Discovery of new non-invasive tests algorithms (NITs-Algo) for liver disease in subjects with metabolic factors, using SAF scoring system. A proof of concept demonstrating the impact of disease definitions.

T Poynard, M Munteanu, F Charlotte, H Perazzo, Y Ngo, O Deckmyyn, W Merrouche, V de Ledinghen, P Mathurin, V Ratziu;

In subjects presumed NAFLD, there is a need of NITs for a simple prediction of liver injury and NASH. The histological diagnosis of NASH was recently improved by the SAF scoring system (A2 or F2 defining significant disease) and the FLIP-algo defining NASH (Bedossa 2014). Authors aimed to propose non invasive tests (NITs-algo) taking into account remaining limitations (Brunt 2016), which impacted artificially the NITs performance: the choice of 5% or 1% for defining steatosis (S), the requirement of S for defining A or NASH, as well as a lack of sufficient controls A0S0. Authors concluded that taking into account the impact of definitions should permit to understand artificial discordances observed between “NAFL-NAFLD-NASH” epidemiological studies, and to construct better biomarkers. “Metabolic liver disease” could be used instead of “NAFL/NAFLD/NASH”.

Diagnostic performance of FibroTest, SteatoTest, and ActiTest in patients with NAFLD using the SAF-score as histological reference


The study aimed to improve the validation of three blood tests used in NAFLD patients as surrogate markers, FibroTest for fibrosis staging, SteatoTest for steatosis grading and ActiTest for inflammation activity grading. A total of 600 NAFLD patients with biopsy (blindly assessed using the new SAF score) and blood tests (FibroMax panel) were included from a single-center cohort (FibroFrance) and from the multicenter FLIP consortium. The median NonBinROCs (95% CI) of tests were all significant (P<0.0001) for all stages and grades. None of the other fibrosis tests (NAFLD Fibrosis Score, BARD score and FIB4 score) had such significant increase between each fibrosis stages as FibroTest had. In conclusion, in patients with NAFLD, SteatoTest, ActiTest and FibroTest are non-invasive tests that may offer an alternative to biopsy and correlate with the simple grading/staging of the SAF scoring system across the three elementary features of NAFLD: steatosis, inflammatory activity, and fibrosis.
Abstract #1105
FibroMax for the longitudinal follow-up of Obese T2DM patients with Endobarrier
Improvement in Non-Invasive Hepatic Parameters of Nonalcoholic Fatty Liver Disease in Obese Uncontrolled Type 2 Diabetes Mellitus Patients who underwent Endoscopic Duodenal–Jejunal Bypass Liner (Endobarrier) Implantation
O Cohen-Ezra, G Segal-Lieberman, A Lang, Yeroham Kleinbaum, Y Inbar, S Katsherginsky, K Tsaraf, Z Ben Ari
The study proposed to investigate the effect of nonsurgical bariatric technique, the Endobarrier (GI Dynamics) on non-invasive hepatic parameters in obese uncontrolled T2DM patients with NAFLD that had performed repeated shear wave elastography (SWE) (Aixplorer SuperSonic Imagine, France) and Fibromax (FibroTest, ActiTest, SteatoTest, and NashTest) (BioPredictive, France) for the noninvasive evaluation of hepatic injury.
By 3, 6 and 12 months following the Endobarrier implantation, the fibrosis stage (FibroTest and SWE) decreased significantly from baseline. In addition, the ActiTest, SteatoTest (fat liver content), and NashTest (steatohepatitis NAS score) from Fibromax panel improved significantly from baseline by 6 month after the Endobarrier removal.
FibroMax panel results were sensitive to detect significant improvement in hepatic fat liver content, steatohepatitis score and fibrosis stage in uncontrolled obese, diabetic, NAFLD patients after Endobarrier procedure.

