE for the entire cohort was 119 Kpa (range 38 to 652) and at follow up, TE decreased to 73.5 Kpa (range 29 to 348) with a median change in TE of -3.4 Kpa (range -353 to +1, p=7.35E-11). At baseline, 45% of the entire cohort were cirrhotic (78% Childs-Pugh A) with median TE of 163 Kpa and FIB-4 of 485. Follow up median TE done in the cirrhotic population after median time of 39 weeks post EOTR decreased to 117 Kpa and FIB4 was 23. The median change of TE in cirrhotic patients was -65 Kpa (range -353 to +1, p=1.04E-7) and for FIB4 was -1.97 (range -17.47 to -0.33, p=1.49E-8). Non-cirrhotic patients (TE<12A) comprised 55% of the entire cohort and their median change of TE was -2.4 Kpa (range -6.4 to 0.7, p=1.53E-6) and FIB4 was -0.68 (range -2.8 to 0.41, p=2.98E-6).48% of the entire cohort down-staged their liver fibrosis as determined by TE. In the cirrhotic group, 59% of the patients had a drop in their stage of liver fibrosis (F4 to F0-2), F3 to F3 (5/27 patients) and there was no correlation in Childs-Pugh Score and failure to achieve improvement in fibrosis stage. 82% of patients that were baseline F3 had a drop in their stage of liver fibrosis (F3 to F0-2). In a multiple logistic regression analysis for factors associated with down-staging in liver fibrosis, we found that patients who were treatment naïve were more likely to improve their fibrosis stage (OR 5.73, p=0.033).

Conclusion: Liver fibrosis stage, as determined by TE, improved after achieving SVR with DAA treatments in most patients. The significant drop in TE measurement post SVR was also correlated with a significant drop in FIB4. Although cirrhotic patients had a more significant drop in their median TE when compared to non-cirrhotic patients, they had a lower probability of improving their fibrosis stage.

29. Poster Presentation  #865

#865: LONG-TERM CLINICAL OUTCOMES IN HCV GENOTYPE 1-INFECTED PATIENTS RECEIVING OMBITASVIR/PARITAPREVIR/RITONAVIR AND DASABUVIR ± RIBAVIRIN: FIRST INTERIM SAFETY AND EFFICACY RESULTS FROM TOPAZ-I

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Introduction: In phase 3 trials, the 3 direct-acting antiviral (3-DAA) regimen of ombitasvir/paritaprevir/ritonavir (paritaprevir identified by AbbVie and Enanta) and dasabuvir ribavirin (RBV) achieved high sustained virologic (SVR) rates with a favorable safety profile in >2300 HCV patients, including those with compensated cirrhosis. TOPAZ-I evaluates the impact of SVR12 on long-term progression of liver disease over 5 years’ post-treatment (PT) follow-up in patients with chronic HCV GT1 infection receiving 3-DAA RBV.

Methods: TOPAZ-I is an on-going phase 3b, international, multicenter, open label study which enrolled HCV GT1-infected treatment-naïve or interferon-experienced patients without cirrhosis or with compensated cirrhosis across 187 centers in 27 countries. Patients were to receive 3-DAA RBV for 12 or 24 weeks, based on subtype and cirrhosis status, as consistent with the approved local labels. First interim results include SVR12 (HCV RNA < LLOQ 12 weeks PT), safety and clinical outcomes. Change in liver fibrosis from baseline was evaluated by FibroScan®.

Results: 1564 patients received study drug (50% male 97% White, 15% compensated cirrhosis). 79% (1228/1564) of patients reached SVR12 time point. ITT SVR12 was achieved in 97% (1190/1228) of patients who reached PTW12 95% and 97% in patients with and without cirrhosis, respectively. In patients who achieved SVR12, mean FibroScan® scores improved over time, with greatest improvements seen in patients with cirrhosis (mean Kpa change from baseline to PTW12: F0-F1 = -0.55, F2 = -1.64, F3 = -2.75, F4 = -6.45). In total, 66% (1024/1564) patients experienced an AE, with fatigue (18%), headache (17%), nausea (11%), pruritus (11%), and insomnia (11%) occurring in >10% of patients. The majority of AEs were mild/moderate in severity, 37 (2%) patients experienced serious AEs, 6 (0.4%) patients discontinued study drug due to AEs. Grade 3-4 laboratory abnormalities were rare. Clinical outcomes are reported in the table.

Conclusion: Data from this large study confirm the efficacy and safety results observed in registraotional trials of 3-DAA RBV in HCV GT1-infected patients. Preliminary data show a beneficial impact on liver fibrosis clinical outcomes were infrequent. Updated safety, efficacy and clinical outcomes will be presented.

30. Poster Presentation  #883

#883: 8 WEEKS TREATMENT UNDER REAL LIFE CONDITIONS WITH LEDIPASVIR/SOFOSBUVIR IN HIV CO-INFECTED TREATMENT-NAÏVE HCV GENOTYPE 1 PATIENTS DEMONSTRATES SIMILAR RESULTS TO MONO-INFECTED HCV PATIENTS: DATA FROM THE GERMAN HEPATITIS C-REGISTRY (DHC-R)

Peter Buggisch1, Klaus H. Boeker2, Rainer Günther3, Gerlinde Teuber4
Introduction: 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. Although the number of patients eligible for 8 weeks according to the summary of product characteristics (SmPC) is high, a large proportion of patients still receives a longer treatment duration. One of the reasons might be the uncertainty whether 8 weeks treatment duration is sufficient in harder to cure populations as HIV co-infected patients, patients on opioid substitution treatment (OST) or older patients (> 70 yrs.). Aim of this analysis was to evaluate the virologic response rates of 8 wks treatment under real world conditions in these patients. Methods: The German Hepatitis C registry is a national multicenter cohort. Patients are treated at the discretion of the physician. Data are collected by a web-based data system and confirmed by plausibility checks and on site monitoring. In this analysis data of patients with 8 or 12 wks treatment with LDV/SOF and available SVR12 data (data cut 2/2016) were included. Baseline characteristics, prior treatment history, safety and effectiveness were investigated. Results: 831 (433 female) pts were treated for 8 weeks. The mean (SD) age was 50.2 (12.9) yrs. In 37% the fibrosis stage was evaluated by elastography (Fibroscan®), the mean (SD) stiffness value was 6.5 kPa (2.4). 674 pts reached the SVR 12 time point and were included in the analysis. Genotype distribution was 99.1% for GT1 and 0.9% for GT4. Baseline viral load was > 6 Mio IU/mL in 2.7%, 8.6% were treatment experienced and 2.5% had liver cirrhosis and were treated for 8 weeks despite these characteristics. The overall SVR 12 rate was 93% (ITT) and 98% (PP). 59 (8.8%) pts had HIV co-infection. SVR 12 in this group was 93.2% (ITT) and 96.6% (PP), only 2 viral relapses occurred. 72 pts received OST, only 1 pt developed viral relapse. 5 pts discontinued therapy and 5 were lost to follow up, thus, SVR12 was 84.7% (ITT) and 98.6% (PP) compared to 94.5% (ITT) and 97.9% (PP) without OST. 48 pts were >70 yrs. with SVR12 rates of 95.8% (ITT) and 97.9% (PP). 65 pts who were pretreated achieved SVR12 rates of 90.8% (ITT) and 95.2% (PP).

Conclusions: Under real world conditions, 8 wks LDV/SOF achieves very high SVR rates in heterogeneous groups like HIV co-infected pts and in other so called harder to cure populations.

#31. Poster Presentation  #900

#900: DACLATASVIR PLUS SOFOSBUVIR PLUS RIBAVIRIN IN HCV GENOTYPE 3 INFECTED PATIENTS WITH CIRRHOSIS CHILD A: A RANDOMIZED TRIAL FOR 16 OR 24 WEEKS

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Background: HCV genotype 3 is still the challenging genotype. With current standard therapy the relapse rates are still considered high, particularly in patients with cirrhosis. The combination of Daclatasvir and Sofosbuvir with or without Ribavirin for 12 or 16 weeks have shown slightly improved SVR rates and lower relapse rates using weight-based dosing of Ribavirin. The goal of our study is to explore the efficacy of 16 weeks versus 24 weeks of Daclatasvir/Sofosbuvir/Ribavirin in cirrhotic patients with HCV genotype 3, and to explore the importance of the initial Ribavirin dosing.

Methods: 49 subjects were screened into the study. 39 were randomized into two arms (16 weeks versus 24 weeks) in 1:1 ratio using IVRS. Baseline demographics and viral parameters were similar in both arms. The mean age was 55.4 7 years; 22 males 21 non-Hispanics. 28 patients were treatment naive and 11 patients were experienced to Peg/ RBV therapy. Cirrhosis was confirmed in all patients by Fibroscan.

Results: 39 patients were randomized into the study, and 32 patients completed the course of therapy. 7 patients are still on treatment. 100% of the patients who completed treatment achieved EOT viral negativity. In the 16-week group, SVR12 was 91% with only one patient relapse. This patient had over 90% adherence to the medication regimen and was receiving 1200 mg/ day Ribavirin. SVR12 in the 24-week group was 100% in the patients who finished the study (17/17). Ribavirin dose started at 800 mg/day in 25 patients and 1000-1200 mg/day in 14 patients. Three patients in each group required a decrease in their Ribavirin dose due to anemia. The starting dose of Ribavirin did not impact the SVR12.

Conclusion: The combination of Daclatasvir/Sofosbuvir/ Ribavirin is recommended for HCV genotype 3 patients. In cirrhotic patients our study shows:

1) 16-week treatment achieved 91.6% SVR12 with only one relapse
2) 24-week treatment achieved 100% SVR12
3) there was no significant difference in SVR between the two arms
4) 800 mg/day of Ribavirin achieved the same viral response as weight-based Ribavirin
5) 16and 24-week treatment was well tolerated in patients with cirrhosis.

32. Poster Presentation  #904

#904: SAFETY AND EFFICACY OF IFNFREE ANTIVIRAL THERAPIES IN ADVANCED HCVASSOCIATED LIVER CIRRHOSIS: RESULTS FROM THE GERMAN HEPATITIS C-REGISTRY (DHC-R)

Katja Deterding, Joerg Petersen, Hartwig H. Klinker, Karl-Georg Simon, Klaus H. Boeker, Eckart Schott, Tim Zimmermann, Markus Cornberg, Rainer Günther, Heike Pfeiffer-Vornkahl, Christoph Sarrazin, Michael P. Manns, Dietrich Hueppe, Heiner Wedemeyer, Thomas Berg, German Hepatitis C-Registry

Introduction: Direct-acting antiviral (DAA) regimes improved the efficacy of chronic HCV treatment. Phase 3 trials suggested lower response rates in patients with liver cirrhosis. However, there is limited information on the efficacy of DAA therapies in interferon-ineligible patients with advanced cirrhosis. To what extent liver function improves in cirrhotic patients receiving interferon-free therapies is unknown.

Methods: The DHC-R (Deutsches Hepatitis C-Register, German Hepatitis C-Registry) is a national multicenter real-world cohort including approx. 9,300 patients. Patients are treated at the discretion of a physician. Data are collected by a web-based system. Data quality is analyzed by plausibility checks and on site monitoring. This data analysis is based on 6,034 patients who were observed for at least
Results: 763 patients had advanced liver cirrhosis (median MELD-Score 9 range 6-32), 632 patients with FU week 12 were included. The majority of patients was infected with HCV-genotype 1 (n=592) HCV-genotypes 2, 3, 4 and 6 were present in 17, 124, 28 and 1 patient, respectively. Patients received different treatment regimens. Overall, SVR was achieved in 88.0% of the patients (ITT). SVR rates according to the regimen ranged from 66 to 100%. DAA therapy lead to SVR rates (ITI) of 91.1%, 80.0%, 72.7% and 82.6% for HCVgenotype 1 (n=460), 2 (n =12), 3 (n=64) and 4 (n=19), 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 88,000/µl at baseline to 111,000/µl during follow-up (p<0.05). Creatinine levels were stable during antiviral treatment. SAEs were reported in 8.1% and 6 patients died during the observation period.

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.

33. Poster Presentation #920

#920: REDUCTION OF LIVER STIFFNESS BY DIRECT-ACTING ANTIVIRALS FOR CHRONIC HEPATITIS C

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Background and Aim: Liver stiffness (LS) by transient elastography (TE) and velocity of shear wave (Vs) by acoustic radiation force impulse (ARFI) have been reported to correlate with fibrosis stages in various liver diseases. The aim of the present study was to evaluate the effect of direct-acting antivirals (DAAs) on LS and Vs in chronic hepatitis C (CHC).

Methods: LS (kPa) and Vs (m/s) were measured in 582 patients with CHC. The changes of LS and Vs were assessed in 300 patients treated with DAAs. 125 patients were treated with daclatasvir (DCV) and asunaprevir (ASV), 115 with sofosbuvir (SOF) and ledipasvir (LDV) for HCV genotype 1, and 60 with SOF and ribavirin (RBV) for genotype 2.

Results: DCV/ASV, SOF/LDV, SOF/RBV treatments achieved high rates of sustained virologic response (SVR) (89, 95, 97%, respectively). LS significantly decreased and Vs did not significantly decrease at end of treatment (EOT) (100, p=0.0005 1.76, p=0.011), and Vs significantly decreased at 6 months after EOT (103, p<0.0001 1.69, p<0.0001) and at 12 months after EOT (123, p=0.0034 1.98, p=0.0062), compared with baseline (12.7, 1.86) in patients with DCV/ASV. LS decreased in tendency (102, p=0.081) but Vs did not significantly decrease (1.62) at EOT compared with baseline (12.0, 1.60) in patients with SOF/ LDV. LS significantly decreased (100, p=0.0097) but Vs did not significantly decrease (1.75) at 6 months after EOT compared with baseline (111, 163) in patients with SOF/RBV. Fibrosis stages were deduced from Vs values according to cut-off values for fibrosis stages in patients with DCV/ASV. The cutoff values determined by ROC analysis were 1.28 for F2, 1.44 for F3, and 1.73 for F4 in 108 patients who underwent liver biopsy. Two points or greater reduction of deduced stage was observed in 19% of patients with DCV/ASV, whose pretreatment deduced stages were F3-F4. Higher platelets counts, lower total bilirubin levels, and lower gamma globulin levels were significantly associated with a 2-point or greater reduction of deduced fibrosis stage. LS and Vs at baseline did not predict SVR in each treatment.

Conclusions: The reduction of LS was observed in patients with DAAs, and can be attributed to regression of liver fibrosis and inflammation. The reduction of Vs was slower than that of LS. This finding may be attributed to the stronger association of LS with inflammation compared with that of Vs. The significant reduction of deduced fibrosis stage was observed in those with milder fibrosis which was indicated by higher platelets counts, lower total bilirubin levels and gamma globulin levels. TE and ARFI were useful for evaluating the effect of DAAs in CHC.

34. Poster Presentation #921

#921: FOUR WEEKS OF SOFOSBUVIR, LEDIPASVIR AND RIBAVIRIN WITH OR WITHOUT INTERFERON GIVE HIGH CURE RATES IN DRUG USERS WITH HEPATITIS C A RANDOMIZED CONTROLLED TRIAL (4WIDUC)

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Background and aims: People who inject drugs (PWID) are the driving force of chronic hepatitis C (CHC) in the western world, but treatment uptake has been low in Direct acting antivirals (DAA’s) cures more than 90% of patients. Outreach treatment programs at drug treatment centers (DTC’s) are feasible but shorter treatment duration is desirable. Four week DAA trials have been disappointing so far. We hypothesise that maintaining ribavirin (RBV) in a 4 week DAA regimen and adding pegylated-interferon 2 alpha (PEG 2a) could give high cure rates in drug users.

Methods: The study was conducted at one DTC. Thirty two patients were randomized 1:1 to either LDV/SOF+RBV or LDV/SOF+PEG 2a for 4 weeks. RBV was dosed weight based and PEG 2a at 180 µg weekly. Main inclusion criteria: Treatment naive patient with CHC (all genotypes), in opium substitution therapy (OST) p< 50 years, weight≥100 kg, viral load<2mill IU/ml and liver stiffness measure (LSM)< 8 kPa. Subjects were allowed any kind of concomitant drug or alcohol use but should be compliant to their OST program. Primary endpoint was sustained virologic response at week 12 after end of treatment (SVR 12) in the intention to treat (ITT) population.

Results: Forty seven persons were screened, and 32 initiated treatment. At date of submission SVR 12 in the ITT population was 92% (12/13) in the interferon arm and 77% (10/13) in the interferon free arm. One virologic relapse was detected. The remaining three failures were due to lost to follow-up or premature withdrawal from therapy. The PP SVR12 is so far 100% in the interferon arm and 91% in the interferon free arm. Full SVR 12 data will be presented at the meeting.

Conclusions: 4 weeks of sofosbuvir, ledipasvir and ribavirin with or without interferon was highly effective in curing CHC in this hard to reach but easy to treat population of non-cirrhotic drug users on OST with only one virologic relapse detected in a PP patient. Delivering treatment at a DTC concurrently with OST was feasible and the SVR rates suggest this short regimen to be evaluated in larger trials.
#36: Poster Presentation #926

**#926: DIRECT-ACTING ANTI-VIRAL THERAPY OUTCOMES IN CANADIAN CHRONIC HEPATITIS C TELEMEDICINE PATIENTS**

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**Background:** There are approximately 245,000 HCV-infected Canadians, many of whom live in under-served and remote areas without access to HCV healthcare specialists. Telemedicine (TM) can provide healthcare to these marginalized patients. We compared patient characteristics and direct-acting antiviral (DAA) treatment outcomes in HCV TM and non-TM patients (The Ottawa Hospital Viral Hepatitis Outpatient Clinic) residing in Eastern Ontario.

**Methods:** A cohort database analysis was performed on 1258 patients followed at The Ottawa Hospital and Regional Viral Hepatitis Program between January 2012 and May 2016. TM (n=148) and non-TM (n=1110) patients were compared by examining baseline characteristics and clinical outcomes.

**Results:** TM patients were younger (49.8 vs 52.4 years), more likely to be Indigenous (7.4% vs 25%), to have injection drug (69% vs 55%) and incarceration (46% vs 35%) histories, and more likely to be genotype 3 infected (27% vs 17%). Groups were comparable in gender (65% male) and cirrhotic stage (23%). 62% of TM patients underwent transient elastography assessment during regional outreach Fibroscan blitzes compared to 60% of our non-TM patients. 24 TM and 214 non-TM HCV-infected patients have completed DAA therapy. Ledipasvir-sofosbuvir+/ribavirin was the most frequently prescribed DAA regimen (79% of TM and 57% of non-TM patients, p=0.15). The SVR rate in the TM group was 95% and 91% in the non-TM group (p=0.059).

**Conclusion:** Our TM program successfully engages and retains a remote population enriched for characteristics associated with barriers to successful HCV treatment. TM patients were able to engage in HCV care, achieving high SVR rates comparable to those obtained by traditional models of care.

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**#35: Poster Presentation #924**

**#924: SOFOSBUVIR/LEDIPASVIR PLUS RIBAVIRIN ACHIEVES HIGH SVR12 IN GENOTYPE-3 PATIENTS WITH COMPENSATED CIRRHOSIS AND SIMILAR TO SOFOSBUVIR PLUS DACLATASVIR. A MULTICENTRE REAL LIFE COHORT**

Mar Rivero-Bariela, Sonia Alonso, Inmaculada Fernandez, Diego Rincón, Yolanda Real, Javier Crespo, Francisco Góa, Antonio Olveira, Jose L. Colleja, Benjamin Pol Lorday, Jose Antonio Carrion, Juan Arenas, Maria Jose Devesa, Carme Bailies, Angeles Castro, Manuel Romero-Gomez, Rafael Granados, Juan Manuel Pascasio, Martin Prieto, Javier Salmeron, Ester Badia, Jose M. Moreno, Xavier Forns, Juan Turnes, Jose Luis Montero, Rafael Esteban, Conrado M. Fernandez-Rodriguez

**Background and aims:** Current antiviral therapy for HCV genotype(GT) 3-associated cirrhosis achieves suboptimal sustained virological response (SVR) rates. Daclatasvir (DCV) + Sofosbuvir (SOF) ribavirin (RBV) is the only all-oral recommended option due to lower SVR rates of SOF/LDV in patients with cirrhosis. We aimed to evaluate the efficacy and safety of 12 and 24-week SOF+DCV or SOF/LDV RBV in a real-life cohort of GT3 patients with cirrhosis.

**Patients and methods:** Multicenter observational study from two different databases: HepaC-AEEH and Community of Madrid Regional registry. All HCV-cirrhotic patients mono-infected by GT 3 and treated with SOF plus a NSSA inhibitor (DCV or LDV) RBV between May 2014 and October 2015 were included.

**Results:** 282 patients were included: 83% male, age 54 years (26-82), 124 (44%) treatment-experienced, 48 (17%) decompensated, 130 (46%) FibroScan >20 kPa and 65 (23%) MELD score>10.195 (69%) received SOF+DCV and 87 (31%) SOF/LDV. Overall, 88% received RBV. The addition of RBV and extension to 24 weeks were higher in the SOF/LDV group (95% vs. 84%, p =0.004 83% vs. 62%, p<0.001). A higher percentage of decompensated patients were treated with DCV (21% vs. 10%, p=0.029). 208 patients have reached week 12 of follow-up. Overall SVR12 was 93.8% (195/208), 94% with SOF+DCV and 93.5% with SOF/LDV. SVR12 rates are summarized in table. 13 failures were observed (9 relapses, 1 virological failure, 3 deaths).Previous treatment did not impact on SVR Platelet<75,000/mL was the only factor associated with nonSVR12 (RR: 3.50 95%CI 1.23-9.94, p =0.019). In patients with MELD <10 or albumin >3.5 mg/dL, type of NSSA inhibitor did not impact on SVR12 (93% vs 97%, RR 0.96, 95%CI 0.89-104; 93% vs 96%, RR 0.97, 95%CI 0.90-105, respectively). Only 16 patients (5.7%) presented serious adverse events (SAE), including 3 deaths (11%) and 6 discontinuations (32%). Percentage of SAEs and deaths was higher in decompensated patients (18% vs. 31%, p<0.001, 4% vs. 0.4%, p=0.008).

**Conclusions:** SOF/LDV+RBV achieved high SVR12 rates in GT3 patients with compensated cirrhosis, similar to SOF+DCV, both with low rates of serious adverse events.
ml/min and changes in the GFR 12 weeks after the end of treatment in those patients with CRI baseline.

Results: 157 individuals were included, with mean age 54 years and 66% male. 68% were pre-treated with PR IP first generation. 132 (84%) had genotype 1 (1a: 32%, 1b:46% and others: 4%), 15 (10%) genotype 3 and 10 (6%) genotype 4. The baseline viral load was > 800,000 IU/mL in 72% and 17% were diabetics. Fibrosis stage: 16 (10%) were F0-F1; 37 (24%) F2; 40 (25%) F3 and 64 (41%) had cirrhosis. 154/157(98,1%) had SVR12. 64/157 (41%) had a CRI baseline. Of these, 63 improved the treatment and 12 weeks of follow-up with 100% SVR12. In this subgroup, the eGFR improved significantly after obtaining SVR12 (Median: 77,81 ml/min vs 82.36 ml/min p = 0.014).

Conclusions: 1) The prevalence of CRI in patients with CIHCV is high (41%), 2) In patients with CIHCV and CRI, the eGFR improves significantly after SVR12.

38. Poster Presentation #936

#936: SERUM CONCENTRATION OF ASUNAPREVIR AFFECTS ALANINE AMINOTRANSFERASE ELEVATION FOR PATIENTS WITH CHRONIC HEPATITIS C AND THE PROTECTIVE EFFECTS OF URSODEOXYCHOLIC ACID

Shuhei Hige, Itaru Ozeki, Ryoji Tatsumi, Masakatsu Yamaguchi, Mutsumi Kimura, Tomohiro Arakawa, Tomoaki Nakajima, Yasuki Kuwata, Takahiro Sato, Takumi Ohmura, Joji Toyota, Yoshiyasu Karino

Background and Aims: Asunaprevir (ASV) is administrated with daclatasvir (DCV) for genotype 1 chronic hepatitis C patients in Japan. Alanine aminotransferase (ALT) elevation is the most frequent adverse event. However, the precise mechanism has not been elucidated. Ursodeoxycholic acid (UDCA) is used as a hepatoprotective medicine in case of liver dysfunction. In this study, we investigated the significance of serum ASV concentration and the relationship with ALT elevation.

Patients and Methods: 132 patients with genotype 1 chronic hepatitis C were treated with 100mg of ASV twice and 60mg of DCV once daily. Pharmacokinetics (PK) of ASV was investigated in 25 cases. Trough concentrations of ASV (C-ASV_trough) at week 2, 4, 6, 8 and 12 were measured. Intensive PK study was performed in 10 cases and C-ASV of 0, 0.5, 1, 2, 4, 6, 8 and 12 hours after ASV administration were measured at day 14. C-ASV_trough at week 1 or 2 was measured for other 117 cases. C-ASV was measured by HPLC. 55 cases were administrated UDCA continuously before the start of the combination therapy and 51 cases were not. Those who improved ALT=30 IU/L and maintained during the treatment period were classified as a stable [Rel(-)] group and those who did not as a relapser [Rel(+)] group.