Abstract #1149
FibroMax for the longitudinal follow-up of Obese T2DM patients Lifestyle Intervention
The Effect of 12-Months of Intensive Lifestyle Intervention on Serum Biomarkers of Hepatic Steatosis, Inflammation and Fibrosis in Adults with Type 2 Diabetes
M Lazo, M Liang, JJ Potter, JM Clark
The authors proposed to evaluate the efficacy of weight loss through diet and exercise as a treatment for NAFLD, in reducing steatosis, in patients with type 2 diabetes. Were included 123 overweight or obese adults with type 2 diabetes enrolled in the Fatty Liver Ancillary Study to the Look AHEAD (Action for Health in Diabetes) trial, with FibroMax (FibroTest, SteatoTest and NashTest) measured on stored serum samples at baseline and after 1 year of the study.
53% had significant steatosis (SteatoTest ≥S2), 18% had NASH (NashTest =N2), 9% had significant fibrosis (FibroTest ≥F3). At 12 months, the percentage with significant steatosis and NASH decreased more among the intensive lifestyle intervention (ILI) group than the group with diabetes support and education (DSE) (all p<0.01). 5% weight loss had a significantly improvement in SteatoTest. There were no significant 12-month changes in FibroTest, by intervention group, or by degree of weight loss.
Authors concluded that FibroMax biomarkers of NAFLD-steatosis and NASH appear to be sensitive to change and may be useful to monitor treatment responses.
Abstract #658

Assessment of serum levels of Chitinase-3-like protein 1 (CHI3L1) improves identification of the NASH patients at risk who should be treated

AJ. Sanyal, SA. Harrison, G Cordonnier, J Brozek, A Roudot, E Praca, F Ben Sudrik, S Megnien, Rémy Hanf, B Staels, P Bedossa, V Ratziu, D W. Hum, R Darteil,

Data and samples from the 274 biopsy proven NASH patients included in the GOLDEN505 phase IIb trial with elafibranor were used for this study that proposed to identify additional biomarkers. The measurements of Chitinase-3-like protein 1 levels (CHI3L1, also called YKL-40) was added to the other measurements including FibroMax panel (FibroTest, NashTest, SteatoTest, ACtiTest). Authors proposed to improve algorithms including than the existing scoring systems such as the NAFLD Fibrosis Score, the Fibrotest, than the existing scoring systems such as the NAFLD Fibrosis Score, the ELF test, the Fibrotest, and FIB-4. The results of the comparisons were not provided in the abstract.

Abstract #1121

Circulating, hepatocyte-derived extracellular vesicles correlate with fibrosis stage and portal pressure in patients with nonalcoholic steatohepatitis


Extracellular vesicles (EVs) are membrane-bound particles released from dying or activated cells. The objectives of this study were to quantify and characterize EVs in serum of patients with nonalcoholic steatohepatitis (NASH) using dynamic light scattering analysis, electron microscopy and flow cytometry in 50 histologically proven NASH patients and 11 controls. Compared with controls, NASH patients had greater numbers of total EVs and the number of hepatocyte-derived EVs correlated with fibrosis stage as per Fibrotest ($p=0.31; P=0.037$).

Abstract #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.

MF. Donato, C Rigamonti, F Invernizzi, G Colucci, M Fraquelli, M Maggioni, BB. Antonelli, S Monico, G Rossi, M Colombo.

This retrospective study aimed to evaluate the diagnostic performance of Fibrotest (FT) and transient elastography (TE) in detecting liver fibrosis as well as additional histological features before and after DAA and the role of DAA on graft fibrosis reversibility. This retrospective study included 31 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. SVR was 97%.

DAA significantly decreased the extent of sinusoidal fibrosis in LT recipients with recurrent hepatitis C. TE showed overall better concordance with histology while both TE and FT properly assessed significant fibrosis and its changes.
Abstract #1635
Liver Transplant

100% Virological response with 3D regimen and significant short-term liver stiffness improvement in patients with recurrent hepatitis C following liver transplantation

S Iacob, I Popescu, L Gheorghe.