Results: In the intensive PK study, median C max was 951 ng/mL (283-4500) and t max was 1.97 hours (0.9-2.1). Mean C-ASVs_trough between week 2 and 12 were widely distributed from 162 to 1958 ng/mL by individuals, but the differences in the same case was small: mean SD was 415% of the mean value. Median C-ASV_trough of cirrhotic cases with Child-Pugh (CP) score 6, CP score 5 and non-cirrhotic cases was 168, 77 and 52 ng/mL (p=0.06). Median C-ASV_trough was significantly correlated with type 4 collagen-7S, FIB-4 index, WFA-M2BP, liver stiffness measurement by Fibroscan™ (r=0.50, 0.40, 0.40, 0.39 p=0.001). The maximum value and the period of ALT elevation was 974 IU/L and 13.7 weeks in UDCA(-) group and 65.4 IU/L and 15.2 weeks in UDCA(+) group. Median C-ASV_trough (ng/mL) in Rel(-) and Rel(+) group was 487 and 925 in UDCA(-) cases (p=0.03), 1125 and 711 in UDCA(+) cases (ns). In UDCA(-) cases, the probability of ALT elevation during the treatment was 25.0% for C-ASV_trough <50 ng/mL cases and 58.6% for C-ASV_trough ≥50 ng/mL cases. C-ASV_trough did not affect SVR (72 ng/mL in SVR cases and 62 ng/mL in non-SVR cases: ns).

Conclusions: ASV concentration correlated with hepatic reserve and the degree of fibrosis. ALT elevation during the combination therapy with ASV and DCV for patients with genotype 1 HCV infection was associated with serum ASV concentration and UDCA reduced ALT elevation.

39. Poster Presentation #937

#937: IN PATIENTS WITH CHRONIC HCV INFECTION, ANTIVIRAL TREATMENT WITH DAAs CAN BE MANAGED BY SPECIALIZED NURSES. RESULTS OF A LARGE REAL-LIFE COHORT

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Background: The availability of effective DAAs for the treatment of chronic HCV infection has resulted in a major increase of the number of patients susceptible to benefit from these new therapeutic approaches. Many of these patients have advanced liver disease and require rapid access to antiviral treatment. Therefore, innovative strategies are needed to optimize patient management, cope with large cohorts of patients and accelerate treatment initiation. The objective of this study was to compare the management of selected HCV patients treated with DAAs between hepatologist physicians and specialized nurses in a tertiary care center.

Methods: 548 patients, candidates for all-oral DAAs regimens, were prospectively allocated to treatment supervised either by a hepatologist physician (n=261, group P) or a specialized nurse (n=287, group N). Key exclusion criteria were Child C cirrhosis, hepatocellular carcinoma, or severe comorbidities. Cirrhosis was defined by FibroScan score>12 kPa, or FibroTest score>0.75. Patients received all-oral regimens according to international guidelines, including mainly SOF+DCRVRB (56.6%), SOF+LDVRB (25%) or SOF+SIMVRB (11.9%).

Results: 606% of patients were male with median age of 59 years at DAA treatment initiation. Cirrhosis was present in 47% 30 patients were Child B median MELD score was 6.108% of patients were organ-transplanted. 13.9% had renal failure, 17.9% diabetes and 37.8% hypertension. 11% had HCV-HIV co-infection. HCV genotype 1 was predominant (61.2%), followed by genotypes 4 (17.7%), 3 (133%), 2 (59%), 5 (11%) and 6 (0.7%). 536% were treatment-experienced patients 86.1% were treated for 12 weeks and 139% for 24 weeks. There were no significant differences in baseline characteristics and treatment duration between both groups (P and N). Overall, SVR12 rate was 92.7% (91.2%, group P vs 94.1%, group N). Premature treatment discontinuations occurred in 1.8% (1.9%, group P vs 1.7%, group N). Severe adverse events were observed in 35% (43%, group P vs 2.8%, group N). Death during treatment period was reported in 0.9% (1.5%, group P vs 0.3%, group N). Loss to follow up (1.8% in the overall population) was significantly more frequent in group P (34%) than in group N (03%) (p=0.008).

Conclusions: This study in a large real-life cohort strongly shows that all-oral DAAs regimens can be safely and successfully managed by specialized nurses. This strategy may accelerate DAA treatment access for
40. Poster Presentation  #940

**#940: IMPACT OF SVR TO INTERFERON-FREE ANTIVIRAL REGIMENS ON LIVER STIFFNESS MEASUREMENT AND LIVER FUNCTIONALITY IN HCV INFECTED PATIENTS WITH SEVERE LIVER DISEASE: A REAL LIFE STUDY**

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**Background:** New interferon-free regimens with 2nd generation Direct Antiviral Agents (DAA) demonstrated high efficacy among HCV-infected patients in registered trials. Nevertheless, little is known about the impact of these therapies on liver stiffness measurement (LSM) and liver functionality in "real-life" settings.

**Aims:** to evaluate the impact of SVR on LSM and clinical and liver parameters indexes of 2nd generation interferon-free DAA therapy on a real-life population of HCV infected patients with Metavir F3 and F4 liver fibrosis.

**Patients and methods:** 282 HCV patients (M/F: 55.6/44.4%, Age: 62.8±10.49, BMI: 25.9±3.69) with F3 or F4 liver fibrosis undergoing antiviral therapy with DAA, were consecutively enrolled from April to December 2015 in three tertiary centers of Hepatology of Southern Italy, decompensated cirrhosis were excluded. Genotypes were: 1b: 62.9%, 1a: 4.0%, 2a: 22.7%, 3: 6.8%, 4: 2.5%. Patients were treated on the basis of EASL/ AASF guidelines with: Sofosbuvir (SOF) + Ribavirin (RBV) (26.0%), SOF + Simeprevir (RBV) (28.8%), SOF + Ledipasvir (RBV) (14.0%), Ombitasvir + Paritaprevir + Ritonavir + Dasabuvir (RBV) (24.8%), Ombitasvir + Paritaprevir + Ritonavir (RBV) (1.4%), SOF + Daclatasvir (RBV) (5.0%). Of every patient clinical, biochemical and imaging data (LSM and Ultrasonography), Child-Pugh and MELD scores were collected at the baseline before therapy starting (T0), at the End of Therapy (EOT) and after 12 weeks, at the Sustained Virological Response (SVR12).

**Results:** of the 282 patients 68.6% were Metavir F4 (LSM>12.5 kPascal) and 31.4% F3. SVR12 was reached in 97.5% of patients. In F3 and F4 patients LSM, and (in F4 patients) Child and MELD score significantly decreased from T0 to EOT (p<0.0001 each). Interestingly, no significant differences between these variables were found between Eot and SVR12 (p>ns). At an univariate analysis of the clinical and liver functionality parameters, baseline Glucose (p<0.005), Type 2 Diabetes (p<0.001), ALT (p<0.001), PLTs (p<0.005), were found associated with a significant Eot LSM (>2kPascal) improvement. At a multiple regression with Age, Sex, BMI, Glucose, Diabetes, ALT, MELD, Child and Platelets levels (PLT) as independent variables, only ALT and PLTs were directly, and Diabetes inversely, associated with significant LSM reduction.

**Conclusions:** Virological response to interferon-free regimens is associated to fibrosis regression and recovery of liver functionality and this can be detected as early as Eot response is achieved, whereas no differences between Eot and 12 weeks post-treatment can be found in SVR patients. Diabetes seem to negatively influence LSM improvement. Further investigations are advised to assess long term effects of SVR.

41. Poster Presentation  #941

**#941: MASSIVE DISPARITY IN INSURANCE APPROVAL; A COMPARISON BETWEEN LEDIPASVIR/SOFOSBUVIR BASED HEPATITIS C THERAPY AND ADALIMUMAB BASED IBD THERAPY**

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2 School of Medicine, Wayne State University, Detroit, MI
3 Gastroenterology, Henry Ford Hospital, Detroit, MI

**Purpose:** We evaluated the success rate for insurance approval for a single center setting for hepatitis C therapy involving ledipasvir/sofosbuvir and compared it to IBD therapy involving Adalimumab.

**Methods:** Pharmaceutical records were reviewed for all patients prescribed ledipasvir/sofosbuvir and Adalimumab between July 2014 and November 2015. Data was extracted including type of insurance, insurance approval, fibrosis staging based on fibroscan for the patients who were prescribed ledipasvir/sofosbuvir and data for type of IBD, severity of anemia, location, extraintestinal manifestations and perianal complications was collected for the patients who were prescribed Adalimumab.

**Results:** 783 patients were prescribed therapy with ledipasvir/sofosbuvir based therapy and the overall approval rate was 77.8%. In comparison among the 55 patients who were prescribed Adalimumab 52 (94.5%) were approved, 2 patients were denied and 1 was still pending approval. Among the patients who were prescribed ledipasvir/sofosbuvir by insurance companies 296 patients (378%) had Medicare, 424 (541%) private insurance and (82%) had Medicaid. The approval rates were 93% for Medicare patients, 79% for private insurances and 32% for Medicaid patients. Amongst private insurances, Private A had approval rate of 87%, Private B had approval rate of 73% and other private insurances had approval of 71%. In the Adalimumab group, 73% patients had Medicare and Medicaid each, 14% patients had Private A, 69% had Private B and 18% had other private insurance. All the patients who had Medicaid or Medicare were approved. Of the 2 patients who were denied one had Private B, Crohn’s disease as the diagnoses and absence of anemia or extraintestinal manifestations. Whereas the second patient had insurance other than Private A or B, Ulcerative colitis as the diagnoses, presence of moderate anemia and no extra-intestinal manifestations.

**Conclusion:** We evaluated insurance approval rates of ledipasvir/sofosbuvir based hepatitis C therapy and Adalimumab based IBD therapy. The over-all approval rate of therapy based on ledipasvir/sofosbuvir was 77.8% and Medicaid patients had a very low approval rate of 32%. The overall approval rate for Adalimumab based therapy was 94.5% and all the Medicare and Medicaid patients were approved. The only patients who were denied had private insurance.

**Figure:** Table showing approval rates in percentage of ledipasvir/sofosbuvir based on insurance type (p-value <0.001).

### Table

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<thead>
<tr>
<th>Insurance</th>
<th>Approval Rate</th>
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<td>Medicaid</td>
<td>32.1</td>
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<tr>
<td>Medicare</td>
<td>92.9</td>
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<tr>
<td>Private</td>
<td>78.9</td>
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42. Poster Presentation  #945

**#945: COMMUNITY-BASED, INDIVIDUALIZED, HEPATITIS C THERAPY IN NEPAL**

Holly A. Murphy1, Sameer M. Dixit2, Andrew Trotter2, Apurva Rai3, Ujjwal Karmacharya3, Patricia Kramarz1, Philippe A. Creach4

1 Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ) GmbH, Kathmandu, Nepal
2 Center for Molecular Dynamics Nepal, Kathmandu, Nepal
3 JPPARSHA Nepal, Kathmandu, Nepal
4 The Global Fund, Geneva, Switzerland

**Purpose:** With direct acting antiviral therapy (DAA) expansion to resource-limited settings there is an urgency to validate best practices...
for population-based screening and treatment of hepatitis C (HCV). The Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ) GmbH (German Development Cooperation) implemented a community-based screening and treatment model for mono-infected and HIV/HCV co-infected persons in Nepal where over 150,000 individuals are living with HCV genotype 3 (GT3: 60%) and genotype 1 (GT1: 40%) (Kinkel, H).

Methods: We “pivoted” HCV screening and treatment within 3 existing opioid substitution treatment (OST) sites screening 600 patients with HCV viral load and GT, AST/Platelet Ratio Index (APRI) and fibroscan enrolling 150 HCV mono-infected and 150 HIV-HCV co-infected for individualized treatment in an ongoing study. Patients with GT3 disease with optimal predictors (baseline HCV viral load <3,000,000 IU/ ml, HIV-negative, no cirrhosis, age <50, body mass index < 30 kg/m², favorable IL28B SNPs) received 12-weeks sofosbuvir/peg-IFN-RBV (SIR vs S/daclatasvir (SD) +/R (cirrhotics). GT1-regimens included: S/ledipasvir (SL) or SD +/R (cirrhotics).

Results: We demonstrated optimal 4-week complete rapid virologic response (RVR) (94%) without significant toxicity among the first 105 patients treated (n=69 HIV+50% with tenofovir disoproxil fumarate (TDF)-containing antiretroviral regimens). Treatment regimens were: 50% SD and 35% SL (with R for 17 patients with compensated cirrhosis), 15% SIR. An APRI cut-off of 2 (compared to fibroscan 10) had 51% sensitivity, 95% specificity (89% negative predictive value) for advanced fibrosis.

Conclusions: Both optimal outcomes and drug tolerability demonstrated the effectiveness of community, OST-based HCV screening and treatment in a resource-limited setting with simple individualized DAA-based therapy. Excellent early outcomes across GT 1 and 3 in this “real-life” setting encompassing HIV-infected and injecting drug users supports simple HCV diagnostic/treatment models implemented through OST sites. These results will be valuable for extending population-based HCV treatment to resource-limited settings.


43. Poster Presentation #949

#949: HIGH EFFICACY OF LEDIPASVIR/SOFOSBUVIR COMBINATION WITH OR WITHOUT RBVIRIN IN THE TREATMENT OF CHRONIC HEPATIS C GENOTYPE 4–INFECTED COMPENSATED AND DECOMPENSATED CIRRHOSIS PATIENTS: REAL LIFE DATA FROM SAUDI ARABIA

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Limited clinical trial data has shown high efficacy of co-formulated ledipasvir/sofosbuvir (LDV/SOF) in the treatment of patients infected with hepatitis C virus (HCV) genotype (GT)-4 infected patients, although the data is limited in cirrhotic patients. This study assessed real-world safety and efficacy of co-formulated ledipasvir/sofosbuvir (LDV/SOF) with or without ribavirin (RBV) in GT4 infected patients with compensated and decompensated cirrhosis.

Methods: In this ongoing, observational cohort, we included HCV GT4 treatment naïve and experienced patients with (n=40) and without (n=118) decompensated cirrhosis for a 12-24 week treatment regimen with LDV/SOF. RBV (55.7% of patients) was dosed by physician discretion between 600 – 1200 mg daily. Patients with prior DAA failure were excluded from the analysis. Decompensated cirrhosis (F4, Metavir) was ascertained by Fibroscan. Decompensated cirrhosis (Child’s Pugh score 7) was ascertained by established clinical, biochemical and radiological criteria. The primary efficacy endpoint was SVR12, and drug discontinuation and/or occurrence of grade 3/4 adverse events. Results: A total of 158 adult patients with a mean age of 59±2.7 years, and HCV RNA 5.80±8 IU/mL were enrolled, 94 (59.5%) were female, and 73 (46.2%) were treatment-experienced to pegylated interferon RBV. All patients have completed 4 weeks on therapy, with HCV RNA undetectable (<15 IU/mL) in 84/158 (53.1%) patients, and all 129 had reached end-of-therapy with undetectable/below range HCV RNA. No virologic breakthroughs were observed in any of the patients. Overall 81/87 (93.1%) patients who had completed 12 weeks of post treatment follow up achieved SVR12 (compensated cirrhosis, n=57 [SVR12 919%], decompensated cirrhosis, n=24 [SVR12 96.0%]). Of the 6 patients who failed therapy (all relapsed), one had decompensated cirrhosis while the other 5 had compensated cirrhosis, including 5 who were treatment naïve and 1 being treatment experienced. Four of the 6 patients who failed therapy received concomitant RBV. Adverse events were grade 1 or 2 and there were no drug discontinuations related to side effects. Two patients with compensated (1 Child’s B and 1 Child’s C) cirrhosis died from underlying disease progression while on therapy. Conclusion: The interim analysis of this cohort shows that LDV/SOF with or without RBV is highly effective with a favorable safety profile in HCV GT4 patients with underlying cirrhosis. SVR12 rates were high in all patient categories regardless of the presence of decompensated cirrhosis or prior treatment experience. Treatment was generally well-tolerated with few side effects.

44. Poster Presentation #958

#958: REGRESSION OF FIBROSIS IN HCV PATIENTS TREATED WITH DIRECT ACTING ANTIVIRALS (DAAS)

Stephanie Hametner, Remy Schwarzer, Alexander Ziachebahi, Rainer Schöfl, Andreas Maieron

Gastroenterology and Hepatology, ElisabethHospital, Linz, Austria

Introduction: sustained virological response (SVR) due to antiviral therapy is associated with changes in biochemical markers of liver function. So far little is known about the effects of SVR on liver fibrosis. Therefore we investigated the effects of DAA based HCV therapy on fibrosis measured by transient elastography (TE).

Methods: over a period of 12 months (03/201403/2015) we treated a total of 154 patients with a DAA-based therapy 121 patients had baseline evaluation including TE and SVR 12 of those, a total of 108 patients were followed up at least 24 weeks post treatment including TE. TE results were classified as very reliable (IQR/M≥10), reliable (IQR/M 30% or 30% and <7,5kPa) and not reliable (IQR/M>30%). Patients were devided into two groups (cirrhosis and non cirrhosis) according to TE results (cut off F4>13kPa).Only patients with correct TE results were included.

Results: 108 patients in total, 43 (39.8%) female, median age 60, (female: 63 (IQR 55-73), male: 58 (IQR 54-63)). Distribution of genotypes was as follows: 1a: 27.8%, 1b: 57.4%, 1: 3.7%, 3: 74%, 4:19% 55.6% were considered cirrhotics69%4 previously had treatment including PI based regimes. All patients included in this evaluation achieved SVR 12. Baseline (BL) and follow-up TE results are shown in table 1. In a subgroup of 47 cirrhotic patients with correct TE=13 kPa, 48% showed a regression of fibrosis to F3 according TE evaluation. In those with proven regression BL TE measured 17.1kPa (IQR: 143209),
FUP TE results showed 89kPa (IQR: 83-108).

**Conclusion:** SVR in HCV patients due to DAA therapy appears to induce regression of fibrosis in our patients. Moreover in a significant proportion of patients with TE proven cirrhosis we noticed stage migration from F4 to F3. This work underlines that down staging of fibrosis even in cirrhotic patients could happen, however histological verification is lacking. One might wonder whether in subgroups of cirrhotics with fibrosis regression TE decline can be translated in less liver related endpoints therefore a longer observation of our patients is planned.

**Figure:** TE results in different patient populations

<table>
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<tr>
<th></th>
<th>TE &lt;8 kPa (n=11)</th>
<th>TE 8-10 kPa (n=22)</th>
<th>TE 11-18 kPa (n=11)</th>
<th>TE &gt;18 kPa (n=12)</th>
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<tr>
<td>no cirrhosis</td>
<td>9 (4.3-11.4)</td>
<td>6.2 (4.6-7.7)</td>
<td>11.8 (5.8-11.0)</td>
<td>13.2 (9.9-21.5)</td>
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<tr>
<td>cirrhosis</td>
<td>25.1 (6.3-31.3)</td>
<td>18.3 (2.8-30.6)</td>
<td>18.3 (6.3-31.3)</td>
<td>18.3 (6.3-31.3)</td>
<td>&lt;0.0001</td>
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</tbody>
</table>

BL (baseline), TE (transient elastography), FUP (follow up)

45. Poster Presentation  #1003

**#1003: DISEASE RECURRENT AND FIBROSIS PROGRESSION IN PATIENTS TRANSPLANTED FOR NONALCOHOLIC STEATOHEPATITIS**

Chandra Bhati1, Maria Rivera1, Michael O. Idowu1, Carolyndiscoll1, Divyanshoo R. Kohli1, R. Todd Stravitz2, Arun J. Sanyal1, HoChong Gilles3, Scott C. Matherly2, Puneet Puri2, Velimir A. Luketic4, Hannah Lee5, Richard K. Sterling5, Mohammad Siddiqui5

1 Virginia Commonwealth University, Richmond, VA
2 VA McGuire Medical Center, Richmond, VA

**Background:** Nonalcoholic fatty liver disease (NAFLD) exists in two predominant histological subtypes: nonalcoholic fatty liver (NAFL) and nonalcoholic steatohepatitis (NASH). NASH is characterized by benign steatosis while NASH is diagnosed when steatosis is accompanied by necroinflammatory activity and fibrosis. NASH is an important cause of cirrhosis and the leading listing diagnosis among new liver transplantation (LT) waitlist registrants. However, little is known regarding disease recurrence and progression after LT in patients transplanted for NAFLD. Thus, the aim of the current study was to systematically evaluate disease recurrence and fibrosis progression in patients who had a LT for NASH.

**Method:** Patients who had a LT for NASH or suspected NASH between 1995 and 2013 at the authors’ institution were included. Disease recurrence was evaluated with either histology or FibroScan®. All alive patients had FibroScan® performed to evaluate hepatic steatosis (controlled attenuation parameter or CAP) and fibrosis (liver stiffness measurements or LSM). The previously described cutoffs for CAP and LSM were used (de Ledinghen et al. Gastroenterol Hepatol 2016, Wong et al. Am J. Gastro 2012). Those who failed FibroScan® were offered a liver biopsy. Charts of deceased patients were reviewed and those having a liver biopsy done >1 year post-LT were included.

**Results:** Of the 103 patients who met entry criteria, 56 had a FibroScan and 34 had a liver biopsy. Steatosis was detected in 75% of patients who had a FibroScan® and were defined to have recurrent NAFLD. Most patients had LSM measurement consistent with either no fibrosis (42.9%) or F1-F2 fibrosis (30.4%). Advanced fibrosis (F3) was noted in 26.8% of the cohort while 5.4% of patients had graft cirrhosis but were clinically compensated. In patients with a liver biopsy, 88.2% had recurrent NAFLD, while 46.7% had recurrent NASH. Bridging fibrosis was noted in 23.3% of patients but no patients had cirrhosis on liver biopsy. Interestingly, serum ALT and AST levels did not correlate with disease recurrence, NASH or fibrosis stage in LT recipients transplanted for NAFLD. Three patients (29%) developed clinically significant graft cirrhosis and died of complications related to endstage liver disease.

**Conclusion:** Recurrent NAFLD is common post-LT and cannot be diagnosed based on serum aminotransferases. Although advanced fibrosis can occur in nearly a quarter of patients, mortality related to graft cirrhosis is rare.

1. Presidential Poster  #1051

Hall C
Saturday, 12 November 2016 – 2:00-7:30

**#1051: PROSPECTIVE PREVALENCE OF NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) AND NON-ALCOHOLIC STEATOHEPATITIS (NASH) AMONG A LARGELY MIDDLE-AGED POPULATION UTILIZING FIBROSCAN®, LIVER MULTISCAN (LMS), MAGNETIC RESONANCE ELASTOGRAPHY (MRE), AND LIVER BIOPSY: INTERIM ANALYSIS**

Angelo H. Paredes1, Katharine K. Roberts1, Induruwa N. Pathirana2, Allyson E. Cochet3, Pedro A. Manibusan4, Christopher J. Lisanti5, Ryan Schwope6, Alan A. George1, Katherine M. Cebe1, James K. Aden1, Jennifer M. Aldridge-Whitehead2, Dustin M. Thomas3, Stephen A. Harrison4

1 Gastroenterology, Brooke Army Medical Center, Fort Sam Houston, TX
2 Radiology, Brooke Army Medical Center, Fort Sam Houston, TX
3 Pathology, Brooke Army Medical Center, Fort Sam Houston, TX
4 Biomedical Statistics, Institute for Surgical Research, Fort Sam Houston, TX
5 Cardiology, Brooke Army Medical Center, Fort Sam Houston, TX

**Background:** NAFLD prevalence is estimated to be as high as 30-46% in the USA. Large prospective studies are lacking correlating demographic, clinical and novel radiographic data to histopathology.

**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 MRElastography (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.

**Results:** To date, 430 participants have been enrolled, of which 284 had results available for interim analysis. Mean age: 566 years mean BMI: 305 kg/m2 57% male 14% diabetic. The prevalence of NAFLD (defined by a proton density fat fraction (PDFF) of >5%) among those who completed all radiographic studies was 35% (N=284) (Fig. 1). PDFF values for NAFLD patients distributed as follows: 5-10%: 49% 10.1-20%: 40%; >20%: 11%. One-hundred-seven biopsies have been performed to date: 29 normal, 62 Non-NASHNAFLD and 16 NASH. Among the NASH patients: 3 stage-0 (0% diabetic), 5 stage-1 (40% diabetic), 6 stage-2 (67% diabetic), and 2 stage-3 (100% diabetic). Patients with diabetes and NAFLD compared to non-NAFLD had higher FibroScan™ LSM (p=0.03), FibroScan™ CAP (p=0.0003), steatosis grade (p<0.0001), and fibrosis stage (p=0.0045). Among those with NASH vs. non-NASH NAFLD mean: FibroScan™ LSM 10314 vs. 58.24 kPa(p=0.005) LiF 2.6016 vs. 215008 (p=0.002) MRE 298028 vs. 2205 kPa (p=0.02). MRI cT1 1897 vs. 92416 (p=0.03).

**Conclusion:** In adult patients without known liver disease interim results from novel radiographic studies and liver biopsy confirm the high prevalence of NAFLD in the USA.
46. Poster Presentation #1058

**#1058: PROSPECTIVE COMPARISON BETWEEN TRANSIENT ELASTOGRAPHY, SUPersonic SHEAR IMAGING, AND ARFI IMAGING FOR PREDICTING FIBROSIS IN SUBJECTS WITH NAFLD**

Won Kim1, M Young Seok Lee2, Young Ho So3, Jung Ho Kim3, Sae Kyung Joo3, Yong Jin Jung3

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2 Radiology, Boramae Medical Center, Seoul, Korea (the Republic of)
3 Pathology, Boramae Medical Center, Seoul, Korea (the Republic of)

**Background and Aims:** To compare the diagnostic performance of transient elastography (TE), supersonic shear-wave imaging (SSI), and acoustic radiation force impulse imaging (ARFI) for staging fibrosis and to identify clinical factors which affect liver stiffness measurement (LSM) in a prospective NAFLD cohort.

**Methods:** Ninety-four subjects with biopsy-proven NAFLD were included. For each subject, liver stiffness was measured using TE, SSI, and ARFI within 1 month of liver biopsy. The diagnostic performance for staging liver fibrosis was evaluated using receiver operating characteristic (ROC) analysis. Anthropometric data using fat impedance analysis were evaluated as covariates influencing LSM by regression analyses.

**Results:** All LSM modalities were correlated with fibrosis stages (p<0.001) and exhibited similar performance for staging fibrosis (p>0.05). The areas under the ROC curves for TE (kPa), SSI (m/s, kPa), and ARFI (m/s) were 0.775, 0.761, 0.759, and 0.657 for significant fibrosis (F2), 0.870, 0.816, 0.809, and 0.873 for advanced fibrosis (F3), and 0.882, 0.900, 0.906, and 0.920 for cirrhosis (F4). ARFI tended to be more specific and SSI tended to be more sensitive in differentiating each fibrosis stage with their best diagnostic performance. Anthropometric data were correlated with failure or unreliability of LSM, especially in SSI. In regression analysis, anthropometric data might be confounders influencing LSM, while serum liver injury-related markers might be confounders influencing TE and ARFI.

**Conclusions:** Diagnostic performances of individual LSM modalities for staging fibrosis in NAFLD were not significantly different. TE or ARFI might fit better for suspicion of advanced fibrosis, while TE or SSI might be more advantageous for suspicion of mild fibrosis. Pre-LSM anthropometric evaluation may help predicting LSM reliability, especially in SSI.

47. Poster Presentation #1060

**#1060: UPREGULATED PALMITIC ACID ABSORPTION WITH ALTERED INTESTINAL TRANSPORTERS IN NON-ALCOHOLIC STEATOHEPATITIS (NASH)**

Hiroki Utsumiya, Yasunari Yamamoto, Eiji Takeshita, Yoshio Tokumoto, Fujimasa Tada, Teruki Miyake, Masashi Hirooka, Inova Health System, Falls Church, VA; Inova Fairfax Hospital, Falls Church, VA Department of Medicine, Masanori Abe, Teru Kumagi, Bunzo Matsuura, Yoshi Ikeda, Yoichi Hiasa; Departments of Gastroenterology and Metabolism, Ehime University Hospital, Toon, Japan

**Background & Aims:** Saturated fatty acids (SFA) are important risk factors for the development of NASH via endoplasmic reticulum stress and oxidative stress. Major sources of hepatic SFA are adipose tissue, hepatic lipogenesis *de novo*, and diet. Reports indicate that amounts of SFA derived from adipose tissue and *de novo* lipogenesis increase in NASH, but changes in dietary SFA absorption are unclear. Thus, we aimed to clarify changes in the absorption of dietary palmitic acid, a common dietary SFA that induces hepatic inflammation. We also assessed their association with the pathogenesis of NASH.

**Patients and Methods:** This study included 33 controls as well as 32 and 41 patients with Brunt stages 1-2 and 3-4 defined as early (e-NASH) and advanced (a-NASH) NASH, respectively. Palmitate labeled with 13C was administered directly into the duodenum using gastrointestinal endoscopy to avoid delays resulting from delivery via the stomach. Breath levels of 13CO2 were then measured to quantify metabolized SFA before and every 30 min after administration for the next 360 min. The expression and locations of SFA transporters were assessed in jejunal biopsy samples by Western blotting and immunohistochemical staining. Associations between breath 13CO2 levels and hepatic steatosis, fibrosis, and insulin resistance were evaluated from laboratory tests, elastography, and liver histology.

**Results:** Significantly more 13CO2 was excreted over the 360 minutes in patients with e-NASH than in controls (P<0.01) and only during the early phase (0-120 min) of patients with a-NASH compared with controls (P<0.01). Western blotting revealed higher levels of glycosylated CD36 and microsomal triglyceride transfer protein (MTPP) in patients with e-NASH and a-NASH than in controls. Immunohistochemical staining revealed strong glycosylated CD36 expression in blood ves-sels. The excretion of 13CO2 by patients with e-NASH during the early phase (AUC 0-120 min%) positively correlated with laboratory values such as type IV collagen 7s (r=0.626) and correlated with the controlled attenuation parameter (CAP) (r=0.505) and liver stiffness measurements (LSM) (r=0.697) determined by elastography. Additionally, AUC 0-120 min% was significantly increased in Brunt stage 2 than in stage 1 (P=0.002). The amount of excreted 13CO2 during the late phase (AUC 120-360 min%) positively correlated with insulin (r=0.556) and HOMA-IR (r=0.436).

**Conclusion:** Dietary palmitic acid absorption was upregulated in the jejunum and apparently associated with the clinicopathological features of patients with e-NASH.

48. Poster Presentation #1069

**#1069: THE IMPACT OF CONTROLLED ATTENUATION PARAMETER ON LIVER STIFFNESS MEASUREMENT USING TRANSIENT ELASTOGRAPHY IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE**

Dong Hyeon Lee, Won Kim, Yong Jin Jung

Internal medicine, SNG-SNU Boramae Medical Center, Seoul, Korea (the Republic of)

**Background:** According to a recent report, severe steatosis is likely to affect liver elasticity (E) as measured by transient elastography (TE) in subjects with non-alcoholic fatty liver disease (NAFLD). However, little is known about the impact of controlled attenuation parameter (CAP) as assessed by TE on the measurement of liver E in subjects with NAFLD.

**Methods:** Two hundred eleven subjects with biopsy-proven NAFLD were included in this prospective analysis. All patients underwent acoustic radiation force impulse elastography (ARFI) and TE with CAP measurement. Logistic regression analysis and discriminant function
analysis were used for calculating two kinds of CAP-adjusted E. Area under ROC curves (AUROC) were used to determine the optimal cut-offs, sensitivity, and specificity of CAP-adjusted E values for detecting advanced fibrosis (F3) and cirrhosis.

**Results:** For diagnosing advanced fibrosis, the AUROCs for TE (CAP-adjusted E) were 0.889 (optimal cut-off, -7.739 sensitivity [se], 85.37% and specificity [sp], 87.06%) by log odds and 0.883 (optimal cut-off, 0.263 se, 82.93% sp, 91.76%) by formula calculated using discriminant function analysis, while, for diagnosing cirrhosis, those for TE (CAP-adjusted E) were 0.903 (optimal cut-off, -5.177 se, 90.91% sp, 88.36%) by log odds and 0.904 (optimal cut-off, 0.381 se, 90.91% sp, 88.36%) by formula calculated using discriminant function analysis. The AUROCs (for F3, 0.893 and for F4, 0.915) for TE (E) were not significantly different from those for TE (CAP-adjusted E). However, specificity (for F3, 5294% for F4, 8466% in TE) was markedly improved after adjustment for CAP without diminishment of sensitivity (for F3, 85.37% for F4, 9091% in TE) at the optimal cut-off values.

**Conclusions:** There was a significant positive correlation between CAP-adjusted E and fibrosis stages in subjects with NAFLD. Although CAP-adjusted E was not superior to E in diagnosing advanced fibrosis and cirrhosis, measurement of CAP-adjusted E might obviate the need for liver biopsy in those with NAFLD.

**Figure:**

### #1071: NOVEL FIBROSCAN-BASED SCORE TO DIAGNOSE NASH AND ITS SEVERITY IN A MULTI-CENTRE UK COHORT OF PATIENTS WITH SUSPECTED NAFLD

Peter J. Eddowes1, Quentin Ansee2, Indra Neil Guha3, David A. Sheridan3, Emmanouil Tschatzis3, Jeremy Cobbold3, Michael E. Allison3, Victor de Ledinghen8, Magali Sasso6, Celine Fournier5, Véronique Miette5, Valerie Paradis10, Pierre Bedossa10, Philip N. Newsome2

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4 NHRI Nottingham DigestiveDiseasesBiomedicalResearchUnit, NHS Trust and University of Nottingham, Nottingham, United Kingdom
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**Background & Aims:** Reliable non-invasive biomarkers are needed for the diagnosis and monitoring of patients with non-alcoholic steatohepatitis (NASH). Our study set out to determine the performance of a new score developed by Echosens to differentiate NASH and simple steatosis based on a single FibroScan examination (liver stiffness and controlled attenuation parameter (CAP)).

**Methods:** Patients with suspected NAFLD prospectively underwent FibroScan examination within 2 weeks of a standard of care liver biopsy (LB) between March 2014 and January 2016 at seven UK centers. LB were read in a blinded manner by two expert pathologists. NASH was diagnosed using the FLIP algorithm. NASH severity was graded according to the NAS score. To develop a score to diagnose NASH the cohort was split randomly into training (80%) and validation (20%) sets. Sample splitting was repeated 100 times leading to the selection of the optimum model. This was tested on an external validation cohort that consisted of 47 NAFLD patients from a single liver centre in France. Patients there underwent FibroScan examination within 1 day of LB, read by the same pathologists.

**Results:** 174 patients with BMI <40 kg/m2 were studied. The following patients were excluded for the score development: LB not interpretable/diagnostic of NAFLD (n=18), FibroScan not possible (n=1), FibroScan unreliable according to Boursier’s criteria (n=10). Patients had a median BMI of 32.9 [IQR=6.9] kg/m2 and age of 54 [21] years. 58% were male, 74% had a NAS score 3 and 58% had NASH. The external validation cohort had a median BMI of 30.0 [8.0] kg/m2 and age of 53 [22] years. 67% were male, 82% had a NAS score 3 and 71% had NASH, 91% had a reliable Fibroscan examination. Performance of the scores is shown in the table.

**Conclusion:** A novel score based on measurement of liver stiffness and CAP from a single FibroScan examination was able to correctly classify 79% of patients with/without NASH as well as correctly staging severity in 86%. This has promise as a non-invasive marker for detecting/staging disease activity in patients with NASH.

**Figure: NASH scores performance**

### #1075: IMPACT OF VITAMIN D REPLACEMENT ON LIVER ENZYMES IN NON-ALCOHOLIC FATTY LIVER DISEASE PATIENTS Suparuedee Boonyagard, Karipong Techathuvanan

**Background:** Non-alcoholic fatty liver disease (NAFLD), which is related to insulin resistance and metabolic syndrome, is a disease most commonly found to progress into steatohepatitis and also evidenced as a major cause of cryptogenic cirrhosis. Several recent studies showed that vitamin D plays an important role in the pathogenesis and the treatment of chronic liver disease from many causes, including NAFLD. However, studies specifically involving a role of vitamin D replacement in NAFLD are extremely limited.

**Objective:** To demonstrate the effect of vitamin D replacement on liver enzymes and inflammatory markers in NAFLD patients

**Methods:** A randomized control trial was conducted at Liver clinic at Vajira hospital from January to December 2015. Sixty eligible NAFLD participants, who have ALT elevation with vitamin D insufficiency, were randomly split into two groups (30 patients per group) and assigned to receive either a vitamin D replacement or a placebo for 20 weeks. During this study, the participants were asked to maintain the same lifestyle and medication as before the experiment, as well as to have their serum calcium level monitored every four weeks for any side effects of hypervitaminosis D. Serum ALT, inflammatory markers, and homeostasis model assessment (HOMA) including Fibroscan® were compared before and after the 20-week vitamin D replacement period to evaluate the anti-inflammatory effect of vitamin D.

**Results:** At the beginning of the study, there was no statistical differences between the two groups of patients on the baseline characteristics, including gender, age, BMI, underlying disease (except T2DM), ALT, inflammatory markers, FibroScan® and INbody®. At the end of the study, ALT (-2743 2461 U/L, p <0.001), IL-6 (-0.45 1.12 pg/mL, p
1: Cirrhosis is one of the leading causes of death worldwide. The diagnosis is usually made in late stages after acute decompensation or liver cancer has developed. Ideally, diagnosis should be made in early stages before cirrhosis occurs, but current analytical and imaging methods are inaccurate for early detection of hepatic fibrosis. Aim of the study was to investigate the usefulness of TE for early detection of silent chronic liver disease with hepatic fibrosis in presumed healthy subjects from the general population.

Methods: Cross-sectional, descriptive, population-based study of subjects aged 18-75 yr randomly identified from people attending 18 primary care centers in Barcelona Metro Area from April 2012 to January 2016. Patients with known liver disease were excluded. Subjects were invited to participate through phone calls and 68% accepted. Medical examination, lab tests, and liver stiffness measurement (LSM) with TE were performed the same day by a single experienced operator. According to published data, LSM 6.8, 7.6, and 8.0 kPa were used as cutoffs of clinically-relevant fibrosis. A liver biopsy was suggested in subjects with abnormal LSM.

Results: 3,076 subjects, 57% females, 94% caucasion, with mean age 54 yr were included. Among them, 28% had metabolic syndrome (MS) and 9% excessive alcohol consumption. Less than 1% were found to be HBV and HCV+ and 24% had high aminotransferase levels. The percentages of subjects with increased LSM according to cutoffs used were 9.3%, 7.1% and 6%, respectively. In multivariate analysis, age, sex, high aminotransferases, and presence of MS were associated with increased LSM. Liver biopsy was performed in 51.5% of eligible patients. The histological diagnosis was NAFLD/NASH in 73, alcohol-related in 7, and normal liver in 4 the degree of fibrosis was F0 to F4 in 46, 13, 20, 2, and 3, respectively. There was a significant relationship between LSM and degree of fibrosis: 8.4±1.9; 7.9±1.5; 10.7±1.6; 15±1.5; and 33.9±10.8 kPa, from F0 to F4, respectively (p<0.001). The percentage of patients with significant fibrosis (>2) was related to the LSM cutoff, being 31%, 38% and 44% for cutoffs of 6.8, 7.6 and 8 kPa, respectively. The cut-off of LSM with greatest accuracy for diagnosis of significant fibrosis (2) was 9.2 kPa with 92% sensitivity and 80% specificity and AUROC of 0.87. Conclusion: A high percentage of presumed healthy adults from the Spanish population, 6% using cutoff of LSM of 8 kPa and 2.6% extrapolating biopsy data, have liver fibrosis, in most cases related to NAFLD. TE is a good non-invasive method for screening of liver fibrosis in the general population.

51. Poster Presentation #1083

#1083: EARLY DETECTION OF CHRONIC LIVER DISEASE WITH FIBROSIS AMONG PRESUMED HEALTHY ADULTS USING TRANSIENT ELASTOGRAPHY (TE). A POPULATION-BASED STUDY

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6. School of Nursing, University of Barcelona, Barcelona, Spain
7. Liver Unit, Hospital Clinic, Barcelona, Spain

Background and aims: Cirrhosis is one of the leading causes of death worldwide. The diagnosis is usually made in late stages after acute decompensation or liver cancer has developed. Ideally, diagnosis should be made in early stages before cirrhosis occurs, but current analytical and imaging methods are inaccurate for early detection of hepatic fibrosis. Aim of the study was to investigate the usefulness of TE for early detection of silent chronic liver disease with hepatic fibrosis in presumed healthy subjects from the general population.

Methods: Cross-sectional, descriptive, population-based study of subjects aged 18-75 yr randomly identified from people attending 18 primary care centers in Barcelona Metro Area from April 2012 to January 2016. Patients with known liver disease were excluded. Subjects were invited to participate through phone calls and 68% accepted. Medical examination, lab tests, and liver stiffness measurement (LSM) with TE were performed the same day by a single experienced operator. According to published data, LSM 6.8, 7.6, and 8.0 kPa were used as cutoffs of clinically-relevant fibrosis. A liver biopsy was suggested in subjects with abnormal LSM.

Results: 3,076 subjects, 57% females, 94% caucasion, with mean age 54 yr were included. Among them, 28% had metabolic syndrome (MS) and 9% excessive alcohol consumption. Less than 1% were found to be HBV and HCV+ and 24% had high aminotransferase levels. The percentages of subjects with increased LSM according to cutoffs used were 9.3%, 7.1% and 6%, respectively. In multivariate analysis, age, sex, high aminotransferases, and presence of MS were associated with increased LSM. Liver biopsy was performed in 51.5% of eligible patients. The histological diagnosis was NAFLD/NASH in 73, alcohol-related in 7, and normal liver in 4 the degree of fibrosis was F0 to F4 in 46, 13, 20, 2, and 3, respectively. There was a significant relationship between LSM and degree of fibrosis: 8.4±1.9; 7.9±1.5; 10.7±1.6; 15±1.5; and 33.9±10.8 kPa, from F0 to F4, respectively (p<0.001). The percentage of patients with significant fibrosis (>2) was related to the LSM cutoff, being 31%, 38% and 44% for cutoffs of 6.8, 7.6 and 8 kPa, respectively. The cut-off of LSM with greatest accuracy for diagnosis of significant fibrosis (2) was 9.2 kPa with 92% sensitivity and 80% specificity and AUROC of 0.87. Conclusion: A high percentage of presumed healthy adults from the Spanish population, 6% using cutoff of LSM of 8 kPa and 2.6% extrapolating biopsy data, have liver fibrosis, in most cases related to NAFLD. TE is a good non-invasive method for screening of liver fibrosis in the general population.

52. Poster Presentation #1100

#1100: TRANSIENT ELASTOGRAPHY IN COMBINATION WITH CLINICAL MARKERS (BARD SCORE, FIB-4, NFS) CAN BE USEFUL IN PREDICTING THE PRESENCE OR ABSENCE OF ADVANCED FIBROSIS IN PATIENTS WITH NON ALCOHOLIC FATTY LIVER DISEASE

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Background: Nonalcoholic fatty liver disease (NAFLD) is increasing in prevalence and may soon be the major cause of end stage liver disease. Noninvasive strategies to define fibrosis stage will be important for disease management. The aim of our study was to determine the utility of transient elastography (TE) either alone or in combination with clinical markers to assess fibrosis stage.

Methods: The electronic medical records of all patients with a diagnosis of NAFLD/NASH undergoing TE from May 2014 to December 2015 at a single institution were reviewed. Patients were included if they had reliable liver stiffness measurements (LSMs) and an adequate liver biopsy sample (> 2.5cm) within 3 years of TE. LSMS were used to divide patients into two groups: advanced fibrosis (≥F3) and absence of advanced fibrosis (<F3). Clinical markers: BARD score, FIB-4 and NFS were calculated in this sub-population and combined with LSM and compared to liver biopsy to determine fibrosis stage.

Results: 49 patients with the diagnosis of NASH/NAFLD had reliable LSMS and a liver biopsy were included in our study. LSMS were consistent with <F3 fibrosis in 25/49 and ≥F3 in 24/49. Fibroscan when used aloneaccurately predictive fibrosis stage in 86% (42/49) of patients, 20/25 with <F3 and 22/24≥F3. There was no difference in the predictive value of any of the individual non-invasive markers of fibrosis and no marker had increased positive predictive value or negative predictive value. LSM and all three clinical markers correlated for fibrosis stage in 33% (16/49), liver fibrosis was accurately predicted in all cases, <F3 (9/9), ≥F3 (7/7). The presence of 2/3 markers correlating with TE led to accurate prediction in those with <F3 (11/13), (1 patient lost >50lbs before liver biopsy). For ≥F3 fibrosis the addition of 1 or 2 clinical markers did not improve accuracy of TE. Conclusion: TE is a valuable tool to detect or exclude the presence of advanced fibrosis in NAFLD/NASH patients. Addition of calculated clinical markers further increases the accuracy of TE. When there is discrepancy between TE and ≥2 clinical markers in <F3 fibrosis, liver biopsy should be considered. Prospective, larger studies utilizing TE, clinical markers and liver biopsy are required to confirm these results.

Figure:

<table>
<thead>
<tr>
<th>Transient Elastography</th>
<th>BARD Score/FB-4/NFS</th>
<th>Accuracy of Liver Biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than F3 Total</td>
<td>89% (23/26)</td>
<td></td>
</tr>
<tr>
<td>≤F3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥F3</td>
<td>92% (22/24)</td>
<td></td>
</tr>
<tr>
<td>≥F3</td>
<td>92% (22/24)</td>
<td></td>
</tr>
<tr>
<td>≥F3</td>
<td>100% (5/5)</td>
<td></td>
</tr>
<tr>
<td>≥F3</td>
<td>90% (15/17)</td>
<td></td>
</tr>
</tbody>
</table>
ELASTOGRAPHY COMBINATION FOR NON-INVASIVE FIBROSIS STAGING IN NAFLD

Paul Cales, Alexandra Ducancelle, Julien Vergniol, Brigitte Le Bail, Francoise Lunel-Fabiani, Victor de Ledinghen, Jerome Boursier

Recent EASL international guidelines have suggested combining a blood test and liver stiffness measurement (LSM) to stage liver fibrosis in NAFLD. However, whether such a combination provides a gain in accuracy compared to its two constitutivetestscan not been demonstrated statistically. Therefore, we sought to compare the accuracies of these three test categorises in NAFLD, and secondly to compare the accuracies of tests between NAFLD and the reference etiology, chronic hepatitis C (CHC), where most tests have been developed and validated. Methods. Populations included 225 patients with NAFLD and 698 with CHC (total: 923). Sixteen tests (13 blood tests, LSM with Fibroscan, and 2 combining LSM and blood markers into unique scores: FibroMetersV2CTE) were evaluated in NAFLD and 13 in CHC. References were Metavir fibrosis staging by liver biopsy and CHC etiology. Accuracy was evaluated mainly by the Obuchowski index (OI) for binary diagnostic targets. Results. 1/NAFLD population: the combined FibroMetersV2CTE had significantly higher OIs and AUROCs for severe fibrosis compared to the other two test. OIs were similar between NAFLD and CHC when ordering accuracy (in NAFLD: FibroMeterV2CTE: 0.846 vs FibroMeterV2G: 0.773 (p = 0.002) or vs LSM: 0.808 (p = 0.014). NAFLD-specific tests were less accurate than PC-specific tests: e.g. OIs: FibroMeterV2G: 0.773 vs FibroMeterV2: 0.716 (p = 0.027) or vs NAFLD fibrosis score: 0.674 (p = 0.005). 2/NAFLD vs CHC: OIs were (respectively NAFLD vs CHC in decreasing order of accuracy in NAFLD): FibroMeterV2CTE: 0.846 vs 0.812 (p = 0.124), LSM: 0.808 vs 0.754 (p = 0.054), FibroMeterALD: 0.802 vs 0.750 (p = 0.039), Zeng score: 0.785 vs 0.734 (p = 0.030), Hepascore: 0.778 vs 0.752 (p = 0.300), FibroMeterV2G: 0.773 vs 0.797 (p = 0.422), Fib-4: 0.693 vs 0.741 (p = 0.174), APRI: 0.676 vs 0.742 (p = 0.081), Fibrotest: 0.670 vs 0.762 (p = 0.006). Conclusion: In NAFLD, single accurate tests developed in CHC performed better than test developed specifically for NAFLD. A test combining biomarkers and LSM outperformed its constitutive tests, validating the recent EASL guidelines in NAFLD. Non-invasive fibrosis evaluation can be simplified in NAFLD by using a single test: LSM (or one of the best-performing blood tests developed).

54. Poster Presentation #1128

#1128: VALIDATION OF GUIDELINES ON BLOOD-MARKERS FOR NON-INVASIVE FIBROSIS STAGING IN NAFLD
outcomes in non-alcoholic fatty liver disease (NAFLD) and there remains a clear need to establish the accuracy of non-invasive markers of fibrosis. This study aims to prospectively compare the diagnostic performance and ability to exclude advanced fibrosis of the following non-invasive tests in NAFLD: FibroScan, FibroMeter V, FibroMeter NAFLD, FibroMeter VCTE, NAFLD Fibrosis score (NFS), Fib4, APRI, BARD and AST/ALT ratio.

Methods: Patients with suspected NAFLD prospectively underwent FibroScan examination and blood sampling within 2 weeks of a standard of care liver biopsy (LB) between March 2014 and January 2016 at seven UK centres. LB were staged in a blinded manner by two expert pathologists according to the NAS CRN system. Diagnostic performance was assessed in terms of area under the ROC curves (AUC). Ability to exclude advanced fibrosis was assessed using published cut-offs except for FibroMeter (FM), for which cut-offs have not yet been published. Cut-offs for FM were determined that maximized the Youden index.