The aim was to present the team’s experience with DAA agents in 72 HCV-LT recipients, as well as to compare pre and posttreatment fibrosis with non-invasive markers. At EOT and at time of SVR12 evaluation only TE was performed.

**Results:** At baseline 56.4% of patients had severe necroinflammation at ActiTest (A2,A3, Fibromax panel), cirrhosis (F4) was encountered in 34.5% of LT recipients and grade S3 steatosis in 43.6% of transplanted patients. 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: 11.9±1.8kPa vs 9.5±1.0kPa (p=0.02) in LT recipients.

Abstract #1636
Liver Transplant

Treatment of Hepatitis C with ledipasvir, sofosbuvir with or without ribavirin in post liver transplant patients in an academic center.

N Pyrsopoulos, VA. Lingiah, S Sanaka, P Fung, M Punnoose.

The study aimed to evaluate sustained viral responses at 12 weeks (SVR12) in 63 HCV-LT patients, treated with once daily sofosbuvir and ledipasvir (sof/led). Main immunosuppression (IS) included cyclosporine (CSA), tacrolimus (FK), everolimus (EVR) or sirolimus (SIR).

Fibrosure (FibroTest) testing was done in 61 out of 63 patients; median was 0.49. Prior to treatment, 5 patients (8%) were stage F0, 11 (17.4%) F1, 20 (31.7%) F2, 6 (9.5%) F3 and 19 (30%) F4.

Authors concluded that in patients with recurrent genotype 1 (a or b),3, 4, 5a and 6 hepatitis C after LT, the combination of sof/led with ribavirin for 12 weeks or sof/led for 24 weeks is generally well tolerated with high response rates. Fibrotest was used in pre-treatment evaluation of fibrosis.
Abstract #1829

**HBV Risk of normal ALT to exclude advanced fibrosis**

Nearly One Third of Asian Adults with Treatment Naïve Chronic Hepatitis B Virus (HBV) Infection with Elevated HBV DNA and Normal Alanine Aminotransferase Have Significant Hepatic Fibrosis

**RJ. Wong, A Le, MT. Nguyen, HN. Trinh, A Huynh, M Ly, H Nguyen, KK. Nguyen, JC. Yang, RT. Garcia, BS. Levitz, E DaSilvera, R Gish**

Significant histologic fibrosis may exist despite normal alanine aminotransferase (ALT) in chronic hepatitis B virus (HBV). Non-invasive measures of hepatic fibrosis may improve and guide HBV therapy in patients not meeting eligibility based on HBV DNA and ALT. This study aimed to evaluate the prevalence of fibrosis among treatment naïve chronic HBV Asian patients with elevated HBV DNA and normal ALT. Hepatic fibrosis was assessed using serologic data (FIB-4, APRI, Fibrotest), imaging data (spleen size, main portal vein diameter), and supersonic (shear-wave) elastography. 105 patients were included 91.7% had F0-F1, 8.3% had F2-F3, no patients had F4 based on Fibrotest. Authors concluded that among treatment naïve Asian adults with chronic HBV with elevated HBV DNA and normal ALT accurate staging of hepatic fibrosis would be improved with combination of tests including indirect tests, imaging, and elastography.

Abstract #1879

**FibroTest in HBV trials**

Characterization of host, viral, and treatment-related factors associated with antiviral efficacy of tenofovir alafenamide (TAF) and tenofovir disoproxil (TDF)

**EJ. Gane, M Saito, S Hyun Bae, P Andreone, JF. Flaherty, K Kim, A Gaggar, RP. Myers, FA. Caruntu, F Wong, X Ma, P Marcellin**