Results: 155 patients (57% male, median age 54 [IQR 20] years, median BMI 33.2 [8.1] kg/m2) had a complete dataset for analysis. Fibrosis distribution was: F0: 23%, F1: 25%, F2: 21%, F3: 25%, F4: 6%. 43% of the patients had a NAS score 5. Performance summary of the tests is presented below in the table.

Conclusion: FibroMeter VCTE, which combines biochemical parameters with liver stiffness measured by FibroScan, has the highest performance characteristics with positive and negative predictive values of 67 and 93% respectively at confirming or excluding F3 fibrosis.

Figure: Performance of non-invasive fibrosis scores

<table>
<thead>
<tr>
<th>Fibrosis stage</th>
<th>AUC</th>
<th>Ability to exclude F3</th>
</tr>
</thead>
<tbody>
<tr>
<td>F0</td>
<td>0.95</td>
<td>100%</td>
</tr>
<tr>
<td>F1</td>
<td>0.89</td>
<td>91%</td>
</tr>
<tr>
<td>F2</td>
<td>0.85</td>
<td>85%</td>
</tr>
<tr>
<td>F3</td>
<td>0.81</td>
<td>81%</td>
</tr>
<tr>
<td>F4</td>
<td>0.71</td>
<td>50%</td>
</tr>
</tbody>
</table>

* AUC significantly inferior from FM VCTE (Delong test). Cutoffs were either as published (‡) or established by maximizing Youden index (‡).

56. Poster Presentation  #1141

#1141: ASSESSMENT OF CHANGE OF INTRAHEPATIC FAT AMOUNT USING CONTROLLED ATTENUATION PERCUSSION IN CLINICAL TRIAL

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2 Department of Internal Medicine, Hanyang University School of Medicine, Seoul, Korea (the Republic of)

Background: Multi-echo modified Dixon (mDixon) sequence (MR-PDF) is a safe and non-invasive alternative for the quantification of hepatic fat content. It has accepted reasonable method to assess the change of hepatic fat amount in phase II study. Recently controlled attenuation parameter (CAP) has been showed good correlation with intrahepatic fat amount compare to liver biopsy as well as MRS data in large cross sectional cohort. However there is little known whether change of CAP scores can be used in clinical trial. We investigated the correlation with CAP and MRS by serial examination in clinical trial setting.

Methods: Sixty-five NAFLD patients were evaluated with MRS and transient elastography including CAP in clinical study. Both MRS and CAP were evaluated after three month probiotic clinical trial in patients with NAFLD.

Results: Baseline CAP and MR-PDF showed good correlation assessing hepatic steatosis (r=0.60, p<0.001). Also, changes of CAP value was also correlated with changes of intra-hepatic fat % using MR-PDF (r=0.35, p=0.008) in clinical trial setting. Concordance rate of improvement or aggravation was comparable in both two methods. However, the less change amount was small in CAP value, the less concordance rate showed more weak with MR-PDF. When the change of CAP value after treatment was less than 20, concordance rate with MR-PDF was decreased to 15/25 (60%).

Conclusion: CAP and MRS have a comparable diagnostic value for the hepatic steatosis quantification as well as assessing changes of hepatic fat amount in clinical trial. However, a careful interpretation of the steatosis change using CAP score should be given when the absolute change value was less than 20 in clinical trial setting.

57. Poster Presentation  #1142

#1142: EMERGING INCREASE IN THE PREVALENCE AND SEVERITY OF NONALCOHOLIC FATTY LIVER DISEASE: EPIDEMIOLOGICAL STUDY FROM GENERAL MEDITERRANEAN POPULATION

Salvatore Pettà1, Carola Buscemi2, Silvio Buscemi2, Davide Corlea2, Vito Di Marco2

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2 Metabolism and Clinical Nutrition Laboratory, Di.Bi.M.I.S., University of Palermo, Palermo, Italy, Palermo, Italy

Background/Aims: The worldwide spread of obesity and diabetes is leading to a drastic increase in nonalcoholic fatty liver disease (NAFLD) and its complications. We aimed to assess prevalence of NAFLD and of its severity among a general Mediterranean population.

Methods: We considered 886 consecutive individuals included in the ABCD study (ISRCTN15840340), a longitudinal observational single-centre study of a cohort representative of the general population of Sicily. All patients were negative for HCV, HBV and HIV infection, had alcohol intake <20 g/day for females and <30 g/day for males. Hepatic ultrasound (US) was used to diagnose steatosis and FibroScan (M+ and XL+ probe) to measure liver stiffness and controlled attenuation parameter (CAP). Liver stiffness>6.9 KPa was considered suggestive of significant liver fibrosis (Petta Set al, Hepatology 2015), and CAP310 dB was considered suggestive of moderate-severe steatosis (de Ledinghen V et al, JHEP 2014).

Results: Steatosis by US was diagnosed in 396 individuals (44%) and was significantly associated with male gender, type 2 diabetes, low HDL, and visceral obesity. When splitting the analysis according to gender, steatosis was independently linked to visceral obesity(OR 2.63, 95%CI 1.12-6.427, p=0.001) and low HDL(OR 2.06, 95%CI 1.10-3.85, p=0.02) in males, and to visceral obesity(OR 2.75, 95%CI 1.80-4.19, p<0.001) and type 2 diabetes(OR 2.19, 95%CI 1.00-4.87, p=0.05) in females. The rate of US steatosis, stiffness > 6.9 KPa and CAP310 progressively increased from males without obesity and low HDL(35.1% steatosis;among them 18.6% CAP310, and 13.5% stiffness >6.9), to those with one risk factor(from 57.7% to 62.1% steatosis;among them 42.8% CAP310, and from 21.4% to 23.2% stiffness >6.9), and further to those with both risk factors(74.2% steatosis;among them 35% CAP310, and 30% stiffness >6.9). Similarly, in females the rate of US steatosis, stiffness > 6.9 KPa and CAP310 progressively increased from patients without obesity and diabetes(23.7% steatosis;among them 6.1% CAP310, and 6.1% stiffness >6.9), to those with only one risk factor(from 33.3% to 50.8% steatosis;among them CAP310 from 30.5% to 54.5%, and stiffness >6.9 from 11.1% to 27.2%), and further to those with both risk factors(74.2% steatosis;among them 47.1% CAP310, and 26.4% stiffness >6.9).

Conclusions: NAFLD is present in more than 40% of general population and its prevalence, as well as the prevalence of liver damage, increases according to the presence of obesity and low HDL in males, and obesity and diabetes in females. The impact of variants of PNPLA3 and TM6SF2 genes on steatosis and liver damage in this population is under...
58. Poster Presentation  #1147

**#1147: USEFULNESS OF THE CONTROLLED ATTENUATION PARAMETER (CAP) FOR DETECTING LIVER STEATOSIS AND METABOLIC SYNDROME IN HEALTH CHECK-UP**

Hiroyasu Morikawa1, Sawako Uchida2, Norifumi Kawada1

1 Department of Hepatology, Osaka City University, Osaka, Japan
2 Department of Premier Preventive Medicine, Osaka City University, Osaka, Japan

**Background & Aims:** Currently more than three million people undergo a comprehensive health check-up for preventive medicine, called Ningen Dock, annually in Japan. Controlled attenuation parameter (CAP) evaluated with transient elastography (FibroScan) is a recent method for non-invasive assessment of steatosis. Its usefulness in clinical practice is unknown. Especially the relationship between CAP and the metabolic syndrome is not revealed. In the health check-up, we introduced CAP for the first time and prospectively investigated the relationships between CAP and clinical or biological parameters.

**Patients and Methods:** All CAP examinations performed in 1120 participants without suspected chronic liver disease from self-report. Liver stiffness and CAP measurements were performed by FibroScan 502 touch with 3.5 MHz standard M+ probe by experienced operators. The following factors were analyzed for their influence on CAP value and the relationships between CAP and clinical-biological parameters: age, gender, body mass index (BMI), waist circumference, hypertension, diabetes, metabolic syndrome, alcohol use, liver stiffness measurement, and different biological parameters.

**Results:** Characteristics of participants were as follows: males 62.6%, median age 56 (21-87) years, mean BMI 23.1 (3.6 kg/m2), 25.2% of participants overweight (BMI >25 kg/m2), and waist circumference 84.6 (85 cm). CAP measurement was unreliable in 98 cases (88%). CAP measurement failure was independently associated with FBS. Steatosis was detected in 41.1% by US (liver/kidney contrast) and 21.5% by CT (liver/Spleen ratio, <1.1) whereas it was detected in 49.6% by the CAP (>238 dB/m). The numbers of subjects with S0 (>238 dB/m): S1 (238 to <260 dB/m): S2 (260 to <293 dB/m): S3 (<293 dB/m) steatosis according to the CAP value were 515: 150: 174: 183, respectively. Simple regression analyses indicated that CAP values were significantly correlated with BMI (r=0.556), waist circumference (r=0.515), visceral fat area (r=0.423), L/S ratio (r=0.395), ALT (r=0.395), Triglyceride (r=0.347), and high density lipoprotein (r=-0.336 p<0.001, 95%CI). By multivariate analysis, factors associated with CAP were BMI, ALT, and Triglyceride.

**Conclusion:** The CAP seems to be useful for immediately detecting hepatic steatosis in the comprehensive health check-up. The association of CAP with the metabolic syndrome could be of interest for preventive medicine.

59. Poster Presentation  #1148

**#1148: THE COMBINATION OF INDEX OF NASH SCORE AND LIVER STIFFNESS IMPROVES THE NONINVASIVE DIAGNOSTIC ACCURACY FOR SEVERE LIVER FIBROSIS IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE**

Ramy Ibrahim Kamal Jouness1, Chiara Rosso1, Salvatore Petta2, Monica Cucco3, Milena Marietti1, Gian Paolo Caviglia1, Maria Lorena Abate1, Calogero Cammà4, Antonina Smideli1, Antonio Craxi1, Giorgio Maria Saracco1, Elisabetta Bugianesi1

1 Department of Medical Sciences, University of Turin, Turin, Italy
2 Sezione di Gastroenterologia, DIBIUMS, University of Palermo, Palermo, Italy
3 Department of Oncology, University of Turin, Turin, Italy

**Background and Aim:** The screening for Non-Alcoholic Steatohepatitis (NASH) in subjects with Non-Alcoholic Fatty Liver Disease (NAFLD) is hampered by uncertainties around the non-invasive tools of liver damage. This study is aimed at: 1. validating the recently developed INDEX of NASH and 2. assessing the diagnostic performance of single and combined noninvasive tools of liver damage in a large cohort of patients with biopsy-proven NAFLD.

**Material and Methods:** We analysed data from 254 Italian patients (136 from southern Italy and 118 from northern Italy) consecutively enrolled and biopsied. The following non-invasive scores of liver fibrosis were calculated according to published algorithms: ION, NFS, FIB-4. The apopotic fragments of CK-18 (M30) were measured by ELISA immunosassortant assay and Liver Stiffness (LS) was evaluated by FibroScan. Liver histology was scored according to Kleiner. NASH was diagnosed by the local pathologist according to joined presence of steatosis, inflammation and ballooning (with or without fibrosis). Severe fibrosis was defined as fibrosis F3. Cut-off points to rule-in or rule-out F3-F4 fibrosis were calculated by the Youden index.

**Results:** In the whole cohort, the AUCs of ION and CK-18 for the diagnosis of NAS showed were 0.622 (PPV 44, PPV 81) and 0.599 (PPV 41, PPV 81), respectively, confirming the poor performance of the tests for the noninvasive diagnosis of NASH. Both tests performed better for the diagnosis of severe fibrosis: the AUCs of ION and CK-18 were 0.724 (NPV 86, PPV 41) and 0.693 (NPV 84, PPV 46). In the same population the AUCs of NFS, FIB-4 and LS for the diagnosis of severe fibrosis were 0.694 (NPV 86, PPV 45), 0.677 (NPV 82, PPV 45) and 0.816 (NPV 88, PPV 57), respectively. Next we tested several combinations of all noninvasive tools in order to improve their diagnostic performance for the risk of severe fibrosis. The combination of ION plus LS, NFS plus LS and FIB-4 plus LS similarly improved the performance of each single test, providing a correct classification in 80%, 81% and 79% of cases, respectively.

**Conclusions:** The combination of LS with either ION, NFS or FIB-4 is better than each single noninvasive test to accurately exclude severe liver fibrosis.

60. Poster Presentation  #1151

**#1151: BASELINE PATIENT CHARACTERISTICS AND NON-INVASIVE IMAGE ANALYSIS IN A PHASE 2 THERAPEUTIC TRIAL OF GR-MD-02 IN NAFLD PATIENTS WITH STAGE 3 FIBROSIS**

Stephen A. Harrison1, Karol Barstow2, Adam E. Allgood2, Peter G. Traber2

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**Introduction:** Non-invasive approaches to the assessment of non-alcoholic steatohepatitis (NASH) with various degrees of fibrosis in the context of clinical trials is an important goal for drug development. Three leading candidates for non-invasive monitoring include multiparametric magnetic resonance imaging (LiverMultiScan, LMS), liver stiffness measurement using vibration controlled transient elastography (Fibroscan, FS), and liver stiffness measurement using magnetic resonance elastography (MRE).

**Aim:** To examine the baseline patient characteristics and the relationship between LMS, FS, and MRE in an ongoing single site trial of the antifibrotic GR-MD-02 in NASH patients with stage three fibrosis. (https://clinicaltrials.gov/ct2/show/NCT02421094?term=GR-MD-02&rank=6)

**Methods:** 30 patients, all with biopsy confirmed NASH and stage 3 fibrosis, were enrolled in a double-blind, placebo-controlled clinical trial comparing placebo (15 patients) with 8 mg/kg GR-MD-02 (15 patients). All enrolled patients had baseline non-invasive assessment within one month of randomization with LMS (Perspectum Diagnostics), MRE (Siemens), and FS (EchoSens).

**Results:** The mean age and BMI of the enrolled patients were 58.2...
years and 35.6 kg/m2, respectively. The cohort included 16 men and 14 women, 29 of whom were white with 12 Hispanic and one Asian and 6 had diabetes. Median (IQR, 25th-75th percentile) values for LMS, FS, and MRE were a cT1 value of 974 (950-1009) milliseconds, 14.6 (11.2-23.9) kPa, and 4.2 (3.3-5.4) kPa, respectively. There was significant correlation between FS and MRE measures of liver stiffness (r = 0.6, P<0.0005), and when two FS outliers were removed the correlation improved (r = 0.81, P<0.0005). In contrast, there was no significant correlation between LMS cT1 and either liver stiffness measurement, FS (P=0.11) or MRE (P=0.12).

**Conclusion:** Liver stiffness measured by FS and MRE, both of which have been shown to relate with the degree of liver fibrosis, are well correlated in this cohort of NASH patients with biopsy proven stage 3 fibrosis. LMS cT1 and LIF, which is a composite if steatosis, inflammation and fibrosis is not well correlated to either measure of liver stiffness, possibly because it evaluates a combination of fibrosis and necroinflammation.

**61. Poster Presentation #1154**

**#1154: ALT AS A NON-INVASIVE BIOMARKER OF HISTOLOGICAL RESPONSE TO PHARMACOTHERAPY IN NASH PATIENTS: INSIGHTS FROM THE ELAFIBRANOR GOLDEN505 TRIAL**

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**Background and aims:** While ALT imperfectly predicts histological severity, a relation between ALT changes and histological response (HR) in treated NASH patients (pts) has been suggested. If confirmed, this will help predict treatment efficacy without the need for a control liver biopsy. We assessed ALT and histological changes in the 1-year GOLDEN505 randomized trial of elafibranor (ELA).

**Methods:** Pts treated with placebo (PBO, N=77) or ELA 120mg (N=77) were included. HR was defined as resolution of NASH without fibrosis worsening. All completers (N=154) and NAS4 (NAFLD activity score) completers (N=129), both with high baseline ALT (N=75), ATLThigh: ALT>1.5 ULN and low baseline ALT (N=79, ALTlow: ALT≤1.5 ULN) were analyzed for effects on ALT and HR. HR was also assessed in pts with ALT decrease (N=99) or with stable or increased ALT (N=53) at end-of-treatment.

**Results:** At baseline, median ALT was higher with increasing NAS: 41 IU/ml in NAS=3 to 63 IU/ml in NAS=6 (p<0.001). ATLThigh had more severe histological lesions than ALTlow (NAS=5.41.2 vs 4.61.2, p<0.001). When considering baseline ALT, the HR rate was higher with ELA than with PBO in ATLThigh pts (22% vs 11%, respectively, OR=11.6, p<0.001) while in ALTlow pts the difference was lower: 22% vs 18%, OR=1.54, p=0.5. This was confirmed in NAS4 pts (ALTThigh: 22% ELA vs 8% PBO, OR=18.6, p<0.001 ALTlow: 19% ELA vs 15% PBO, OR=1.97, p=0.4). Compared to PBO, ELA reduced ALT both in ATLThigh and in ALTlow (LSmeanSE was -9.910.1 % and -13.912.3 % respectively). When considering ALT changes on treatment, the HR rate was higher in pts with an ALT decline than in those with stable or increasing ALT (26% (26/99) vs 4% (2/53), p<0.001). Also, ALT changes were larger in HR (N=28) than in non responders (N=126): -29.23% vs +157% p<0.001. In both ELA and PBO, a progressive decrease in ALT was observed in HR but not in non-responders. In ELA, ALT reduction was higher in HR (N=17) than in non-responders (N=60): 3423% vs -367, p<0.05. Similarly, in PBO, ALT reduction was higher in HR than in non-responders (N=66): -2021% vs +547%, p<0.05. In pts with declining ALT, ELA had higher HR rates than PBO (30% vs 22%, OR = 2.05, p<0.145) with a stronger difference for NAS4: 30% vs 16%, OR = 3.21, p<0.05).

**Conclusion:** A decline in ALT is associated with histological improvement, particularly on active pharmacotherapy. Pts who resolve NASH have the strongest time-dependent reduction in ALT. A higher baseline ALT is associated with more active disease and better response of HR to ELA over PBO. Although ALT reduction is not an absolute predictor of HR it may provide important insight on treatment effect.

**62. Poster Presentation #1161**

**#1161: IMPROVED NONINVASIVE PREDICTION OF LIVER FIBROSIS BY LIVER STIFFNESS MEASUREMENT IN PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE ACCOUNTING FOR CONTROLLED ATTENUATION PARAMETER VALUES**

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**Background and aims:** Liver stiffness measurement (LSM) frequently overestimates the severity of liver fibrosis in Nonalcoholic Fatty Liver Disease (NAFLD). Controlled Attenuation Parameter (CAP) is a new parameter provided by the same machine used for LSM, and associated with both steatosis and BMI, the two factors mostly affecting LSM performance in NAFLD. We aimed to determine whether prediction of liver fibrosis by LSM in NAFLD patients is affected by CAP values.

**Methods:** Patients (n=324) were assessed by clinical and histological (Kleiner score) features. LSM and CAP were performed using the M+ probe. CAP values were grouped by tertiles (lower from 132 to 298, middle from 299 to 338, higher form 339 to400 dB/m).

**Results:** Among patients with F0-F2 fibrosis, mean LSM values expressed in kPa increased according to CAP tertiles (68 vs. 86 vs. 94 pt=0.001), and along this line the AUC of LSM for the diagnosis of F3-F4 fibrosis was progressively reduced from lower to middle and further to higher CAP tertiles (0.915, 0.848-0.982 0.830, 0.753-0.908 0.806, 0.723-0.890). As a consequence, in subjects with F0-F2 fibrosis, the rates of false-positive LSM results for F3-F4 fibrosis increased according to CAP tertiles (72% in lower vs.166% in middle vs. 18.1% in higher). Consistent with this, a decisional flow-chart for predicting fibrosis was suggested by combining both LSM and CAP values.

**Conclusions:** In patients with NAFLD, CAP values should always be taken into account in order to avoid overestimations of liver fibrosis assessed by TE.

**63. Poster Presentation #1167**

**#1167: HEPATIC STEATOSIS IN CROHN’S DISEASE – NON-INVASIVE COMPARISON BETWEEN NASH AND CROHN’S**

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Recent studies indicate an increasing prevalence of hepatic steatosis and non-alcoholic steatohepatitis (NASH) in several alimentary tract diseases, including inflammatory bowel diseases (IBD). We and others have shown that NASH in IBD patients is associated with an increased susceptibility for acute-on-chronic liver failure. To date, little is known about the mechanisms leading to hepatic steatosis in IBD. With this study, we aimed to analyze and compare non-invasive predictors of liver injury in patients with NASH and individuals with Crohn’s disease (CD). Therefore we included patients with established NASH and patients with established CD without a history of liver disease and analyzed serum markers of liver injury, a breath test for small intestinal bacterial overgrowth (SIBO) and transient elastography as well as controlled attenuation parameter (CAP) to assess hepatic steatosis. As expected, patients with NASH had a significantly higher BMI compared to CD. Accordingly ALT and AST levels were significantly higher in NASH vs. CD. SIBO occurred in only two individuals and was not associated with steatosis. Interestingly, while transient elastography revealed increased liver stiffness in NASH vs. CD, there was no significant difference in CAP as a measure for hepatic steatosis between the groups. In fact, 43.8% of CD patients had a CAP > 283 dB/m, a previously established cutoff value for significant hepatic steatosis with a maximum CAP of 400 dB/m in one patient. Although most patients remained within normal limits, AST and ALT were significantly higher in CD patients with CAP > 283 dB/m compared to CD patients with lower CAP results. In order to identify conditions associated with higher CAP results, we reviewed the patients’ drug regimens. To our surprise, steroid therapy was not associated with CAP in this cohort. However, individuals with CAP below 283 dB/m were more likely to be treated with biologicals. In fact, CAP was significantly lower in patients on biologicals as compared to other treatment strategies (237.3 11.7 vs. 306.2 20.6 dB/m p<0.05). Thus, in this cohort, NASH was associated with higher BMI, transaminase levels and liver stiffness, while hepatic steatosis as assessed by CAP was not pronounced compared to CD. In CD patients with significant steatosis, higher transaminase levels indicate subclinical hepatic inflammation, despite being within normal limits. Treatment with biologicals seems to protect CD patients from hepatic steatosis. In conclusion, we identified a high rate of hepatic steatosis in CD with alterations in transaminase levels and a potential association with biologicals.

#64. Poster Presentation #1168

#1168: A PROSPECTIVE STUDY TO EVALUATE THE EFFICACY OF A STANDARDIZED LOW CALORIE DIET ACCORDING TO PNPLA3 GENOTYPE IN PATIENTS WITH NON ALCOHOLIC FATTY LIVER DISEASE (NAFLD) – WEEK 2 DATA INTERIM ANALYSIS

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Background: Approximately 30% of the Western population suffers from NAFLD, rising up to 90% in obese people. Complications of NAFLD include Non Alcoholic Steatohepatitis (NASH), liver cirrhosis, hepatocellular carcinoma as well as aggravation of diabetes and cardiovascular diseases. PNPLA3 is an important genetic factor associated with NAFLD. Aim of the study is to analyze the efficacy of a standardized low calorie liver diet (HEPAFAST, Bodymed, Kierkel, Germany) especially compounded for NAFLD patients (pts) and the influence of PNPLA3 genotypes on treatment outcome.

Methods: In this study 81 non cirrhotic patients are stratified according to PNPLA3 genotypes (27 patients per group CC, CG, GG). All patients receive a protein shake therapy (HEPAFAST) for 2 weeks and instructions to follow a low glycemic and insulinemic (LOGI) diet for another 6 weeks (EOT). All patients are seen longitudinally for four time points (baseline, week 2, 2 months and 6 months follow-up). At each time point liver fat content is assessed by an independent/blinded investigator with Fibroscan CAP. Additionally Fatty Liver Index (FLI), waist circumference (WC), BMI, HbA1c, triglycerides (TG) and GGT are analyzed.

Results: To date 31 patients were included in this study, 26 pts [age 439.6 (meanSD m:19, f:7 PNPLA3 genotypes: CC:15, CG:8, GG:3] finished the HEPAFAST Shake therapy from baseline to week 2. All outcome variables decreased till week 2 (second time point): (1) Fibroscan CAP 322.931.6 dB/m2 to 270.736.0 (52.232.0 p<0.001), (2) FLI 79.416.1 to 60.022.0 (p<0.001), (3) WC 109.785.5cm to 106.290.0 (p<0.001), (4) BMI 32.437.7 to 30.830.0 (p<0.001), (5) HbA1c 5.40.3% to 5.30.0 (p=0.092), (6) TG 128.777.6mg/dl to 86.773.0 (p<0.001) and (7) GGT 44.731.1U/l to 30.818.0 (p<0.001). Evaluation according to PNPLA3 genotype revealed a higher Fibroscan CAP drop for PNPLA3 G-allele carriers [CC: 316.435.1 to 271.543.6 (44.935.5) vs G-allele carriers 331.725.0 to 269.623.8 (62.231.0) p=0.12]. 16 patients finished the HEPAFAST Shake therapy from baseline to week 2. All outcome variables decreased till week 2 (second time point): (1) Fibroscan CAP 322.931.6 dB/m2 to 270.736.0 (52.232.0 p<0.001), (2) FLI 79.416.1 to 60.022.0 (p<0.001), (3) WC 109.785.5cm to 106.290.0 (p<0.001), (4) BMI 32.437.7 to 30.830.0 (p<0.001), (5) HbA1c 5.40.3% to 5.30.0 (p=0.092), (6) TG 128.777.6mg/dl to 86.773.0 (p<0.001) and (7) GGT 44.731.1U/l to 30.818.0 (p<0.001). Evaluation according to PNPLA3 genotype revealed a higher Fibroscan CAP drop for PNPLA3 G-allele carriers [CC: 316.435.1 to 271.543.6 (44.935.5) vs G-allele carriers 331.725.0 to 269.623.8 (62.231.0) p=0.12]. 16 patients finished 2 month treatment period including LOGI diet. Fibroscan CAP further decreased from baseline to 2 months [328.927.8 to 248.631.9 (80.328.0) p<0.001].

Conclusion. A low calorie diet with HEPAFAST shakes is a very effective strategy to significantly lower liver fat in NAFLD patients. This effect seems to be more pronounced in patients carrying the PNPLA3 G-allele.

#65. Poster Presentation #1178

#1178: CYTOKERATIN 18 AND TRANSIENT ELASTOGRAPHY WITH CONTROLLED ATTENUATION PARAMETER AS SCREENING TOOLS FOR NONALCOHOLIC STEATOHEPATITIS IN HIV MONO-INFECTED PATIENTS

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Background: Persons living with HIV are at high risk of nonalcoholic steatohepatitis (NASH). However, data on NASH in HIV mono-infection are scarce.

Methods: We conducted a prospective screening study of prevalence and predictors of NASH in unselected HIV mono-infected patients by the serum biomarker cytokeratin 18 (CK-18) and transient elastography (TE) with associated controlled attenuation parameter (CAP). Patients with significant alcohol intake or coinfection with hepatitis B or C were excluded. NASH was defined as presence of fatty liver (CAP >238 dB/m) and CK-18 >246 U/L. Those cases defined as NASH were offered a liver biopsy. Significant liver fibrosis and cirrhosis (stage 2 and 4 out of 4, respectively) were defined as TE measurement 7.1 and 13 kPa, respectively. Predictors of NASH were determined using multivariable logistic regression analysis.

Results: 159 consecutive HIV mono-infected patients (median age 52.7, IQR 46.58.8 years, 81.5% men, median CD4 count 605, IQR 451-798 cell/ul, 90% on antiretrovirals) were included. Fatty liver and NASH were diagnosed in 49.7% and 9.4% of cases, respectively. Significant liver fibrosis and cirrhosis were more frequent in patients with NASH.
than those without NASH (see Figure, p<0.001). After adjusting for age and BMI, elevated ALT (OR=12.4, 95% CI 2.9-54.1, p=0.001) and TE measurement >7.1 (OR=7.8, 95% CI 1.9-31.8, p=0.004) were independent predictors of NASH. 13 out of 15 patients with a non-invasive diagnosis of NASH agreed to undergo a liver biopsy and histology confirmed NASH in all cases.

**Conclusion:** Hepatic steatosis diagnosed by CK-18 and TE with CAP is very frequent in HIV mono-infected persons, particularly in case of elevated ALT and TE measurement. A non-invasive diagnostic strategy employing these non-invasive tools can help early identification of NASH and initiation of interventions by reducing the need for liver biopsy in persons living with HIV.

**Figure:**

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**66. Poster Presentation #1179**

**#1179: CONTROLLING HIV USING CART CONTRIBUTES TO METABOLIC DISORDER AND HEPATIC STEATOSIS**

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**Objectives:** Available data on the prevalence of hepatic steatosis (HS) in a real-life HIV-infected population are scarce and discrepant. Controlled attenuation parameter (CAP) determination is accurate in identifying significant hepatic steatosis (fat accumulation in >10% of hepatocytes). The aim of this study was to assess the prevalence and factors associated with significant hepatic steatosis in HIV-infected patients.

**Methods:** 364 HIV-infected patients were included in this prospective, cross-sectional study. All patients underwent controlled attenuation parameter (CAP) determination. Steatosis was classified as S1 (significant steatosis) in CAP>238 dB/m, S2 in CAP>260 dB/m, S3 in CAP>292 dB/m. Logistic regression and Cox-regression univariate and multivariate analyses were performed to analyze the associations between HS and demographics, metabolic data, virologic factors and antiretroviral therapy.

**Results:** 287 (79%) were HIV mono-infected, 20 (6%) were HBsAg-positive, 57 (16%) were anti-HCV-positive, of which 31 (54%) had achieved sustained virologic response (SVR). Significant hepatic steatosis was detected in 149 (41%) patients (S1:229%, S2:34%, S3:37%). Interestingly, less severe steatosis was observed in patients with a longer duration of known HIV-infection (10 [0-29] vs. 12 [0-29] yrs, p = 0.031), and longer cART naive periods [2 [0-20] vs. 3 [0-21] yrs, p = 0.037]. As expected, patients with significant steatosis showed higher mean HbA1c levels [5.3 (2.7-8.1) vs. 5.5 (3.6-11.4), %, p=0.015], higher mean BMI [23 (15-41) vs. 26 (19-38) kg/m2, p < 0.001], higher triglycerides [153 (28-1549) vs. 228 (43-1193) mg/dl, p < 0.001] and lower HDL cholesterol [50 (8-127) vs. 45 (18-100) mg/dl p = 0.002] compared to patients without steatosis. Interestingly, multivariate analysis revealed that while BMI was independently associated with steatosis [OR, 1.24, 95% CI, 1.12-1.37, p < 0.001], longer cART-naive periods [HR, 0.90, 95% CI, 0.83-0.94, p < 0.001] were associated with less hepatic steatosis development. No impact on severity of steatosis was identified for any antiretroviral drug class.

**Conclusions:** Hepatic steatosis is highly prevalent among HIV-infected patients. Obesity is an independent predictor of steatosis development, while suppression of viral replication might contribute to hepatic steatosis, which however was not related to antiretroviral drugs known to cause metabolic changes.

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**67. Poster Presentation #1186**

**#1186: COMPARISON OF NON-INVASIVE MARKERS FOR ASSESSING FIBROSIS IN ASIAN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE**

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**Background and aims:** The prevalence of non-alcoholic fatty liver disease (NAFLD) is increasing 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:** A total of 214 patients who underwent liver biopsy and concomitant TE were recruited from a tertiary hospital in Korea and analyzed between November 2011 and December 2014. Liver fibrosis was assessed using AST to Platelet Ratio Index (APRI), NAFLD fibrosis score, and Fibrosis-4 (FIB-4).

**Results:** The study population were separated into a control group (n = 103) and a NAFLD group (n = 111) based on liver biopsy results. Patients with NAFLD had a mean age of 39.7 years and there was a male predominance (n = 85, 76.6%). The accuracy of CAP for detecting steatosis grade, assessed by the area under the receiver operating curve (AUROC), was 0.882, 0.906, and 0.870 for S1, 281 dB/m for S2, and 315 dB/m for S3. 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. Moreover, the AUROC for LS for detecting fibrosis grade were 0.996, 0.980, and 0.980 for F2, F3, and F4, respectively. The optimal cut-off values for liver 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 values for detecting F3 and F4 were good (F3: 100% and 72%, respectively, and F4: 80 and 98%, respectively), and were better than other noninvasive markers, including APRI, NAFLD fibrosis score, and FIB-4. Approximately 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.

**Conclusion:** TE resulted in the accurate detection of not only steatosis but also fibrosis in patients with NAFLD. In addition, TE had better sensitivity and specificity for detecting advanced fibrosis and cirrhosis than other noninvasive markers.

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**68. Poster Presentation #1429**

**#1429: HOW TO DEFINE SPLENOMEGLYAL IN THE DIAGNOSIS OF LIVER CIRRHOSIS?: SIGNIFICANCE OF SPLENIC VOLUME MEASUREMENT USING ULTRASONOGRAPHY**

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**Background:** To date, there is no acceptable criterion of spleen size for the clinical diagnosis of liver cirrhosis even though the recent Baveno consensus states splenomegaly is an adjunctive finding to define liver cirrhosis. We evaluated how relevant spleen volume (SV) measured by ultrasonography is to liver fibrosis stage and investigated the optimal
Methods: Total 431 patients whose SV was measured by ultrasonography (length x height x width x l/6) and got a liver biopsy were included in this study. The measured SV by ultrasonography was validated with computed tomography. Spleen volume/body surface area (SV/BSA) in each patient was used for sensitivity analysis. Fibroscan (kPa) was compared to SV for the relation with liver fibrosis stage.

Results: The baseline characteristics of the patients were as follows: mean age (49±11.22), hepatitis B (190, 44.1%), Child-Pugh class [(A/B/C, 339(78.7%)/75(17.4%)/17(3.9%)], fibrosis stage [F0/F1/F2/F3/F4, 35(8.1%)/40(9.3%)/60(14.5%)/61(16%). SV was significantly larger in young age (<40), male sex, viral hepatitis, high BSA, high MELD and Child-Pugh score. SV was well correlated with fibroscan score (r=0.059, p<0.001). Mean SV (ml) according to fibrosis stage was F0 (16959), F1 (18999), F2 (19882), F3 (23679), F4 (457283). AUROC's of SV and SV/BSA for predicting cirrhosis were 0.891 (95% confidence interval, 0.862-0.921), 0.905 (95% CI, 0.878-0.932). Optimal cut-off of SV and SV/BSA for the diagnosis of cirrhosis were 268ml, 161ml respectively.

Conclusions: Spleen volume measured by ultrasonography was gradually increased according to liver fibrosis stage. SV measurement using ultrasonography is useful as a supplementary method for the diagnosis of liver cirrhosis.

Methods: For 69 patients who require NSBB treatments due to severe PHT were included and both LSM and HVPG measurements before and after 3 months NSBB treatment. The correlations between LSM and histological fibrosis grade using collagen proportion area (CPA), and HVPG, before and after 3 months NSBB treatment were compared.

Results: The etiologies of cirrhosis were composed of alcohol (n=56, 81.2%) and HBV (n=13, 18.8%). 43 patients (62.3%) were NSBB responders. In total population, the mean CPA was 28.67 ± 11.80% and the mean baseline LSM was 44.28 ± 17.96 kPa. The baseline CPA was significantly correlated with baseline LSM (R=0.593, p<0.001). After treatment, the LSM was 31.92 ± 15.70 kPa, and the baseline CPA was more significant correlated with post-treatment LSM (R=0.819, p<0.001). In NSBB responder, the correlation between LSM and CPA was more significant and stronger after NSBB treatment (R=0.723, p<0.001) than pre-treatment (R=0.483, p=0.001). These trends were also shown in NSBB non-responder, the correlation was more significant and stronger after NSBB treatment (R=0.765, p<0.001) than pre-treatment (R=0.725, p<0.001). The baseline CPA was statistically significant greater in NSBB non-responder than NSBB responder (24.13 ± 7.60% vs. 36.18 ± 13.69%, p<0.001). The baseline HVPG and after treatment HVPG were 16.90 ± 3.66 mmHg and 12.86 ± 4.67 mmHg. Both baseline HVPG-LSM and post-treatment HVPG-LSM correlation showed significant correlation respectively ((R=0.430, p<0.001), (R=0.646, p<0.001)). In responder group, LSM was more closely correlated with HVPG after NSBB treatment (R=0.620, p<0.001) compared to baseline LSM-HVPG correlation (R=0.435, p=0.004).

Conclusion: The hepatic congestion by severe portal hypertension can influence on LSM. The closer correlations between LSM and CPA after NSBB treatment suggest that LSM include not only static but also hemodynamic component that can reflect PHT. However this hemodynamic component is prominent in histologically less collagen accumulated cirrhosis.

#1445: AVAILABILITY OF CONTRAST-ENHANCED ULTRASONOGRAPHY FOR THE EVALUATION OF PARTIAL SPLENIC EMBOLIZATION IN CIRRHOTIC PATIENTS WITH HYPERSPLENISM

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Aims: The present study investigates whether contrast-enhanced ultrasonography (CE-US) using perfluorbutane can be therapeutically applicable as an evaluation modality of partial splenic embolization (PSE) compared with contrast-enhanced computed tomography (CE-CT).

Methods: From January 2013 to August 2015, 39 cirrhotic patients (mean age=65.4 years, female/ male=16/14, hepatitis B virus/hepatitis C virus/alcohol/ others=2/17/8/3, Child-Pugh class A/B/C=17/12/1) with hypersplenism were treated by PSE with the aim of increasing platelet count. Wedged hepatic venous pressure (wHVP) was measured immediately before and after the PSE procedure. CE-US, CE-CT, and transient elastography (TE) were performed before and 1 week after PSE.

Results: Embolization of splenic artery resulted in a significant decrease in both splenic venous volume (241.2 to 107.5 ml/min, p<0.01) and portal venous volume (PVV, 1335.0 to 986.3 ml/min, p<0.01) ultrasonographically. PSE significantly reduced wHVP (292.1 to 244.7 mmH2O, p<0.01), and values for liver stiffness measured by TE showed a decreasing tendency following PSE (18.5 to 15.2 kPa, p=0.09). In addition, there was a positive correlation between a decrease in PVV and a reduction not only in wHVP but also in values
for liver stiffness post-PSE, indicating that changes in portal venous pressure and liver stiffness following PSE might reflect changes in portal-splenic hemodynamics induced by the procedure. Meanwhile, platelet count increased significantly from 54.4 x 109/L before PSE to 125.9 x 109/L 1 month after PSE (p<0.01), with mean number and mean rate of increase in platelet count of 69.2 x 109/L and 264.2 %, respectively. The splenic infarction ratio (SIR) measured by CE-US was almost equivalent to that measured by CE-CT (76.5 % vs. 78.0 %), and a statistically significant correlation was observed between them (r=0.61, p<0.01). In addition, the SIR by CE-US was positively associated with both the number and the rate of increase in platelet count 1 month after PSE [r=0.56 (p<0.01) and r=0.41 (p<0.05), respectively], compared favorably with that by CE-CT [r=0.50 (p<0.01) and r=0.20 (p=0.27), respectively]. These results suggested that CE-US could replace CE-CT as the standard modality to evaluate the SIR post-PSE.

Conclusions: The US can evaluate hemodynamic changes in portal-splenic venous system in response to PSE, unlike the CT scan. Moreover, CE-US would be comparable to CE-CT in terms of SIR measurements after PSE. Consequently, the US, especially CE-US, will be therapeutically applicable as a less-invasive modality that is useful for the evaluation of PSE for cirrhotic patients with hypersplenism.

71. Poster Presentation  #1449

#1449: LDV/SOF COMBINATION IS ASSOCIATED WITH 100% SVR IN PATIENTS WITH THALASSEMIA MAJOR: A PRELIMINARY REPORT FROM AN ITALIAN MULTICENTER STUDY

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Background and aims: The combination of interferon (IFN) and ribavirin (RBV) for the treatment of chronic hepatitis C in patients with thalassemia major is complicated by poor tolerability. We evaluated the efficacy and safety of the IFNand, most importantly, RBV free regimen of ledipasvir/sofosbuvir (LDV/SOF) for 12 weeks, in both IFN naïve and treatment experienced chronic genotype 1 and 4 HCV infected patients with thalassemia major.

Methods: We planned to treat, at 5 different Italian centres, 100 patients with thalassemia major and chronic HCV infection with LDV/SOF (90/400 mg) FDC once daily for 12 weeks. Patients were stratified by treatment history and presence of cirrhosis. Cirrhosis was defined by a liver biopsy (Metavir score 4) or by Fibroscan (value >12,5 KPa). The presence of compensated or decompensated cirrhosis and concomitant previous IFN and RBV treatment failure was an exclusionary criterion. The primary endpoint was undetectable HCV RNA 12 weeks after the end of treatment (SVR12), by an assay with sensitivity of 12 or 15 HCV RNA IU/ml. An interim analysis was planned.

Results: Fifty-five of 100 patients are included in this analysis. The remaining patients are on screening or just started treatment. Overall SVR4, currently available in 43 of 55 patients, will be presented. At baseline, the majority of patients were male (56%), mean age was 42 yrs (33-54) most patients were infected with 1b HCV (90%), had viral load 800.000 IU/ml (78%), 76% carried IL28B non-CC genotype. Compensated cirrhosis was diagnosed in 14.6% of cases, 67% were treatment naïve. At baseline, mean Hb value was 10.5 g/dl (8.1-13.5), mean ferritin value was 339 ng/ml (92965), mean LIC was 7.3mg/kg/dry weight. All but 2 patients achieved undetectable HCV RNA 4 weeks after the start of treatment. All patients with available data achieved SVR4. No increase in the number of blood transfusion was observed during treatment.79% of patients experienced at least one side effect. The most frequent side effects were headache (18%), asthenia (10%), and fatigue (11%). All were of mild severity. No side effects assessed as treatment related were reported. No drug to drug interactions were registered, regardless of the chelation treatment adopted.

Conclusions: In HCV GT 1 and 4 patients with thalassemia major and HCV chronic infection, LDV/SOF treatment for 12 weeks appears safe and effective. 100% SVR rates were observed at this interim analysis and treatment was well tolerated.

72. Poster Presentation  #1475

#1475: HCV CURE: INCREASES BODY WEIGHT AND LIVER FAT CONTENT

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Background: FibroScan with Controlled Attenuation Parameter (CAP) offers a novel, non-invasive means of assessing steatosis along with liver stiffness. We previously reported that hepatitis C virus (HCV) cure is accomplished by an increase in body mass index (BMI), Chekuri et al., PlosOne, in press). The impact of sustained virologic response (SVR) on steatosis remains to be described. Objective: To measure changes in BMI, body weight and liver fat content in patients who achieve SVR after HCV treatment with direct acting antiviral drugs.

Methods: Demographic, virologic and anthropometric data were collected on all adult patients with pre-treatment (Tx) and post-SVR weight and CAP measurements who were treated for chronic HCV at Mount Sinai between July 2015 and May 2016. Liver stiffness and liver fat content were measured by transient elastography (TE) in combination with CAP (a validated method for assessing hepatic steatosis). Overweight and obesity were defined by a body mass index (BMI) of 25.0 – 29.9 kg/m2 and >30.0 kg/m2, respectively. Cirrhosis was defined by a FibroScan score 12.5 KPa. Pre-Tx and post-SVR weights, CAP scores, BMI, and proportion of cohort with advanced steatosis (CAP>300 dB/m) were compared using paired t-tests, while correlation between percent weight and percent CAP changes was calculated using Spearman’s rank coefficient.

Results: Fifty-three patients were included 66% (n=35) were male, and the median age was 56 years (range 27-77). Eight (15%) were co-infected with HIV and 23% (n=12) were cirrhotic. Most (n=48) patients had genotype 1 infection, three had genotype 3 and two had genotype 4. Median pre-Tx BMI was 25.9 kg/m2 (range 18.139.1), and median pre-Tx CAP score was 233 dB/m (range 100-381). SVR was associated with a median weight gain of 4 (range -16 +17) pounds, increase in BMI of 0.64 kg/m2 (range -2.93 +3.33) and increase in CAP of 20 dB/m (range -71 +233) (all p<0.01). There was a net increase of 22% in patients with steatosis, 11% with advanced steatosis and 4% with obesity. Changes in weight were positively correlated with changes in liver fat (p=0.028). There was no correlation between change in liver stiffness and weight change or CAP change. In males, SVR was associated with a median weight gain of 4 pounds (range -13 +17), increase in BMI of 0.7 kg/m2 (range -1.4 – 3.33) and an increase in CAP of 25 dB/m (range -71 +128) (all p<0.01). These parameters did not
change significantly in females.

Conclusion: HCV cure is accompanied by modest increases in, BMI, weight, and liver fat content. Further investigation is needed to determine the clinical significance of these changes.

73. Poster Presentation  #1635

#1635: 100% VIROLOGICAL RESPONSE WITH 3D REGIMEN AND SIGNIFICANT SHORT-TERM LIVER STIFFNESS IMPROVEMENT IN PATIENTS WITH RECURRENT HEPATITIS C FOLLOWING LIVER TRANSPLANTATION

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Background: Over recent years, interferon-free regimens offer the prospect of treating the high-risk patient groups (liver cirrhosis/liver transplant recipients) with high SVR rates across all genotypes.

Aim: To present our experience with DAA agents in LT recipients, as well as to compare pre and posttreatment liver stiffness.

Methods: Our cohort consisted of 72 patients with recurrent hepatitis C after LT. All patients received associated ribavirin. The 3rd regimen was administered 24 weeks. FibroscanÒ and FibromaxÒ were performed in all patients before DAA therapy. At EOT and at time of SVR12 evaluation only Fibroscan was performed.

Results: There were analyzed 32 females and 40 males with a mean age of 55±27 years. Median time since LT was 266 months (range 46-1769 months). At baseline 56±4% of patients had severe necroinflammation at Fibromax, cirrhosis (F4) was encountered in 34±5% of LT recipients and grade 3 steatosis in 43±6% of transplanted patients. On treatment virologic response was 100%. End of therapy in this cohort of LT patients was 100%. However, at week 2 after beginning of therapy, only 13±9% of LT recipients were HCV RNA undetectable. Undetectable HCV RNA at 4 weeks of therapy was present in 66±7% of patients with recurrent hepatitis C, but at week 8 all patients were HCV RNA undetectable. Viral load positivity at week 4 was not influenced by baseline HCV RNA or stage of fibrosis. Liver stiffness (LS) differed statistically significant according to the activity grades (p=0.02) and fibrosis stages (p=0.0001) at Fibromax. There was a significant improvement in LS between antiviral therapy start and EOT: 11918kPa vs 9510kPa (p=0.02) in LT recipients.

Conclusion: Virological response was 100% at EOT LS can reliably assess both inflammation and fibrosis in LT recipients and can be used to follow these patients after HCV eradication. LS significantly decreased after EOT and suggests improvement in liver damage. Data regarding LS at SVR12 will be available at the meeting.

74. Poster Presentation  #1643

#1643: THE EFFECT OF A 12-MONTH WEIGHT LOSS PROGRAM ON NON-ALCOHOLIC FATTY LIVER DISEASE IN OBESE PATIENTS

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Background: 20-30% of the Western population is estimated to have Non-alcoholic fatty liver disease (NAFLD), and 2-3% of the population has Non-alcoholic steatohepatitis (NASH). [i] Lifestyle modification programs for weight-loss are the current accepted standard of care for these patients. The effect of long term weight control on liver stiffness is still lacking. The goal of this weight loss program is to evaluate the association of % total body weight loss and the improvement in alanine-aminotransferase (ALT), aspartate-aminotransferase (AST), and fibrosis scores as measured by transient elastography using FibroScan (Echosens).

Methods: 37 patients were enrolled in a year-long nutritional counseling program. 34 of these patients successfully completed the program 2 patients voluntarily resigned, and 1 was lost to follow-up. Blood tests, including ALT and AST values prior to the start of the program, at the 6-month point, and at the end of the program, were done. 31 of the patients had transient elastography at the same time points. Categorical variables were analyzed with descriptive statistics. Paired t-tests to evaluate changes in weight, ALT, and AST.

Results: 34 patients completed the program. The mean weight was 220.8 lbs. 28, and BMI was 36.2 ± 0.5. Laboratory values initially were ALT 27.1 ± 21 and AST 22.2 ± 12. Liver stiffness using FibroScan was 6.43 kPa ± 0.7. Four patients had liver fibrosis 2/4. At 12 months, the mean weight was 195.7 ±66 (range 155.2-298.5) [p=0.001] and BMI was 34.5 ±3 (range 28.3-42.8) [p=0.000]. Serum ALT 18.9 ±12 (range 7-72) and AST 17.3 ±7 (range 11-42) decreased significantly [p=0.001]. Liver stiffness significantly improved to 5.69 kPa ± 5.7 (range 1.5-21.3 kPa) [p=0.000]. The data shows that a mean of 1.1% (0.3-4%) total body weight loss is associated with improvement in ALT, AST, and liver stiffness scores as measured by serial laboratory tests and transient elastography.

Conclusion: Weight loss of 0.2-4% showed significant improvement in 1) transaminases (ALT, AST), 2) BMI, and 3) liver stiffness. Although study subjects had near to normal transaminases, weight loss resulted in significant drop in their transaminase levels. This study confirms the value of lifestyle changes resulting in weight loss and underscores the normal levels for ALT and AST.

75. Poster Presentation  #1684

#1684: BIOLOGICAL SIGNIFICANCE OF CONNECTIVE TISSUE GROWTH FACTOR AND ITS POTENTIAL AS A NOVEL THERAPEUTIC TARGET IN HEPATIC FIBROSIS

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Background and aim: Connective tissue growth factor (CTGF) is one of secreted matricellular proteins related with several systemic diseases. We analyzed the biological significance of CTGF in hepatic fibrosis.