The objective of this study was to determine host, viral, and treatment-related factors associated with HBV DNA persistence after 48 weeks of treatment with TAF or TDF in adults with CHB enrolled in two Phase 3 studies of TAF 25 mg QD vs. TDF 300 mg QD (Study GS-US-321-0108 and GS-US-321-0110). Authors examined the associations between host factors (i.e age, sex ALT, FibroTest, etc), viral, and treatment-related factors with HBV DNA persistence. 1,246 randomized subjects (96%) had available HBV DNA at Week 48 and are included. Authors concluded that a high proportion of after 48 weeks of treatment with TAF or TDF. HBeAg-positivity, high BL viral load, HBV genotype D, prior antiviral treatment and lower antiviral adherence are independent predictors HBV persistence with these therapies.
Abstract #1904
Characterization Of Changes In FibroTest Values During Treatment With Tenofovir Alfenamide (TAF) Or tenofovir disoproxil fumarate (TDF) In Patients With CHB
N Izumi, O Tak Yin Tsang, S Hoon Ahn, S Gurel, P W. Angus, J F. Flaherty, K Kim, A Gaggar, V Suri, M Subramanian, C Cooper, H Won Hann, SK. Acharya
In two large Phase 3 studies of TAF, a novel prodrug of tenofovir, versus TDF in patients with chronic hepatitis B, repeat FibroTest measurements were assessed during the first 48 weeks of treatment. For analyses, a FibroTest score of <0.49 = Ishak F0-F2 fibrosis stage, a score of 0.49-0.75 = Ishak F3-F4 fibrosis and a score of >0.75 = Ishak F5-F6 fibrosis.
Subjects treated with TAF had greater mean declines in FibroTest scores at Week 48 compared to subjects treated with TDF. The strongest predictors by multivariate analysis for fibrosis stage improvement as per FibroTest included higher baseline ALT (> 5xULT), and lower HBsAg levels (log10 IU/mL). While FibroTest changes favored TAF, the change in FibroTest score was driven mainly by changes in Apolipoprotein A1 and likely represents the known lipid-lowering effect of TDF. The significance of this FibroTest score decline with respect to fibrosis stage in TAF versus TDF patients requires further investigation.

Abstract #824
Regression of Liver Fibrosis assessed by non-invasive methods in Patients with Chronic Hepatitis C who Achieved Sustained Virologic Response after DAAs Treatment
Y Davidov, Y Kleinbaum, O Cohen-Ezra, E Veitsman, T Berdichevski, P Weiss, S Katsherginsky, H Avishag, K Tsaraf, Z Ben Ari
Authors evaluated the regression of liver fibrosis after the cure of HCV following DAAs therapy (during non-invasive measures FibroTest, elastography shearwave (SWE), APRI score and FIB-4. 130 patients were enrolled.
Authors reported the majority of the subjects (44.8%) demonstrated improvement in liver fibrosis stage by non-invasive methods. Some of the clinical parameters were negative predictors of liver fibrosis regression. Longer follow up period is required to determine the impact of the DAAs treatment in HCV patients.
Abstract #1918

Impact of steatosis and metabolic syndrome on the SVR rate with DAA

Metabolic syndrome, hepatic steatosis and genotype 1b C virus compensated liver cirrhosis in the era of Direct Acting Antiviral therapy

C Mihai, A Trifan, C Stanciu, L Gheorghe, S Iacob, M Diculescu, C Cijevschi

The aim was to assess the effect of DAA therapy - paritaprevir, ritonavir, ombitasvir, dasabuvir and ribavirin (PrOD+R) on steatosis (HS) and the metabolic syndrome (MS) in patients with compensated genotype 1b HCV Child A cirrhosis as per FibroTest. Fibrosis and steatosis were assessed by FibroTest and SteatoTest from the FibroMAX panel.

356 consecutive patients were enrolled. The prevalence of significant HS (S2-3) was 50.6%, MS parameters prior to treatment was obesity (38.5%), type 2 diabetes (T2D) (27.2%), hypertension (21.9%) and hyperlipidemia (19.4%). There was statistically significant positive correlation between steatosis as per SteatoTest and T2D, obesity, hyperlipidemia. Steatosis and MS are common finding in patients with compensated cirrhosis but do not seem to influence the SVR rate (100%) after PrOD+R. DAA therapy for cirrhotic HCV patients seems to improve individual components of the metabolic syndrome, especially hyperlipidemia and hypertension.

Abstract #805

Predicting cirrhosis complications with FibroTest

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)?


The aim of this case-control 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.

Actitest-Fibrotest, along with other blood markers and transient elastography (TE) were analysed every 6 months between months 0 to 36. 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: 0.72±0.18 vs 0.84±0.10. This significant difference was found in SVR patients except for TE. After adjusting for SVR, all markers remained associated with the occurrence of a complication.

FibroTest was able to early predict the occurrence of complications especially HCC in patients with post hepatitis C cirrhosis. Authors proposed to monitor more accurately patients with high initial values, threshold remaining to be determined.
Abstract #1979

Dynamics of AFP in cirrhotic patients with virological response following 3D therapy and severe necro-inflammation at Fibromax

S Iacob, L Gheorghe, A Trifan, C Stanciu, R Sirli, I Sporea, R Lupusoru, C Cijevschi, V Arama, C Brisc, I Rogoveanu, R Iaco, C Gheorghe

The aim of this study was to assess if and which patients should be more aggressively screened for HCC during long term follow-up after viral eradication with interferon-free regimens.

393 consecutive patients with HCV genotype 1b liver cirrhosis and without HCC were treated with 3D-Abbvie and ribavirin for 12 weeks in 6 tertiary centers from Romania. All patients had Fibromax done at the beginning of antiviral therapy. The distribution of activity score at Fibromax was A1 7.9%, A2 25.2% and A3 66.9%. Steatosis grade S2 and s3 was encountered in 42.1% of patients. There was a significant association between severe inflammation and moderate-severe steatosis (p=0.0007). ALT and GGT were significantly decreased at the end of treatment (EOT). However, only in patients with A1-A2. In this cohort, high activity HCV cirrhosis characterized by $A \geq 3$ at Fibromax evaluation and increased AFP was associated with a significant lower decrease in AFP at EOT. In the setting of HCV macronodular cirrhosis, the persistent AFP above ULN, should rise the question of intensifying HCC surveillance within the first 2 years after "virological cure", even in patients with pretherapeutic CT/MRI assessment.

Abstract #2006

Safety of DAA treatments in patients aged >65 years with cirrhosis as per FibroTest

Efficacy and safety of paritaprevir/ritonavir, ombitasvir and dasabuvir + ribavirin for treatment of HCV genotype 1b compensated cirrhosis in patients aged 65 years or older


The aim of this study is to analyze efficacy and safety of paritaprevir/ritonavir; ombitasvir and dasabuvir and ribavirin (3D+R) for 12 weeks treatment of hepatitis C virus (HCV) genotype 1b- compensated cirrhosis as per FibroTest in patients aged 65 years or older included across 10 academic centers in Romania. 527 patients were included. Authors concluded that treatment with 3D+R regimens in patients aged 65yrs or older with HCV genotype 1b compensated cirrhosis as per FibroTest is highly effective and safe, similar to that in younger patients.
Abstract #1920

Impact portal hypertension on the SVR rate with DAA

The influence of clinical significant portal hypertension (stage Baveno 2) on safety, tolerability and efficacy of paritaprevir, ritonavir, ombitasvir, dasabuvir and ribavirin (PrOD+R) in a real-world large cohort of genotype 1b HCV liver cirrhosis patients


The aim of our study was to evaluate the safety and efficacy of PrOD+R in patients with clinical significant portal hypertension (Baveno 2), genotype 1b compensated cirrhosis diagnosed by FibroTest.

360 (68.3%) were Baveno 1 and 167 (31.7%) were stage Baveno 2. Treatment with PrOD+R in patients with Baveno 2 stage genotype 1b compensated HCV cirrhosis as per FibroTest is highly effective and safe, similar to that in Baveno 1 stage. However, the liver decompensation events are more frequent and a note of caution need to be taken.