Methods/Results: We examined CTGF gene expression under approval of institutional ethics committee. In 97 liver biopsy samples, CTGF expression levels increases along with the progression of fibrosis score and positively correlated with those of other fibrosis-related genes such as β-SMA, TGFb1, and Colla1a1. In addition, CTGF expression showed positive correlation with several fibrosis markers including serum hyaluronate and type 4 collagen levels, FIB-4 index, and shear wave velocity of ultrasound elastography, and negative correlation with platelet count. In mice experiments, CTGF was also up-regulated in the liver after bile duct ligation (BDL). CTGF was up-regulated both in primary liver parenchymal cells (PC) and non-parenchymal cells (NPC) isolated from mice underwent BDL compared with those isolated from sham-operated mice. In vitro experiments revealed that the treatment of TGF-b, an inducing factor of CTGF, increased CTGF production in hepatocyte cell lines and a hepatic stellate cell (HSC) cell line LX-2, but not in a macrophage cell line, suggesting that hepatocytes and HSC might mainly produce CTGF in the fibrotic liver. Recombinant CTGF treatment induced the activation and collagen production in LX-2. In turn, siRNA-mediated knockdown of CTGF decreased the viability of LX-2. In addition, CTGF treatment induced the production of pro-fibrotic cytokines such as PDGF, TGFb1, and TIMP-1 from hepatocyte cell line PLC/PRF/5. These results suggest a promoting effect of CTGF in liver fibrosis. We subsequently evaluated the influence of CTGF deficiency after BDL in 3 strains of conditional CTGF knockout mice HSC-specific CTGF deficient mice (GFAP-Cre+ CTGF flox/flox mice CTGFHSC mice), hepatocyte-specific CTGF deficient
mice (Alb-Cre+ CTGF flox/flox mice CTGF Hep mice), and poly IC-induced PC and NPC CTGF deficient mice (MX1-Cre+ CTGF flox/flox mice CTGFPC+NPC mice). As a result, compared with Cre/interm, CTGF expression levels in the liver significantly decreased in CTGF Hep and PC+NPC mice. Only in CTGFPC+NPC mice, fibrosis-related genes such as B5MA, PDGF, TGFβ1, and TIMP-1 were also down-regulated and liver fibrosis was markedly attenuated, evidenced by reduced collagen expression and Sirius Red-stained area.

**Conclusion:** CTGF is produced both from PC and NPC in the fibrotic liver. CTGF acts on HSC and hepatocytes and promotes hepatic fibrosis. CTGF could be a promising therapeutic target against liver fibrosis.

### 76. Poster Presentation  #1707

**#1707: SCREENING OF OESOPHAGOGASTRIC VARICES IN VIRUS-RELATED COMPENSATED ADVANCED CHRONIC LIVER DISEASE: BAVENO VI CRITERIA AND BEYOND**

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**Background:** Recent consensus (Baveno VI) suggests the use of threshold values for Transient Elastography (TE) and platelet count for screening of oesophagogastric varices (OV) in virus-related compensated advanced chronic liver disease (cACLD). According to these criteria, patients with liver stiffness <20 kPa and/or platelet count >150,000/mm³ could safely avoid endoscopy because of a very low risk of varices requiring prophylactic treatment.

**Aims:** 1. To assess the accuracy of Baveno VI criteria in a cohort of HBV and HCV cACLD patients undergoing endoscopic screening for varices. 2. To assess the accuracy of less conservative threshold values for TE (<25kPa < 30KPa) and platelet count (>125,000/mm³; >100,000/mm³).

**Methods:** cACLD HCV and HBV viremic patients undergoing endoscopic screening for upper gastrointestinal varices were evaluated. Exclusion criteria were: TE unavailable or unsuccessful, current hepatocellular carcinoma or other neoplasm, portal vein thrombosis, previous liver decompensation, known OV, splenectomy, Interferon exposure within one year. Laboratory data (within 6 months) and liver stiffness (within 12 months) were retrospectively collected.

**Results:** 165 of 318 patients fulfilled inclusion criteria. Forty three (26%) had varices of these, 14 (8%), all with at least one criterion, had varices requiring prophylaxis. Baveno VI criteria had 100% sensitivity and 100% negative predictive value with low specificity (26%) and positive predictive value (11%). According to these criteria 42 (25%) patients could have safely avoided screening endoscopy. Other, less conservative criteria for TE (<25kPa or <30 KPa) and platelet count (>125,000/mm³) could maintain the highest accuracy (100% sensitivity and 100% negative predictive value) and would have safely avoided endoscopy in 44% and 49% of patients, respectively (p = 0.001 vs Baveno VI criteria). However, further lowering the platelet count threshold to 100,000 would result in additional saving of endoscopies (up to 56% or 64% for <25 kPa or <30 kPa cutoff value), but 7% or 15% patients with large OV would have been missed, respectively.

**Conclusions:** Baveno VI criteria to rule out OV requiring prophylaxis are valid and reproducible in virus-related cACLD and allow sparing 25% endoscopies. Less conservative threshold values for TE (up to <30 KPa) and platelet count (up to >125,000/mm³) could further spare up to 49% endoscopies without losing accuracy. These data need independent validation on larger cohorts of patients.

### 77. Poster Presentation  #1709

**#1709: VIBRATION-CONTROLLED TRANSIENT ELASTOGRAPHY (VCTE) IS USEFUL IN IDENTIFYING CLINICALLY SIGNIFICANT PORTAL HYPERTENSION IN PATIENTS WITH NASH CIRRHOSIS**

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**Introduction:** Portal pressure, as assessed by the hepatic venous pressure gradient (HVPG) is a validated predictor of the development of complications of cirrhosis, particularly in patients with compensated viral/alcoholic cirrhosis where an HVPG 10 mmHg predicts varices and decompensation and an HVPG 12 mmHg predicts variceal hemorrhage. However, measuring HVPG is invasive, expensive and requires special expertise.

**Aim:** To examine the relationship between LSM by VCTE and HVPG in patients with compensated cirrhosis secondary to non-alcoholic steatohepatitis (NASH).

**Methods:** In an ongoing phase 2 multicenter trial of an antifibrotic agent (GR-MD-02), patients with compensated NASH cirrhosis and portal hypertension (HVPG 6 mmHg) (NCT02462967) who underwent both LSM and HVPG (measured within 4 weeks from each other at baseline) were included in this analysis. LSM was obtained using Fibroscan® 502 Touch while HVPG values were obtained from centrally-read HVPG tracings. Identifying patients with HVPG 10 mmHg or 12 mmHg was the primary interest.

**Results:** Seventy four patients with mean age, BMI and MELD score of 59.9 years, 34.6 kg/m² and 7.2 1.3 respectively were eligible for this analysis. Their median [IQR, 25th-75th percentile] LSM was 25.1 (18.1-39.4) kPa and median HVPG was 12.0 (9.0-15.6) mmHg. There was significant correlation between LSM and HVPG (r = 0.4, P = 0.001). The median LSM in 49 patients with HVPG 10 mmHg was 27 (21.3-46.9) kPa and the median LSM in 42 patients with HVPG 12 mmHg was 29.9 (21.7-50.4) kPa. The AUROCs of LSM for identifying HVPG 10 mm Hg was 0.73 (95% CI: 0.60-0.85, P = 0.002) and for identifying 12 mm Hg was 0.74 (95% CI: 0.62-0.86, P<0.001). The LSM cut-offs for identifying HVPG 10 and 12 mm Hg with 90% sensitivity were 15.6 and 16.7 kPa respectively. The LSM cut-offs for identifying HVPG 10 and 12 mm Hg with 90% specificity were 46.1 and 48.0 kPa respectively.

**Conclusion:** In patients with compensated NASH cirrhosis, LSM by VCTE can non-invasively identify NASH cirrhosis with HVPG 10 mmHg or 12 mmHg.

### 78. Poster Presentation  #1732

**#1732: THE NORTHWELL HEALTH REAL WORLD EXPERIENCE: A NOVEL TEAM APPROACH IS SUCCESSFUL IN OVERCOMING BARRIERS OF ACCESS TO OBTAINING HCV DIRECT ACTING ANTI-VIRAL THERAPIES AND OBTAINING SVR RATES OF 97%**

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**Introduction:** Hepatitis C (HCV) is almost universally curable. The greatest barrier to cure has become patient (pt) access to direct
acting anti-viral (DAA) therapies due to non-medical restrictions imposed by payers. In order to overcome these restrictions and obtain access to therapy for all patients (pts), we center created a dedicated team to work on behalf of our HCV pts.

**Methods:** We created a team comprised of a pharmacist, pharmacy technician, patient navigator and physician whose responsibilities included DAA acquisition and delivery, patient education, and data collection. DAA acquisition included completing prior authorizations and letters of appeal to payers and the NY State external review board. The program was piloted in a single office and then expanded to multiple sites in the New York area.

**Results:** We report initial results for the period 1/1/2015-6/6/2016. During that time, 917 pts with HCV entered our process for DAA acquisition. Pts with all insurances including 20 commercial plans, 12 managed Medicaid plans and straight Medicaid were included. Medication was requested for all pts regardless of fibrosis stage and genotype. During the evaluated period, 810 pts were approved for treatment (88%), 764 have received medication (83%), 107 patients still have final approval/denial pending. 3/917 patients have had their DAA treatments denied (<1%). As of 6/6/2016, 46 pts were approved but did not start therapy. Reasons for not starting included: needing counseling by PharmD (19), personal reasons such as surgery, vacation (18), and needing medication delivery (9). Of our approved cohort, 454 were treatment-naive and 356 treatment-experienced. Genotype breakdown: G1 not subtype 3, G1a 483, G1b 237, G2 33, G3 41, G4 12, G6 1. Fibrosis score by biopsy: Fibroscan: F0 25, F1 241, F2 130, F3 89, F4 272. 53 patients had no fibrosis score. Approved DAA’s were: SOF/ LD+ ribavirin (RBV) 639, Sofosbuvir (SOF)/RBV 42, PrOd + RBV 91, Daclatasvir/SOF+RBV 31, ELB/GZR + RBV 5, Pr+RBV 2. As of 6/6/2016, 664 patients completed therapy. Approximately 190 patients are in the follow-up period. SVR rate for the completed patients is ~97%. To date, 18 patients have relapsed following cessation of therapy.

**Conclusions:** Implementation of a dedicated team to obtain access to HCV DAA therapies overcomes standard barriers to treatment access and greatly improves the ability to obtain these treatments for all pts with HCV, regardless of insurance, fibrosis stage or genotype with overall medication acquisition 88% and absolute denial rate < 1%. Outcomes from this program include SVR rates of 97%, improved patient satisfaction scores and improved staff experience.

79. Poster Presentation #1743

**#1743: PATIENT REPORTED ASSESSMENT OF DIFFERENT DIAGNOSTIC IMAGING TESTS FOR LIVER DISEASE – VISUAL REPRESENTATION AND OWNERSHIP OF RESULTS IMPROVES UNDERSTANDING.**

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**Background:** Liver disease is rising in prevalence; early intervention followed by action (eg. dietary improvement) prevents later stages of disease and associated costs. Good patient experience and understanding leads to better outcomes in chronic disease, and thus information delivery is important to earlier positive outcomes.

**Methods:** 41 patients with experience of liver disease underwent Transient Elastography (FibroScan) and quantitative MRI analysed by LiverMultiScan. Results were fed back in a standard format. For FibroScan, a Liver Stiffness number, with comparison to coloured fibrosis score chart. For LiverMultiScan, a standard report featuring statistical summary of key parameters and coloured MRI scan. This was followed by a qualitative interview and questionnaire into patient experience and understanding. The interview was thematically analysed.

**Results:** 38 patients touched on the imagery of LiverMultiScan, 37 positively. Imagery theme summary was that access to the coloured visual image enhanced understanding, and so reassured patients of their health status. No discernible difference was seen by condition, though those with patchy disease commented strongly. 26 patients commented on information ownership and its effects, 25 positively. Patients spoke of frustration in terms of access to their information, and importance of access for personal empowerment and subsequent lifestyle action. On the questionnaire, done before and after scanning, patients rated understanding of the health of their liver. Mean scoring increased from 6 to 93 on a 10-point scale and the changes were significant at the 1% level using the Wilcoxon Signed-Rank test.

**Conclusion:** Giving patients access to their own reports in an understandable and visual format may enhance patient experience and understanding of liver health, and so potentially form part of health interventions for liver disease. Patient empowerment in chronic liver disease merits further research.

**Figure:**

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80. Poster Presentation #1748

#1748: COMMUNITY APPROACH TARGETING CIRRHOSIS AND HEPATOCELLULAR CARCINOMA (CATCH) COMMUNITY CIRRHOSIS PREVALENCE IN VIRAL HEPATITIS

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The aim of this study was to estimate the prevalence of significant fibrosis and cirrhosis in an at-risk population in the community using transient elastography (TE) to measure liver stiffness (LSM).

**Methods:** Participants were recruited from 21 primary care centers across Melbourne, Australia. Inclusion criteria included age >18yrs, with hepatitis B (CHB) or hepatitis C (CHC) with duration >6months, absence of prior or recent (<18months) specialist input and no current or prior HCC Clinical assessment and TE (Fibroscan® 402) were performed in primary care. LSMs of 8.0kPa and 12.5kPa were used as cut-offs for significant fibrosis (F2) and cirrhosis (F4) respectively. The
Results: From October 2014 to April 2016, 752 community participants were assessed (498 CHC / 253 CHB). LSM failure occurred in one patient (0.13%) and phlebotomy failure in 6 (0.80%). TE was performed using the M+ probe in 95.5% (n=717) and the XL+ probe in 4.5% (n=34). The control cohort of 247 participants (179 HCH/68 HCB) only differed demographically by having an older median age in HCH (p=0.001). In the cCHC the mean LSM was 99kPa and in the cCHB it was 56kPa. There was no difference between mean LSM in the community and control cohorts (CHC p=0.773/CHB p=0.067). An LSM8kPa in the community was observed in 298% (418% cCHC/ 63% cCHB p<0.001) and a LSM12.5kpa seen in 99% (all cCHC-151%). Three cCHB patients were diagnosed as cirrhotic (1.2%) on clinical and radiological grounds (all LSM>11.0). This was at a lower prevalence than our HCB (5.9% p=0.039). The distribution of LSM12.5kPa was no different between cCHC and HHC (p=0.739). On multivariate analysis advanced age (OR 1.062 p=0.001), elevated BMI (OR 1.128 p=0.002), at risk (>140g/p.w) alcohol consumption (OR 2.549 p=0.001) and genotype 6 (OR 8.347 p=0.009) were associated with an LSM12.5kPa in cCHC.In cCHB elevated viral load (OR 2.063 p=0.023), BMI (OR1.518 p=0.019) and viral phase 2 (OR 21.818 p=0.033) were associated with increased risk of cirrhosis however were not significant on multivariate analysis.

Conclusion: This study demonstrates that a community-based screening program using LSM is practical with an acceptable uptake in the CHC and CHB population. Based on the LSM data, the prevalence of fibrosis and cirrhosis in the community CHC patients is significant and comparable to that seen in a tertiary hospital cohort. These results have considerable importance with respect to allocation of healthcare resources.

81. Poster Presentation #1762

#1762: LACK OF COMPLIANCE TO HEPATOCELLULAR CARCINOMA (HCC) SCREENING GUIDELINES IN HEPATITIS B (HBV) OR C (HCV) VIRUS CO-INFECTED HIV PATIENTS WITH CIRRHOSIS

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Background: The incidence of HCC in HBV or HCV HIV-co-infected patients is increasing possibly due to an increase in the prevalence of cirrhosis. Guidelines recommend HCC screening every 6 months in patients with cirrhosis. We assessed compliance with HCC screening guidelines in HBV and HCV HIV-co-infected patients with cirrhosis.

Methods: Patients were enrolled from 4 cohorts from The Netherlands, France, Austria and Italy participating in the COHERENCE collaboration (www. Coheren.org) and followed between 1 January 2005 and 1 January 2015. HBV co-infection was defined as being HbsAg positive and HCV co-infection as HCV antibody-positive. Assessment of liver cirrhosis was based on a) clinical diagnosis reported in the chart, b) liver biopsy, c) fibroscan result (>118 kPa for HBV and >126 kPa for HCV), or d) APRI score >2.0.Compliance to national and European HCC screening guidelines was defined as at least one ultrasound every 65 months. Generalized estimating equation (GEE) models adjusted for repeated measurements were fitted to determine the predictors of the lack of compliance to HCC screening guidelines.

Results: 1,743 HCV-infected patients with HBV and/or HCV co-infection and liver cirrhosis were included. Of the 1,743 patients, 1,306 (75%) were HCV co-infected, 320 (18%) HBV co-infected and 117 (7%) were HBV/HCV co-infected. The majority of patients were male (80%), Caucasian (83%) and infected with HIV by injecting drug use (IDU 44%), homosexual contact (MSM 32%) or heterosexual contact (14%). Median age at cirrhosis diagnosis was 43 years (IQR: 36–48) and median follow up time since diagnosis of cirrhosis was 6.0 years (IQR: 4–10) 96% of the patients used cART at time of diagnosis and 79% had HIV RNA<400 copies/ml. Screening (6.5 months) was performed in 5% of the individuals in 2006, and 7% in 2014. Injecting drug use and longer time since diagnosis of cirrhosis were associated with a higher compliance to HCC screening, whilst HBV/HCV co-infection, lack of ALT measures and assessment of cirrhosis by APRI score were associated with a lower compliance (figure 1). Sensitivity analyses, in which all patients with a cirrhosis assessment by APRI score were excluded, and in which the allowed time between ultrasound measures was extended to 9, 12, 15 and 24 months, all showed comparable associations.

Conclusion: Compliance to HCC screening recommendations in at-risk HBVand/or HCVHIV-co-infected patients is low in Europe. In the light of an aging population and subsequently an increasing prevalence of liver cirrhosis this is a situation that needs to be addressed urgently.
.0 kPa cutoff wrongly excluded significant fibrosis in 24% (9/37) of patients. Mean LS scores during PEG-IFN therapy declined by Week 48 (Group A: -0.49 kPa [-8%]; Group C: -1.52 kPa [-22%]), in contrast to untreated patients where mean LS scores increased (Group B: +0.38 kPa [+7%]).

Conclusions: To date, this is the largest study of TE in children with CHB. TE showed poor discriminatory ability in staging liver fibrosis, partly due to low prevalence of cirrhosis in this population; thus, clinical utility of TE in children with CHB appears to be limited.

82. Poster Presentation  #1793

#1793: US ASIAN HBV PATIENTS HAVE LIVER STEATOSIS AND METABOLIC SYNDROME AT LOWER BMI THAN NON ASIANS

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Background: Metabolic Syndrome (MS) affects 35% of U.S. adults and is associated with the development of nonalcoholic fatty liver disease. Asians have increased risk of cardiovascular disease and diabetes at lower BMI than other populations. There is limited data on MS and steatosis in chronic HBV patients, so we examined the prevalence of MS and steatosis and their impact on liver disease severity in our predominantly Asian US cohort.

Methods: This was a single-center retrospective cohort study of all chronic HBV patients with an abdominal ultrasound between 2004-2015. Demographics, clinical variables, ultrasound and transient elastography (TE) were collected and their association with MS, steatosis and HBV status was analyzed. Metabolic syndrome was defined as 3 or more of 5 risk factors: obesity, dyslipidemia, hypertension, hypertriglyceridemia and Diabetes. Obesity was defined using WHO guidelines (BMI 25 for Asians, BMI 30 for non-Asians).

Results: 617 HBV patients with a mean age of 53 years were included in this study. Patients were predominantly male (57%), Asian (88%, of whom 70% were Chinese), on HBV therapy (64%) and 65% had undetectable DNA. 21% had MS with 4 or more risk factors of which hypertension (41%), hyperlipidemia (41%) and obesity (32%) were most common. 25% of patients had 2 risk factors, 28% and 100% respectively. 42% had steatosis and 14% had cirrhosis by ultrasound. Of 204 patients (33%) with TE, 81% had low fibrosis scores (F0-1). Patients with steatosis were more likely to have MS (38 vs 16%) [p<0.001] and a higher ALT (31 vs 24) [p<0.001]. Similarly, patients with MS were older [p<0.001] more likely to have steatosis (40 vs 17%) [p<0.001] and a higher ALT (29 vs 25) [p=0.003]. Asian patients had a lower BMI than non-Asians (mean 24 vs 26, p=0.001) but had similar prevalence of the other four MS risk factors and steatosis. If the obesity cut off of BMI 30 was used for all patients, then 49 Asians were downgraded from 3 to 2 risk factors: but the prevalence of steatosis remained the same as in patients with MS (39% vs 40%).

Conclusions: Asian HBV patients have lower BMI than non-Asians yet have the same prevalence of steatosis and other risk factors for MS, supporting guidelines that suggest lower BMI targets in Asians. We found a strong association between MS, steatosis and elevated ALT in HBV patients. Given that MS is modifiable, we advocate for MS evaluation and aggressive lifestyle modification counseling in HBV patients, especially in those Asian patients with lower BMI.

83. Poster Presentation  #1808

#1808: DYNAMIC CHANGES OF LIVER STIFFNESS PREDICT HISTOLOGICAL REVERSE OF LIVER FIBROSIS IN CHRONIC HEPATITIS B PATIENTS TREATED WITH ENTECAVIR

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Aim: The dynamic change of liver stiffness measurement (LSM) and its relation to histological reverse of liver fibrosis in chronic hepatitis B (CHB) patients on antiviral therapy were still unknown. The aim of the present study was to elucidate the predicitive value of dynamic change of LSM for histological reverse of liver fibrosis in CHB patients treated with entecavir.

Material and methods: We measured HBV DNA, liver function tests and LSM in CHB patients at baseline and every 26 weeks during a 78-week entecavir therapy. Liver biopsies were taken before and 78 weeks of treatment and histological reverse of liver fibrosis was defined as Ishak fibrosis score decreased >=1. Piecewise linear mixed-effects model was used to examine the dynamic changes in liver stiffness.

Results: Among 93 CHB patients on entecavir therapy, histological reverse of liver fibrosis was observed in 44.1%. Dynamic changes of liver stiffness measurement (LSM) showed a two-phase declining manner. The fast-declining phase was seen after 26 weeks of treatment: in the reverse group the LSM went down from 12.6 Kpa to 7.6 Kpa (Rate of decrease=39.7%), whereas in the non-reverse group it went down from 113 Kpa to 8.7 Kpa (Rate of decrease=230%). The slow-declining phase was observed from 26 to 78 weeks of treatment: in reversed group the LSM further went down to 7.1 Kpa and 6.4 Kpa at week 52 and 78 week, whereas in the non-reverse group the LSM was 8.4 Kpa and 7.7 Kpa, respectively. Multivariate regression analysis showed that histological fibrosis reverse was associated with patient age, histological inflammation score, and changes of LSM. The AUROC of liver fibrosis prognostic model for prediction of reverse was 0.73 (95%CI: 0.60-0.85).

Conclusion: Dynamic changes of LSM could predict histological liver fibrosis reverse in CHB patients treated with entecavir.

84. Poster Presentation  #1820

#1820: SUBCIRRHOTIC LIVER STIFFNESS BY TRANSPARENT ELASTOGRAPHY CORRELATES WITH LOWER RISK OF HEPATOCELLULAR CARCINOMA IN PATIENTS WITH HBV-RELATED CIRRHOSIS

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Backgrounds/Aims: The risk of developing hepatocellular carcinoma (HCC) varies, even among in the context of cirrhosis. We investigated the relationship between liver stiffness (LS) in subc Innocative range, assessed via transient elastography (TE), and risk of HCC development in patients with chronic hepatitis B (CHB)-related cirrhosis.

Methods: Data on 540 patients presenting with clinically evident CHB-related cirrhosis between April 2006 and December 2014 were reviewed retrospectively. Subc Innocative range of LS was defined by TE values @13 KPa.
Results: Of the study population, 214 (39.6%) had LS values in the subcirrhotic range. During follow-up (median, 54.1 months), 81 patients (15.0%) developed HCC. In conjunction with age, male gender, and diabetes mellitus, subcirrhotic LS value (hazard ratio=0.462) was an independent predictor of HCC development in multivariate analysis (all p<0.05). Cumulative HCC incidence was significantly lower for patients with subcirrhotic (vs. cirrhotic) LS range (log-rank test, p<0.05). In our cohort, the modified REACH-B (mREACH-B) score performed better than did other prediction models, namely REACH-B, CU-HCC, and LSM–HCC scoring systems (area under receiver operating characteristic curve [AUROC]: 0.717 vs. 0.669, 0.578, and 0.624, respectively, for 7-year HCC risk).

Conclusions: A significant association between subcirrhotic range of LS values and lower risk of HCC development was identified in patients with clinically evident CHB-related cirrhosis. Thus, different TE-based HCC surveillance strategies may be required even in patients with an identical liver cirrhosis disease category.