Abstract #943

FibroTest could be easily integrated in telemedicine

Telemedicine-based Hepatitis C Virus (HCV) Management for Individuals on Opioid Agonist Treatment (OAT)

AH. Talal, P Andrews, A McLeod, Y Chen, M Markatou, C Sylvester, L Brown

Telemedicine (two-way videoconferencing) permits direct interaction between patients and specialists in distinct locations and might be useful for HCV treatment of OAT patients. Over 14-months, 54 HCV RNA-positive patients received an HCV evaluation via telemedicine. Fibrosure (FibroTest) revealed: mild (stage 0-1) in 14/44 (32%), moderate (stage 1-2) in 15/44 (34%), and severe (stage 3) in 15/44 (34%) patients. Medication adherence has been excellent.

Authors concluded that telemedicine-based HCV care is a feasible, reimbursable model for HCV treatment delivery in an OAT program with excellent initial patient acceptance that strengthens over time. Telemedicine can virtually integrate specialty-based care into the OAT clinic.
Effectiveness of Sofosbuvir/Ledipasvir and Sofosbuvir/ Simeprevir for the Treatment of Hepatitis C Genotype-1: Real World Analysis  
A Abdulameer, P Leff, K Joshi, A Hepner, A Moore, K Arendt, J Reynolds, R Gish, R Manch, A Kohli

The aim was to evaluate retrospectively the effectiveness of SOF/LDV and SOF/SIM for treatment of HCV genotype 1 (GT1) in a real-world patient population. 588 patients with GT-1 who received treatment with either SOF/LDV or SOF/SIM were identified. 34% of patients had cirrhosis by radiology, Fibrosure-FibroTest or liver biopsy. Full results of SVR12 and SVR12 stratified by cirrhosis, treatment experience and provider setting will be presented in AASLD Liver meeting. Patients with cirrhosis and those who are treatment experienced were more likely to relapse. DAA regimens have transformed treatment options for patients with chronic HCV, providing well tolerated, shorter course, high effectiveness regimens. Characterization of treatment failures is essential for modifying therapy for these at-risk patients.

Trials using FibroTest/FibroSure

- #114 ENDURANCE-4: Efficacy and Safety of ABT-493/ABT-530 Treatment in Patients with Chronic HCV Genotype 4, 5, or 6 Infection ; T Asselah et al.
- #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 ; GR. Foster et al.
- #937 In patients with chronic HCV infection, antiviral treatment with DAAs can be managed by specialized nurses. Results of a large real-life cohort ; G Scoazec et al.
- #1927 Efficacy and safety of sofosbuvir and daclatasvir for 8 weeks in treatment-naïve non-cirrhotic patients with chronic HCV Genotype 3 Infection ; C Hezode et al.
- #1989 High efficacy of ombitasvir/paritaprevir/ritonavir and dasabuvir with ribavirin for 12 weeks in treatment of genotype 1b HCV infected cirrhotic patients: a large real world cohort ; I Girleanu et al.
- #826 Stage 3-4 Fibrosis does not guarantee access to direct-acting antivirals in patients with state-funded insurance: An analysis of a HCV referral program ; P Santos et al.
- #927 Hepatitis C Virus Treatment Response to Ledipasvir/ Sofosbuvir among patients co-infected with HIV and HCV: Real World Data in a Black Population; J Banga et al.
- #1465 Rapid intrahepatic and peripheral blood HCV RNA decline and HCV-specific immune response increase during IFN-free DAA therapy in HCV treatment-naïve patients ; S A. MacParland et al.
- LB-16 Eight weeks treatment duration with Ledipasvir/Sofosbuvir (LDV/SOF) is effective for appropriately selected patients with genotype 1 Hepatitis C virus (HCV) infection: an analysis of multiple real world cohorts totaling >6,500 patients ; V Sundaram et al.