Figure:

85. Poster Presentation #1835

#1835: VALIDATION OF A DIAGNOSTIC STRATEGY COMBINING THE TRANSIENT ELASTOGRAPHY LIVER STIFFNESS VALUE AND ENHANCED LIVER FIBROSIS TEST TO ASSESS THE FIBROTIC BURDEN IN PATIENTS WITH CHRONIC HEPATITIS B

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Background/Aims: Liver stiffness (LS) determined using transient elastography (TE) and the enhanced liver fibrosis (ELF) test assess the fibrotic burden accurately. Recently, a sequential combination of the LS value and ELF test was proposed to increase the chance of avoiding a liver biopsy (LB). We investigated the diagnostic performance of LS and ELF, validated the LS-ELF algorithm, and investigated whether the sequential LS-ELF algorithm performs better than their concomitant combination in chronic hepatitis B (CHB) patients.

Methods: Between 2009 and 2013, 222 CHB patients (men 144, women 78 median age 48 years) who underwent a LB, along with LS measurement and the ELF test, were recruited for retrospective analysis.

Results: The median alanine aminotransferase level, HBV DNA level, LS value, and ELF score were 42 IU/L, 616,000 IU/L, 10.2 kPa, and 9.7, respectively. Advanced fibrosis (F3) and cirrhosis (F4) were identified in 23 (10.4%) and 118 (53.2%) patients, respectively. The areas under the receiver operating characteristic curve of the LS value that predicted F3 (0.887 vs. 0.703) and F4 (0.853 vs. 0.706) were significantly higher than those of ELF test (all p<0.001). Based on the LS-ELF algorithm, 60.4–71.6% and 55.7–66.3% of the patients could avoid a LB to exclude F3 and F4, respectively, whereas 68–78.7% and 63.5–66.1% of the patients could avoid a LB to confirm F3 and F4, respectively. When both confirmation and exclusion strategies were applied, 67.1–67.6% and 61.3–66.2% of the patients could avoid a LB to diagnose F3 and F4, respectively. The proportions of patients who correctly avoided a LB for predicting F3 (69.4–72.5% vs. 42.3–59.0%) and F4 (608–653% vs. 239–495%) based on the sequential LS-ELF algorithm were significantly higher than those of the concomitant LS-ELF algorithm (all p<0.05).

Conclusion: The ability of the LS value obtained by TE to predict F3–4 and F4 was significantly higher than that of the ELF test. The sequential LS-ELF algorithm conferred a greater chance of avoiding a LB in CHB patients to diagnose advanced fibrosis and cirrhosis and performed significantly better than the concomitant algorithm.

86. Poster Presentation #1836

#1836: PROFILE OF VIRAL, BIOCHEMICAL AND NON-INVASIVE FIBROSIS MARKERS IN A COHORT OF INACTIVE EUROPEAN HEPATITIS B (HBV) CARRIERS: 3 YEARS FOLLOW-UP OF A PROSPECTIVE LONGITUDINAL STUDY (ALBATROS STUDY)

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Background: The aim of the present study was to analyze potential predictors of disease progression in a cohort of inactive HbsAg carriers from Europe during long-term follow-up.

Methods: In the European prospective ALBATROS study so far 920 patients with HbeAg-negative lowreplicative chronic HBV were enrolled for long-term follow-up over 10 years. Definition of lowreplicative HBV without indication for antiviral therapy at study inclusion was based on international guidelines. Biochemical, virological and non-invasive fibrosis parameters including FibroScan and APRI score were performed at BL as well as during annual follow-up.

Results: 80/920 patients (8.7%) were lost to follow-up. Data of the present interim analysis at year 3 of follow-up (FU3) were available in 205 patients, mainly infected with HBV genotype A (13%) and D (40%). There was a predominance of Caucasian ethnicity (53%). Table 1 classifies patients according to HBV DNA, ALT levels and fibrosis stage measured by FibroScan at BL and FU3 and identifies any group switch within 3 years. Patients with constantly normal ALT had significantly lower APRI scores (p<0.0001) compared to those who had at least once ALT elevation. In addition, patients with constantly normal ALT had lower fibrosis stage by FibroScan (p=0.015) in comparison to those with transient or persistent ALT increase. There was a significant positive correlation between APRI score and liver stiffness (p=0.002). We could not show any significant association between viral dynamics and fibrosis stage by FibroScan. In Caucasian patients higher body mass index turned out to be the only predictive parameter (p=0.04) to be correlated with advanced fibrosis stage.

Conclusion: Risk of progression to advanced fibrosis stage within 3 years FU was low in patients with low-replicative chronic HBV infection and permanent normal ALT. Higher fibrosis stage with concomitant
increase of transaminases was rather due to metabolic factors, but not to viral parameters, in the subgroup of Caucasian HbsAg carriers.

Figure:

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>FIB4</th>
<th>Any group switch</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) HBV DNA negative (n=391)</td>
<td>27 (13%)</td>
<td>27 (13%)</td>
<td>18 (9%) (1=18)</td>
</tr>
<tr>
<td>(b) HBV DNA pos (n=120)</td>
<td>30 (63%)</td>
<td>143 (79%)</td>
<td>2 (5%) (1=1)</td>
</tr>
<tr>
<td>(c) HBV DNA pos 2000 (n=99)</td>
<td>44 (54%)</td>
<td>35 (17%)</td>
<td>20 (12%) (1=1)</td>
</tr>
<tr>
<td>(d) ALT normal (n=30)</td>
<td>182 (61%)</td>
<td>167 (55%)</td>
<td>17 (5%) (2=1)</td>
</tr>
<tr>
<td>(e) ALT &gt;1 AALN (n=30)</td>
<td>23 (10%)</td>
<td>33 (10%)</td>
<td>3 (2%) (2=1)</td>
</tr>
<tr>
<td>(f) ALT &gt;2 AALN (n=30)</td>
<td>0 (0%)</td>
<td>5 (2%)</td>
<td>2 (1%) (2=1)</td>
</tr>
<tr>
<td>(g) P1 fibrosis (n=10)</td>
<td>152 (63%)</td>
<td>132 (61%)</td>
<td>10 (7%) (1=3)</td>
</tr>
<tr>
<td>(h) P2 fibrosis (n=10)</td>
<td>11 (5%)</td>
<td>2 (2%)</td>
<td>12 (0%) (1=3)</td>
</tr>
<tr>
<td>(i) P3 fibrosis (n=10)</td>
<td>10 (7%)</td>
<td>11 (7%)</td>
<td>3 (3%) (2=3)</td>
</tr>
</tbody>
</table>

87. Poster Presentation  #1839

#1839: DIAGNOSTIC PERFORMANCE OF APRI, FIB-4 AND FIBROSCAN FOR ASSESSMENT OF HEPATIC FIBROSIS IN CHRONIC HEPATITIS B PATIENTS RECEIVING ORAL ANTIVIRAL THERAPY; 7-YEAR REAL LIFEDATA

Ifthihar Koksal, Gurdal Yilmaz, Ilknur Yavuz,

Background: Regression of advanced liver fibrosis is one of the new concepts in hepatology. The effect of long-term suppression of replication of hepatitis B virus (HBV) by antiviral medications to the fibrosis regression is not known exactly in the chronic hepatitis B (CHB) patients. Since liver biopsy is an invasive process, the importance of non-invasive tests in determining fibrosis is increasing over recent years. Non-invasive fibrosis markers have a lot of advantages such as absence of risks, patient acceptance and being easy and repeatable. These tests can be used for follow-up liver fibrosis in CHB patients.

Aims: To evaluate the performance aspartate aminotransferase-to-platelet ratio index [APRI] and fibrosis index based on four factors [FIB-4 index], and Fibroscan (Transient Elastography) for the measurement of liver fibrosis in CHB patients receiving oral antiviral therapy in long-term follow-up period.

Methods: Demographic, histologic, clinical, and laboratory data of CHB patients receiving tenofovir disoproxil fumarate and entecavir were recorded. Predicted fibrosis stage, based on established scales and cut-off values for APRI, FIB-4 scores, and Fibroscan was compared with Ishak scores obtained from liver biopsy at baseline and at 7 years follow-up period.

Results: A total of 168 patients with CHB (36.3% HBeAg positively) were analyzed. The majority of patients (65.5%) were taking tenofovir disoproxil fumarate. Seventy-nine percent of patients with a baseline liver biopsy had Ishak fibrosis stage ≥2 (14.3% had cirrhosis [Ishak 5 or 6]). The median APRI score was 0.69 (inter quartile range: 0.44–1.41), the median FIB-4 score was 1.19 (range: 0.72–2.02), the median Fibroscan was 7.4 (inter quartile range: 5.9–9.5). FIB-4 scores (r=0.253, p=0.001) and Fibroscan (r=0.292, p=0.002) correlated with fibrosis stage. APRI did not correlate with fibrosis stage. The median Fibroscan and FIB-4 scores at years 7 was 6.5 (inter quartile range: 5.5–9.1) and 1.06 (range: 0.85–1.54). There is a significant decrease in those values in both tests compared to pre-treatment values in the 7th year of the treatment (P<0.022, P<0.001).

Conclusions: Fibroscan and FIB-4 scores are suitable for assessment of hepatic fibrosis in CHB patients. Long-term suppression of HBV can lead to regression of liver fibrosis and cirrhosis.

88. Poster Presentation  #1854

#1854: THE EFFECTS OF NON-ALCOHOLIC FATTY LIVER DISEASE ON LIVER FIBROSIS IN CHRONIC HEPATITIS B PATIENTS ON NUCLEOSIDE ANALOGUE THERAPY: RESULTS FROM A MATCHED-CASE CONTROL STUDY

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Background: The potential synergistic effect of non-alcoholic fatty liver disease (NAFLD) and chronic hepatitis B (CHB) on hepatic fibrosis has not been well-investigated. Liver stiffness (LS) and controlled attenuation parameter (CAP) are non-invasive methods to quantify hepatic fibrosis and steatosis respectively. This study aims to use LS and CAP to determine the effect of NAFLD on fibrosis in CHB patients on long-term nucleoside analogue (NA) therapy.

Methods: From December 2014 onwards, we recruited CHB patients on NA therapy and without concomitant hepatitis C or alcoholic liver disease. Liver biochemistry, serum hepatitis B virus (HBV) DNA and metabolic parameters were measured. Recruited patients underwent LS and CAP measurements using transient elastography (Fibroscan, Echosens, Paris). Significant fibrosis was defined using the European Association for the Study of the Liver guidelines (9 kPa for patients with normal alanine aminotransferase). Metabolic syndrome was defined using the International Diabetes Federation criteria. CHB patients with significant fibrosis and without significant fibrosis (controls) were matched according to age, sex, NA type and duration of treatment in a 1:3 ratio.

Results: 568 CHB patients (mean age 573 years, 732% male, 9505 hepatitis B e-antigen negative) were recruited, with 142 fibrosis patients and 426 controls. Median duration of NA therapy was 76.7 months (range 6–213 months). There was no difference in the proportion of patients with undetectable HBV DNA between fibrosis patients and controls (92.3% vs 92.5%, p=0.938). Patients with significant fibrosis, when compared to controls, had significantly higher CAP (255 dB/m vs 240 dB/m, p=0.009), HBV DNA (6.0% vs 5.7%, p<0.001) and body mass index (BMI) (25.0 kg/m² vs 23.8 kg/m², p=0.001) and significantly lower platelet count (135 vs 192 x 10^9/L, p<0.001). Patients with significant fibrosis were also more likely to have metabolic syndrome, central obesity and raised fasting glucose when compared with controls (all p<0.05). In multivariate analysis, CAP, raised fasting glucose and BMI were independently associated with significant fibrosis (odds ratio 1.0005, 2.233 and 1.116, respectively, all p<0.05), while platelet count was inversely associated with significant fibrosis (odds ratio 0.982, p<0.001).

Conclusion: Steatosis and metabolic abnormalities were independent predictors of significant fibrosis, implying that they could contribute to the persistence of fibrosis in CHB patients on NA therapy. Identification
and management of NAFLD and metabolic conditions in on-treatment CHB patients may potentially assist regression of hepatic fibrosis.

89. Poster Presentation #1877

SILIBININ TREATMENT FOR HEPATITIS D: IN VITRO AND IN VIVO

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Background and aim: Hepatitis D virus (HDV) infection causes the most severe form of chronic viral hepatitis. HDV is a defective satellite virus which requires the hepatitis B virus (HBV) and its surface antigen for transmission and replication. About 15 to 20 million people are chronically infected by HDV worldwide. Interferon-alpha (IFN)-based therapies for hepatitis D are effective in only about 25% of patients. Therefore, identifying new therapeutic targets is urgently needed. Silibinin, extracted from milk thistle (Silybum marianum sp.), has been long used as a hepatoprotective and antioxidant compound, and is well tolerated and has potent antiviral activity against hepatitis C with the ability to achieve cure. It is not known whether SIL has antiviral activity against hepatitis D in vitro or in vivo.

Methods: In vitro studies were carried out using the pharmaceutical form of silibinin, Legalon®SIL in HepaRG differentiated cells and primary human hepatocytes. Time-of-addition experiments were performed to separately analyze entry and post-entry stages of viral infection. To test SIL effect on HDV infection, a 39-year-old male HDV/HBV coinfected patient with cirrhosis by fibroscan, who developed severe side effects during a previous course of IFN, initiated monotherapy with intravenous 1400 mg/day of SIL for 4 weeks. Blood samples were collected every week. HDV RNA was measured by RT-qPCR.

Results: The in vitro results indicate SIL dose-dependent antiviral activity in the fMolar range. This activity was more prominent at the viral entry stage than at later stages of the HDV life cycle, with a 50% decrease in HDV infection. Interestingly, an additive inhibitory effect was observed when SIL was combined with therapeutically-achievable doses of IFN, reaching an 80% inhibition of infection. To test in vivo whether SIL blocks HDV production, SIL was administered to a chronic HDV-infected patient with a high pre-treatment HDV RNA level of 1.85x107 cp/ml. While SIL treatment was safe and without any side effects, HDV RNA levels did not decline during treatment (mean 2.4x107 cp/ml).

Conclusion: SIL exhibited antiviral activity against HDV in vitro, targeting the viral entry stage, with minimal effect on HDV production, which is partly confirmed in vivo by the lack of reducing HDV levels during 4 weeks of SIL treatment. Larger studies with longer treatment durations with SIL alone or in combination with IFN (and other anti-HDV drugs) are needed to further explore SIL use against HDV.

90. Poster Presentation #1887

POST-TREATMENT DYNAMIC CHANGES OF LIVER STIFFNESS TO PREDICT FIRST 2-YEAR OUTCOMES IN HBV COMPENSATED CIRRHOSIS

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Background: Baseline liver stiffness measurement (LSM) using FibroScan accurately assesses the degree of liver fibrosis and the risk of hepatocellular carcinoma (HCC) and decompensation development in patients with chronic hepatitis B. However, the effect of LSM dynamic change after anti-HBV treatment on predicting early outcomes is still unclear. This study investigated the usefulness of post-treatment dynamic changes of liver stiffness to predict first 2-year outcomes in HBV compensated cirrhosis.

Methods: A total of 630 HBV patients with compensated cirrhosis between January 2013 and October 2015 were enrolled in this prospective study. Patients were under entecavir or tenofovir-based anti-HBV therapy, and were assessed at baseline, at every 26 weeks for liver stiffness. After anti-HBV treatment, patients attended regular follow-up as part of a surveillance program for the detection of HCC and decompensation. The hard-endpoint was the presence and degree of ascites or encephalopathy, bleeding gastric or esophageal varices, the development of hepatocellular carcinoma, or death related to liver disease. Linear model was used to fit two slopes of LSM dynamic change (slope1 for 0-26week and slope2 for 26-104week). Cox proportional hazard model was used to evaluate the effect of LSMdynamic changes on hard-endpoints.

Results: During the follow-up period (median, 15.6 months range, 6.0-24.0 months), hard-endpoints developed in 35 patients. On multivariate analysis, together with LSM baseline and slope1, were at a significantly greater risk of hard-endpoint development, with the following hazard ratios: 1.04 (95% confidence interval [CI], 1.02-1.08 P=0.003) for LSM baseline and 6.98 (95% CI, 250-1945 P<0.001) for LSM slope1. The area under the ROC curve was 0.73 (95% CI, 0.60-0.85 P=0.002).

Conclusion: Our data suggest that dynamic change of LSM during the first 26weeks could be a useful predictor of hard-endpoint development in patients with compensated cirrhosis during HBV treatment.

91. Poster Presentation #1905

LIVER STIFFNESS AND VIROLOGIC OUTCOMES AFTER INTRODUCING TENOFOVIR AS PART OF ANTIRETROVIRAL THERAPY IN LAMIVUDINE-EXPERIENCED ADULTS WITH HIV AND HEPATITIS B VIRUS (HBV) CO-INFECTION IN GHANA: FOUR-YEAR FOLLOW UP OF THE PROSPECTIVE HEPIC COHORT

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INTRODUCING TENOFOVIR AS PART OF ANTIRETROVIRAL THERAPY IN LAMIVUDINE-EXPERIENCED ADULTS WITH HIV AND HEPATITIS B VIRUS (HBV) CO-INFECTION IN GHANA: FOUR-YEAR FOLLOW UP OF THE PROSPECTIVE HEPIC COHORT

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Results: During the follow-up period (median, 15.6 months range, 6.0-24.0 months), hard-endpoints developed in 35 patients. On multivariate analysis, together with LSM baseline and slope1, were at a significantly greater risk of hard-endpoint development, with the following hazard ratios: 1.04 (95% confidence interval [CI], 1.02-1.08 P=0.003) for LSM baseline and 6.98 (95% CI, 250-1945 P<0.001) for LSM slope1. The area under the ROC curve was 0.73 (95% CI, 0.60-0.85 P=0.002).

Conclusion: Our data suggest that dynamic change of LSM during the first 26weeks could be a useful predictor of hard-endpoint development in patients with compensated cirrhosis during HBV treatment.
Introduction: Until recently lamivudine was the only available agent to treat hepatitis B in the context of HIV infection in sub-Saharan Africa. Tenofovir is gradually becoming available although access remains far from universal. Long-term outcomes of introducing tenofovir as part of antiretroviral therapy (ART) in subjects previously extensively exposed to lamivudine as the sole HBV-active agent in the region are unknown.

Methods: We report from a prospective cohort of HIV/HBV co-infected adults attending for HIV care in Kumasi, Ghana, where HBsAg prevalence is 14%. HbsAg-positive subjects were invited to attend for transient elastography (TE) and blood sampling before the introduction of tenofovir (T0) as part of ART, and within 1 year (T1) and 4 years (T2) of starting tenofovir. Adherence and alcohol consumption were determined by a questionnaire-based interview.

Results: Overall 178 patients underwent evaluation at T0/T1, of whom 98 (55%) also attended for assessment at T2. Remaining patients were lost to follow up (50, 28%) died (10, 6%), declined to attend (17, 10%), or were excluded due to pregnancy (2, 1%) or invalid TE (1, 1%). Of the 98 subjects, 94 had started tenofovir-based ART and had received tenofovir for median 4 years (IQR 3.8, 4.1), while continuing previous lamivudine (Table 1). By multivariable linear regression, female gender, no history of alcohol excess, and higher HBV DNA level, higher liver stiffness, and lower platelet count at T0/T1 were significant predictors of decreasing liver stiffness between T0/1 and T2. No treatment-emergent resistance mutations in HBV polymerase were observed by Sanger sequencing among subjects with HBV DNA>100 IU/ml at T2 one subject showed M204V+V173L+L180M at both T0 and T2.

Conclusions: This is the first report of the long-term impact on liver stiffness and virologic parameters of introducing tenofovir as part of ART in extensively lamivudine exposed HIV/HBV co-infected patients in sub-Saharan Africa. Significant reductions in liver stiffness and improved HBV control were observed at four years.

Figure: Prospective analysis of 94 subjects who introduced tenofovir Continuous variable are presented as median (IQR).
recorded prior to therapy (median 3 months, range 0 to 5 years) and within 18 months after HCV therapy were evaluated. Changes in TE values were correlated with FIB-4 and APRI Scores as well as histological results where available.

**Results:** Median TE prior to DAA treatment was 12.6 kPa (IQR 11.85), median TE post treatment 895 kPa (IQR 105). This equals a TE regression of 2839% within 16 months after successful treatment (median 111 days, IQR 103 days, range 0-490 days). Liver enzymes correspondingly showed significant reduction, often already during DAA treatment. Average FIB-4 and APRI prior to therapy were 386 and 198 respectively. Average post treatment FIB-4 was 278 while post treatment APRI was 076. This results in a decrease in FIB-4 of 2801% and a regression in APRI of 6185%. Thus both values fall below the published cutoff values for significant liver fibrosis following successful DAA treatment of chronic HCV.

**Conclusion:** Patients with SVR after DAA therapy showed a rapid and significant regression of TE values within 18 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.

**94. Poster Presentation #1924**

**#1924: FAVORABLE EFFICACY OF COMBINATION THERAPY WITH DIRECT-ACTING ANTIVIRALS TO ELDERLY AGED 70 AND OLDER WITH HCV GENOTYPE 1**

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**Background:** All-oral combinations with direct-acting antivirals for patients with HCV infection show the favorable efficacy, but treatment efficacy and pretreatment predictors of efficacy for elderly aged 70 and older is unclear. The first aim of this study was to determine treatment efficacy and pretreatment predictors of efficacy, especially in elderly. The second aim was to determine the impact of treatment to AFP levels and Liver Stiffness that might be useful as one of predictors of early hepatocarcinogenesis in HCV patients without hepatocellular carcinoma.

**Methods:** 914 patients, with chronic HCV genotype 1b infection, introduced the regimen of daclatasvir 60 mg once daily plus asunaprevir 100 mg twice daily for 24 weeks. Resistance-associated variants (RAVs) of NS5D168 and NS5A-L31/Y93 were evaluated using cycling-probe real-time PCR combined with direct sequencing and/or PCR prediction assay. Quantitative analysis of NS5A-Y93H mutation more than 20% was evaluated as significant. Liver stiffness levels were evaluated at baseline and at point within 6 months after the stop of treatment. FibroScan 502 was used for measurement with the M+ probe and XL+ probe.

**Results:** Sustained virological response (SVR) rates, based on intention to treat analysis, were 87% and 88% in overall patients and elderly aged 70 or more, respectively. SVR rates of patients, without RAVs in NS5 and/or NS5A region by direct sequencing, were 94% and 94% in overall patients and elderly aged 70 or more, respectively. In both groups of overall patients and elderly aged 70 or more, multivariate analysis identified NS5A-Y93H mutation (<20%), pretreatment (failures to treat except for triple therapy with simeprevir, or treatment naive), and levels of viremia (<6.0 log IU/ml) as independent pretreatment predictors of SVR. Frequencies of patients with NS3-D168 mutation at baseline, by direct sequencing, in failures to triple therapy with simeprevir (44%) were significantly higher than those of the others (2%). Levels of AFP and Liver Stiffness after the stop of treatment were significantly lower than those at baseline, in both groups of SVR and non SVR.

**Conclusions:** All-oral combinations with daclatasvir and asunaprevir achieved the high SVR rates to HCV genotype 1b patients, including the elderly aged 70 and older. Viral factors, including RAVs in NS3 and/or NS5A region, mainly affected poor response. The induction of treatment improved levels of AFP and Liver Stiffness as surrogate marker of hepatocellular carcinoma, regardless of treatment efficacy. Further study should be performed to investigate whether viral eradication in elderly might improve the prognosis.

**9.5. Poster Presentation #1927**

**#1927: EFFICACY AND SAFETY OF SOFOSBUVIR AND DACLATASVIR FOR 8 WEEKS IN TREATMENT-NAÏVE NON-CIRRHOtic PATIENTS WITH CHRONIC HCV GENOTYPE 3 INFECTION**

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**Background:** HCV GT 3 is the second most common GT world-wide after GT 1. For non-cirrhotic patients with HCV GT 3 infection, the AASLD and EASL guidelines recommend treat-ment with the IFN- and RBV-free regimen of DCV + SOF for 12 weeks according to the results of the phase 3 ALLY-3 study, in which this patient group achieved 96% SVR12 rate. The objective of this pilot study was to investigate the efficacy and safety of an 8-week treatment of DCV + SOF in treatment-naïve patients with HCV GT 3 infection without cirrhosis.

**Methods:** This ongoing pilot study is, a multicenter, open label, single arm trial that enrolled patients without cirrhosis who were HCV treatment-naïve. Key exclusion criteria included presence of cirrhosis, as determined by either a FibroScan score ≥12.5 kPa, or a FibroTest score of ≥0.75 and baseline HCV RNA level >6,000,000 IU/mL. The regimen was DCV 60 mg and SOF 400 mg once daily for 8 weeks. Efficacy was calculated as the percent of patients achieving SVR12 (HCV RNA <LLD). Additional endpoints included patients experiencing virologic breakthrough or relapse. Adverse events and clinical laboratory abnormalities were monitored to assess safety and tolerability. Analysis of baseline RASs is ongoing and will be presented; if a patient does not achieve SVR12, additional resistance test-ing will be performed.

**Results:** 29 patients, mean age: 49±10 years, mean FibroScan score: 7.8 kPa (range: 5.9-10.2), mean HCV RNA level: 5.3±1.05 Log10 IU/mL, were included. At the time of the present analysis, 14 patients had reached post-treatment week 4; of these, 13 (93%) achieved SVR4. One patient relapsed at post-treatment week 4.

**Conclusions:** The efficacy and safety of an 8-week DCV + SOF regimen for chronic HCV GT3, in treatment-naïve patients without cirrhosis is being investigated. Baseline characteristics, safety, SVR12 results and resistance analysis for all patients will be presented at the meeting.

**96. Poster Presentation #1929**

**#1929: THE EFFICACY AND SAFETY OF SOFOSBUVIR PLUS RIBAVIRIN WITH OR WITHOUT PEG-INTERFERON IN TREATMENT OF NAÏVE AND EXPERIENCED VIETNAMESE PATIENTS WITH CHRONIC HCV INFECTION**

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**Aims:** To evaluate the antiviral efficacy of sofosbuvir (SOF) + ribavirin (RBV) peg-interferon (PegIFN) by the proportion of subjects with sustained virologic response (SVR) 12 weeks after discontinuation of
therapy. To evaluate the safety and tolerating of SOF+ RBV PegIFN -To consider which factors contribute to predicting the SVR.

Patients and methods: We conducted an open-labeled randomized trial of naive and experienced patients with HCV genotype 1 and 6 at Medic Medical Center in Ho Chi Minh City. 120 chronic hepatitis C patients with genotype 1 and 6 were classified into 4 groups: -Group IA included 40 patients with genotype 1 who received 12 weeks of treatment with SOF+ RBV+ PegIFN Group IB included 20 patients with genotype 1 who received 24 weeks of treatment with SOF+ RBV Group IIa included 40 patients with genotype 6 who received 12 weeks of treatment with SOF+ RBV+ PegIFN Group IIb included 20 patients with genotype 1 who received 24 weeks of treatment with SOF+ RBV. SVR was defined as undetectable HCV RNA after 12 weeks of follow-up. Ages, genders, BMI, IL28B, FibroScan, naive and experienced of patients were the factors for evaluating the effectiveness of the treatment and the prognosis.

Results: SVR of group IA was 100%, IB was 90%, IIa was 100%, IIb was 100%. (p<0.05). Two patients of group IB relapsed: one naive, genotype 1b, FibroScan F4 and another experienced, genotype 1b, FibroScan F4. The adverse events were rare in groups with SOF and RBV treatment. Some adverse events in groups with SOF+RBV + PegIFN were slight and did not necessitate medication or reduced dosage of RBV.

Conclusion: Regimes of therapy SOF plus RBV with or without PegIFN were effective and safe for Vietnamese patients with chronic hepatitis C genotype 1 and 6. SVR in genotype 6 was better than that of genotype 1. SVR was the same between naive and experienced subjects. IL28B factor did not impact SVR.

97. Poster Presentation #1977

#1977: EFFECTS OF INTERFERON-FREE TREATMENT ON SERUM CHOLESTEROL LEVELS ARE DIFFERENT BETWEEN THE TWO SOFOSBUVIR-BASED REGIMENS IN CHRONIC HCV-INFECTED PATIENTS

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Background: It has been reported that sofosbuvir and ribavirin (SOF+RBV) therapy increased serum LDL levels and particle size as early as 4 weeks of therapy in chronic genotype (GT)-1 or GT-2 HCV-infected patients, and an altered balance of lipogenesis following removal of lipid metabolism perturbation induced by HCV was proposed as its mechanism. However, whether this phenomenon could be confirmed, irrespective of treatment regimens or liver fibrosis stages, has never been investigated.

Aim: To explore the effects of SOF+Ledipasvir (LDV) or SOF+RBV on serial changes of serum cholesterol levels (Total-C, LDL-C, HDL-C) and to attempt to predict the responsiveness.

Methods: The patients who completed 12 weeks of SOF+LDV for GT-1 or SOF+RBV for GT-2 and received at least 8 weeks of follow-ups were enrolled. The patients treated with statins were excluded. At pretreatment, measurements of body mass index (BMI) and liver stiffness (FibroScan®) were performed. Serum Total-C, LDL-C, HDL-C and HCV RNA (RT-PCR) were serially determined at week 0, 2, 4, 8, 12 during treatment and at week 4, 8, 12 after cessation of treatment. Total-C and LDL-C (at week 4 from baseline) were calculated and compared between chronic hepatitis (CH) and liver cirrhosis (LC). Decision tree analysis was performed to determine the predicting factors for the higher response.

Results: Seventy-three patients were registered (6612 y.o., M/F = 26/47, CH/LC = 49/24, SOF+LDV/SOF+RBV = 56/17). SOF+LDV increased serum Total-C and LDL-C levels in CH and serum. Total-C levels in LC, within 4 weeks of therapy, significantly earlier than SOF+RBV. In CH, Total-C and LDL-C were significantly higher in SOF+LDV than in SOF+RBV (39 21 vs 1 18 mg/dL, P<0.001 and 38 17 vs 01 13 mg/dL, P<0.001, respectively), while in LC, no difference between the two regimens. However, in each regimen, Total-C and LDL-C were not statistically different between CH and LC. The determinants for the higher response over the median value of Total-C (330 mg/dL) and LDL-C (250 mg/dL) were treatment regimens (SOF+LDV, P<0.001) and lower BMI (P<0.024, P=0.002) for the former, and treatment regimens (SOF+LDV, P<0.001) and lower baseline LDL levels (%125 mg/dL, P=0.008) for the latter.

Conclusions: Rapid increases in serum Total-C and LDL-C levels were demonstrated in patients who were treated with SOF+LDV for GT-1 HCV, and in more favorable metabolic conditions. This phenomenon might be unafflicted by liver fibrosis stages, and unrelated to the supposed mechanism of viral interference with de novo lipogenesis per se, since 95% of the patients could achieve disappearance of serum HCV RNA within 4 weeks of therapy.

98. Poster Presentation #1981

#1981: SAFETY AND EFFICACY OF REGIMENS INCLUDING DIRECT ACTING ANTIVIRALS (DAAS) IN CHRONIC HEPATITIS C (CHC) PATIENTS OVER THE AGE OF 70 YEARS

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Background-Aims: Elderly CHC patients tend to have more advanced liver disease and several comorbidities that negatively impact their likelihood of receiving or tolerating interferon-based antiviral regimens. Although DAAs offer new treatment possibilities to the elderly, little information on the outcomes and potential serious adverse effects (SAEs) is available. We assessed the safety and efficacy of DAAs regimens in elderly patients treated in everyday clinical practice in Greece.

Patients-Methods: Data on patients with CHC over the age of 70 years who received treatment with DAAs were analyzed. The stage of liver disease was assessed histologically or by transient elastography. Monitoring for AE was performed at least every month during
treatment and as needed after treatment.

Results: 114 patients (females 61%) with median age of 73 years (range 70-88) were included. The main source of infection was blood transfusion (35%), and unknown in most cases (60%). Diabetes was present in 32 patients (28%). Seventy nine patients (69%) had failed to previous regimen(s) including pegylated interferon (PEG)+ribavirin (R) in most (n=55, 70%) and DAAs in some of them (n=11, 14%). The majority of patients had either compensated (n=72, 63%) or decompensated cirrhosis (n=19, 17%). The genotype distribution was: G1a: 5%, G1b: 54%, G2: 9%, G3: 10%, G4: 20%, G5: 2%. Median baseline lab values were: AST 52.5 IU/L, ALT 51 IU/L, creatinine 0.9 mg/dl, albumin 3.8 g/dl, HCV RNA 1.6x10^6 IU/ml. The regimens used were: Peg+R+sofosbuvir (SOF) x12wks (n=9), SOF+R x12 (n=13) or x24wks (n=2), SOF+subtreatment x12wks (n=21), SOF+daclatasvir x12 (n=6) or x24wks (n=3), SOF/ledipasvir x12 (n=22), x8wks (n=1) or x24wks (n=3), ombitasvir+ritonavir boosted paritaprevir (2D)+dasabuvir (3D) x12wks (n=23), 2D+R x12wks (n=11). 4AEs during treatment were observed in 5 patients (4%) and included two deaths in patients with cirrhosis (one due to newly diagnosed HCC and one to a non-liver related cause). One patient with decompensated cirrhosis had an episode of hepatic encephalopathy and two presented skin reactions. However, there were no additional early treatment discontinuations. Sustained virological response (SVR) has been achieved in 92% (71/77) of patients who have completed post-treatment follow-up. No significant differences in SVR rates between genotypes were observed, whereas all non-cirrhotic patients (n=20) achieved SVR.

Conclusions: Treatment of CHC with different DAAs regimens in patients over the age of 70 is safe and effective. Elderly patients with CHC should be offered treatment with DDAs according to local guidelines.

99. Poster Presentation #1992

#1992: EFFICACY OF ALL-ORAL HCV THERAPY IN PEOPLE WHO INJECT DRUGS (PWID)

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People who inject drugs (PWID) represent a significant proportion of the HCV infected population. In current practice, all-oral regimens are replacing interferon-based regimens, demonstrating higher rates of sustained virologic response (SVR) and comparatively favorable side effect profiles, offering the possibility of cure for almost all patients. This study seeks to assess the efficacy of all-oral therapies in PWID and, as such, provide further support for the prospect of HCV treatment of this vulnerable population without a mandated abstinence period. A retrospective cohort analysis was performed on all HCV-infected patients who were treated at an academic clinic in downtown Vancouver and had a history of recent and/or ongoing injection drug use. All participants had access to integrated multidisciplinary care addressing psychiatric, addiction-related, social, and medical needs. Specific treatment regimens and medical follow-up were implemented according to contemporary guidelines, but included, at a minimum, assessment every 4 weeks while on treatment, then 4, 12 and 24 weeks thereafter. The primary endpoint was achievement of SVR, secondary endpoints being correlates of treatment success and detection of early recurrent viremia following SVR. To date, 50 PWID have completed all-oral HCV therapy within our cohort. Of these, 36 (72%) were on 12 week or shorter regimens and 14 (28%) completed durations longer than 12 weeks. In addition, 21 (42%) patients completed regimens that included ribavirin and 10 (20%) patients were cirrhotic (fibroscan >12.5 kPa). Key demographic parameters include: mean age 52 (34-75) years, 74% male, 66%/62%/46% using heroin/cocaine/other stimulants, and 40% on opiate substitution therapy. All 50 patients completed treatment. No serious adverse events or treatment-limiting toxicity were observed. Of 50 patients completing treatment, 44 (88%) achieved SVR, with all 6 non-SVR cases due to virologic relapse. No cases of early re-infection were detected. Using a multidisciplinary model of care, the treatment of HCV-infected PWID with currently available all-oral regimens is both safe and highly effective, replicating the efficacy reported in clinical trials of these agents. With our strategy of ongoing care post-SVR, recurrent viremia was not observed. These data support current guidelines that all HCV-infected individuals (including active PWID) be considered for therapy, as clinically indicated.

100. Poster Presentation #1995

#1995: TREATMENT OF US VETERANS WITH HEPATITIS C VIRUS (HCV) GENOTYPE (GT) 1 INFECTION: EFFECTIVENESS OF LEDIPASVIR/ SOFOSBUVIR (HARVONI®) AND OMBITASVIR/ PARITAVIR/ RITONAVIR/ DASUBUVIR (VIEKIRA PAK®) REGIMENS

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Background and aim: Compared to highly controlled clinical trial populations, substantial comorbidity has contributed to traditionally lower sustained virologic response rates (SVR) in US veterans. We therefore assessed the effectiveness of Harvoni® or Viekira Pak®, with or without ribavirin, given for 8-24 weeks in veterans at a single VA transplant center.

Methods: From January 2015 until end of April 2016, 402 veterans with GT1 infection (GT1: 41, GT1a: 269, GT1b:92) were started on either Harvoni® or Viekira® and for which SVR data will be available by November 2016. In treatment-experienced veterans ribavirin was added to Harvoni® to shorten treatment duration to 12 weeks a total of 35 veterans with low viral load were eligible to receive Harvoni® for 8 weeks. Diagnosis of cirrhosis was based on one of the following: i) liver biopsy, FIB-4>3.25, ii) FibroScan >12 kPa or iv) signs or portal hypertension. Treatment experience was defined as having received at least one dose of interferon. Undetectable HCVRNA 12 weeks or later following end of antiviral therapy was defined as SVR12.

Results: Of the 402 veterans with GT1, 311 had completed treatment with available SVR12 data by May 30th 2016. Mean age was 62 yrs (34-76), 94% were male, 67% (n=209) were cirrhotic and 99 (32%) were treatment-experienced. A total of 12 veterans had a liver transplantation. Viral breakthrough and relapse occurred in 6 and 12 veterans, respectively.6 veterans expired during or after therapy due to events unrelated to drug therapy. Early termination of therapy occurred in <4% veterans. Of the entire cohort, SVR12 was achieved in 97% compared to 96% and 93% for those treated with Harvoni® and Viekira®, respectively. Failure rate in those treated with 8 weeks only was 6%. Among all cirrhotic veterans, SVR 12 rates were 96% and 83% for those being treated with Harvoni® and Viekira®, respectively. SVR12 data for the entire cohort of 402 veterans will be presented.

Conclusions: In this large, single center cohort of treatment-naive and -experienced veterans, high SVR 12 rates, similar or even better than registration trial or “real-world” cohorts were obtained with either Harvoni® or Viekira®, respectively. Elimination of HCV among all US veterans that are suitable treatment candidates is now a realistic goal.


101. Poster Presentation #2009

#2009: REAL-LIFE HEPATITIS C TREATMENT: EFFECTIVENESS OF 8 OR 12 WEEK SOFOSBUVIR/LEDIPASVIR IN GENOTYPE 1 NON-CIRRHOTIC TREATMENT-NAIVE MONO OR HIV-COINFECTED PATIENTS
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Background and Aims: Short course of DAAS therapy might be an attractive option to reduce treatment costs and/or drug toxicity. According to clinical trials, genotype 1 (GT1) treatment-naive patients without cirrhosis and with low HCV viral load can be considered for shortening treatment to 8 weeks.

Methods: To determine HCV cure rates among GT1 patients receiving 8 or 12 week DAAs-based treatment in a real-world clinical setting.

Results: 171 patients from two large teaching hospitals in Madrid (Spain) who started treatment with Sofosbuvir/Ledipasvir for 8 (n=38) or 12 weeks (n=133). Median age 51 years (47-55). Male 132 (77 .1%), HIV/HVC 154 (90%). Median CD4+ T-cell count 572 (412-778). Median Transient Elastography 8 .7 (6 .3-8 .5). No differences were found between 8wk and 12wk groups.169 patients were GT1 (98 .8%). 69 patients (40 .8%) were treatment-naive, non cir-rhotic, with a viral load below 6 million. 34 (49 .3%) were included in the 8wk treatment group and 35 (50 .7%) in the 12wk treatment group. 32 (91 .4%) pts reached SVR after 12wk treatment and 34 (97%) after 8wk treatment (p=0 .33). 3 pts early discontinued the treatment none of them because of adverse events: 1 in 8wk group and 2 in 12wk group and 1 more patient was a treatment failure in 12wk group.

Conclusions: GT1 non-cirrhotic treatment-naive patients achieved similar SVR12 rates for 8 or 12 weeks of SOF/LDV II is also noteworthy the high rate of HIV-coinfected patients in our study.

102. Poster Presentation #2016

#2016: TREATMENT OF CHRONIC HCV INFECTION WITH THE NEW DIRECT ACTING ANTIVIRALS (DAAs): A REAL WORLD EXPERIENCE IN BRAZIL
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Introduction: Treatment of patients with chronic hepatitis C virus (HCV) infection is currently in a transition phase with the arrival of the new direct acting antivirals (DAAs). Several phase 3 and Real World studies conducted mainly in the United States and Europe have showed rates of sustained virologic response (SVR) around 90% with DAA therapy. However, there is a paucity of data with this new therapy in Latin America.

Objective: The aim of the present study is to describe safety and efficacy of DAA therapy in a cohort of DAA treatment naive chronic hepatitis C patients from three hepatology centers in Brazil.

Methods: This is a historical cohort analysis including all consecutive patients with chronic HCV infection that were treated since February 2014 with the new DAAs in three hepatology centers in Brazil, one located in Sao Paulo and two in Porto Alegre. Only patients with HCV RNA result available twelve weeks after the end of therapy were included in this analysis.

Results: A total of 273 patients started DAA treatment. Among them, 141 had an HCV RNA result twelve weeks after the end of therapy and were included. Mean age was 58.4 ± 10.9 years (range: 29-85) and 86/141 (61%) were male. Genotype 1 was present in 112 (79.5%) of the patients (1a 29.5%, 1b 70.5%) Genotypes 2, 3, and 4 were detected in 3 (2.1%), 24 (17%) and 2 (1.4%), respectively. Cirrhosis, defined as transient hepatic elastography 12.5kPa or liver biopsy, was present in 62 (44%) patients. Eighty one patients (57.4%) were treatment experienced with previous failure to pegylated interferon+ ribavirin (PEG+RBV) based therapy. The following DAA therapies were used: sofosbuvir (SOF)+RBV in 6 patients SOF+simprevir RBV in 67 SOF+PEG+RBV in 3 SOF+daclatasvir in 23, SOF+ledipasvir in 41, and ombitasvir + paritaprevir/ritonavir + dasabuvir in one patient. Twelve weeks treatment duration was used in 75% of the patients and 24 weeks in the remaining 25%. SVR-12 was achieved in 182/214 (93.6%). Nine patients failed therapy. All failures were due to relapse: 6 were cirrhotic, 5 were treatment experienced, and 4 were either genotype 3 or 1a. Three patients died during treatment, all because of hepatic decompensation. No death or serious adverse event was attributed to the DAA therapy.

Conclusion: Real world experience with DAA therapy in three Brazilian centers showed a high rate of SVR and excellent tolerability, with results similar to the published phase 3 studies conducted with the same DAA therapies. Failure to achieve SVR was only observed among patients with at least one of the following negative predictors: cirrhosis, previous failure to PEG-IFN therapy, and either genotype 3 or 1a.

103. Poster Presentation #2017

#2017: EFFECTIVENESS AND SECURITY OF 3D/2D TREATMENT IN HCV/ HIV COINFECTED CIRRHOTIC PATIENTS
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Aim: Analyze 2D (Paritaprevir + Ombitasvir) and 3D (Paritaprevir + Ombitasvir + Dasabuvir) combinations + Ribavirin (RBV) in HCV/HIV coinfected cirrhotic patients.

Methods: Retrospective, multicentric and per-protocol study, based on 169 HCV/HIV coinfected cirrhotic patients (Fibroscan >12.5 kPa) from 7 Basque Country and Navarra (Spain) hospitals. The data have been collected at the end of treatment (EOT) and 12 weeks after to assess the sustained viral response (SVR) of schemes 2D+RBV for genotype 4 and 3D+RBV for genotypes 1a, 1b and mixed 1a-4 according to data sheet.

Results: We studied 169 patients, 76.9% men, with an average age of 51 years (SD=4.49). Cirrhotic patients with an average fibrosis grade of 21.8 kPa (SD=11.75) 130.7/mm3 platelets (SD=70.68) (38.0% thrombocytopenia <100/mm3) and 4.27 g/dl albumin (SD=0.44) (4.1% hypoalbuminaemia <3.5 g/dl). HCV infection, 94.7% with undetectable viral load (VL) (87.0% <20 copies/ml) and a CD4 average of 626 cells/mm3 (SD=350), (57.4% CD4 nadir <200). 71.1% patients needed antiretroviral treatment (ART) modification and 23.7% withdrawal of antiretroviral therapy. No death or serious adverse event was attributed to the DAA therapy.

Conclusion: Real world experience with DAA therapy in three Brazilian centers showed a high rate of SVR and excellent tolerability, with results similar to the published phase 3 studies conducted with the same DAA therapies. Failure to achieve SVR was only observed among patients with at least one of the following negative predictors: cirrhosis, previous failure to PEG-IFN therapy, and either genotype 3 or 1a.
obtained a SVR of 90.7%, this result being better in mixed genotype (100%) and genotype 1b (96.3%) and worse in genotype 1a (88.9%) and genotype 4 (87.5%). Most RBV adjustments were done before the 4th week of treatment because of hemoglobin decrease. There was not impact in the final response. When ART therapy is adjusted, we observed a good safety profile.

**Figure:** Treatment results

### 104. Poster Presentation #2022

**#2022: CHANGES IN LIVER STIFFNESS AND CLINICAL OUTCOMES AFTER SVR IN PATIENTS WITH ADVANCED FIBROSIS OR CIRRHOSIS FROM HEPATITIS C VIRUS**

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**Background:** The follow-up assessment of fibrosis in patients who achieve sustained virologic response (SVR) is important in terms of predicting risk of liver related complications. Liver stiffness by transient elastography has been shown to have havelong term prognostic value in patients with hepatitis C virus (HCV), however few longitudinal studies exist after treatment that have patients with advanced fibrosis and/or cirrhosis included in the study population and do not correlate with clinical outcomes. Purpose: Evaluate the long-term change Fibroscan scores in HCV patients with advanced fibrosis who achieve SVR and correlate with occurrence of hepatocellular carcinoma, liver imaging and liver related complications.

**Methods:** This is a prospective study evaluating Fibroscan scores in HCV patients with advanced fibrosis undergoing treatment. Liver stiffness was measured prior to initiation of treatment and then repeated at end of treatment, 12 weeks after end of treatment (PTW12), 1 year after the end of treatment and then annually thereafter for a total of 5 years after end of treatment. Clinical outcomes were also collected. This is an interim analysis of all patients currently enrolled.

**Results:** Fourteen patients have currently completed treatment and had PTW12 follow-up. All fourteen patients achieved SVR 12. Mean baseline Fibroscan score was 13.2kPa (range 9.5-23.1). Average reduction in Fibroscan score by EOT was 3.44kPa (range -0.4-13.1). The average reduction after SVR 12 was 433kPa (range -01-131). Nine patients (64%) had at least a 10% improvement in Fibroscan score by PTW12. Three patients had had reduction in liver size and one patient had resolution of splenomegaly. No patients developed HCC. No patients had evidence of hepatic decompensation. On univariate and multivariate statistical analysis, there was no significant association of improvement in Fibroscan score by PTW12 with baseline Fibroscan score, baseline platelets, change in liver size, change in spleen size (p=ns). One year follow up data will also be reported.

**Conclusions:** Successful treatment of HCV in patients with advanced fibrosis results in a reduction in liver stiffness per Fibroscan by PTW12 and no evidence of hepatocellular carcinoma or hepatic decompensation, suggesting stabilization and possibly improvement in liver disease. No clinical predictors correlate with reduction in Fibroscan score, however, one year follow up data is pending and may offer further insight.

### 105. Poster Presentation #2057

**#2057: NOVEL SERUM BIOMARKERS PREDICT OUTCOME IN COMPENSATED CIRRHOSIS**

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**Background:** Compensated cirrhosis is an asymptomatic state, with growing evidence for an immunological basis for disease progression. Clear identification and stratification of cirrhosis associated immune dysfunction could identify key disease stages that may be amenable to targeted therapeutic interventions. The objective of this study was to identify novel inflammatory and metabolic biomarkers that reflect the underlying pathophysiology of cirrhosis progression, and could provide prognostic information.

**Methods:** This is a prospective study of patients with compensated cirrhosis, of mixed aetiology, with clinical and radiological evidence of cirrhosis or biopsy proven cirrhosis. All patients received a Fibroscan™ examination at baseline with blood samples collected for routine disease staging and serum biomarker analysis. The primary outcome was the development of a decompensating event (ascites, encephalopathy, variceal bleeding).

**Results:** 17 (123%) of 138 patients enrolled in the study developed an outcome. The median follow up was 34 months (range 2-46 months). Aetiology was viral in 37% and alcohol liver disease in 38%. 88% were Childs Pugh score B7. On univariate analysis, expected clinical factors such MELD-Sodium score, liver stiffness score, and Child PughScore were associated with an outcome (all p<0.001). All of the following biomarkers were also significantly associated with an outcome (p<0.001): Resistin, VACM1, IP10, IL33, HGF, Leptin, sFas, Thrombomodulin, IL1RA, E-Selectin, HSP70, Adiponectin, CRP, siCAM1. Multivariate logistic regression analysis identified a composite risk score consisting of VACM1 (p=0.0005), CRP (p=0.0006), and HGF (p=0.0071). A ROC curve of this risk score (AUROC = 0.901, p<0.0001) versus outcome generated a risk threshold that on Kaplan Meier analysis predicted 2 year outcome (Log Rank 567, p<0.0001, decomposition risk 55.7% versus 97%).

**Conclusions:** Abnormalities in the activation of adhesion and migration leukocyte molecules, and in cytokine and chemokine levels demonstrate significant immune dysfunction in asymptomatic, compensated cirrhosis. A score derived from these serum biomarkers accurately predicts future decomposition risk at 2 years. There is need for further validation studies to develop risk scores and novel staging of compensated cirrhosis based on immunological phenotyping.