FibroTest Scientific Publications
Key Publications for 2017

Ratziu 2016
FibroMax NASH

SteatoTest and FibroTest sensitive markers of improvement in NASH trial using Elafibranor

Elafibranor, an agonist of the peroxisome proliferator –activated receptor α- and δ, induces resolution of nonalcoholic steatohepatitis without fibrosis worsening

Ratziu V, Harrison SA, Francque S et al. GOLDEN-505 Investigator Study Group. Gastroenterology 2016;150:1147–1159

FibroTest was used as a surrogate marker of liver fibrosis in the international, randomized, double-blind placebo-controlled trial of patients with nonalcoholic steatohepatitis (NASH) using Elafibranor, an agonist of the peroxisome proliferator activated receptor α- and peroxisome proliferator activated receptor- δ.

In line with the histologic changes, FibroMax panel's surrogate markers of steatosis – SteatoTest- and fibrosis – FibroTest - showed significant reductions in patients treated with elafibranor 120 mg compared with placebo.

Authors concluded that the noninvasive serum panels of steatosis– SteatoTest- and fibrosis – FibroTest - are likely more sensitive and earlier response indicators to treatment than histology.

Friedman 2016
FibroTest NASH

FibroTest compared against the histological endpoints in NASH trial CENTAUR

Efficacy and safety study of cenicriviroc for the treatment of non-alcoholic steatohepatitis in adult subjects with liver fibrosis: CENTAUR Phase 2b study design

Friedman S, Sanyal A, Goodman Z, et al. Contemporary Clinical Trials 2016;47:356–65.

FibroTest was used as a surrogate marker of liver fibrosis in the Phase 2b, randomized, double-blind, placebo-controlled multinational study (CENTAUR; NCT02217475) that proposed to assess histologic and non-invasive markers of NASH lesions after administration of Cenicriviroc (CVC), a dual-CCR2/CCR5 antagonist.

FibroTest, included as a marker of NASH progression, was analyzed against the histological endpoints and results will be provided soon.

FibroTest Scientific Publications
Key Publications for 2017

Munteanu 2016
FibroTest
FibroMax
NAFLD
FLIP

Validation of FibroTest and FibroMax panel in NAFLD

Blood tests of liver injury are less well validated in non-alcoholic fatty liver disease (NAFLD) than in patients with chronic viral hepatitis

Munteanu M, Tiniakos D, Anstee Q et al. & the FLIP Consortium and the FibroFrance Group. Aliment Pharmacol Ther. 2016;44:877-89.

A new multicenter study included two NAFLD cohorts - the European FLIP and the French (FibroFrance) - revalidated the diagnostic tests for elementary lesions of NAFLD -steatosis, activity and fibrosis (SAF) – from the FibroMax panel: SteatoTest, ActiTest and FibroTest, respectively.

This study has several strengths: the size of the cohort (600 NAFLD patients), the use of a new histological classification (SAF score, Bedossa et al. 2012) and an efficient statistical methodology (NonBinAUROC).

The results confirmed once again the excellent diagnostic value of FibroMax panel for histological SAF lesions. The FibroTest was superior to the FIB-4 tests and BARD, based on transaminases.

FibroTest was the only test discriminating between fibrosis stages F1 vs F2, unlike the FIB-4, BARD and NAFLD-score.

In patients with NAFLD, the FibroMax panel offers reliable non-invasive tests that are correlated with the histological classification of SAF.

Houot 2016
FibroTest
TE
FIB-4,
APRI
Meta-analysis

FibroTest is superior to TE by Fibroscan, APRI and Fib-4 using direct comparisons meta-analysis

FibroTest better than TE by Fibroscan, APRI and Fib-4: A meta-analysis of 71 studies

Houot M, Ngo Y, Munteanu M, et al. Aliment Pharmacol Ther. 2016;43:16-29

The statistics using direct comparisons have helped to improve the standard methods of meta-analysis and comparisons between non-invasive tests. 71 studies with biopsy in chronic hepatitis B and C were selected for the 185 direct comparisons between the most used noninvasive tests: FibroTest, TE by Fibroscan, APRI and FIB-4.

FibroTest has a better diagnostic performance compared to the TE by Fibroscan for significant fibrosis (12,725 F2F3F4 METAVIR patients) and has a similar performance for cirrhosis (F4 METAVIR 10,929 patients)

The applicability of FibroTest was higher than TE by Fibroscan (99% versus 88%)

FibroTest performance was superior to the tests based on the transaminases – APRI and FIB-4, both for cirrhosis and advanced fibrosis.

FibroTest Scientific Publications
Key Publications for 2017

Herman 2016
HCV
FibroTest
APRI
FIB-4

Lack of accuracy of APRI and Fib-4 compared to FibroTest

Letter: APRI and FIB-4 do not correlate with FibroTest in the evaluation of liver fibrosis in hepatitis C patients

Herman M, Okoji O, Castaneda D, et al. Aliment Pharmacol Ther 2017; 45: 181–191 191.

In this letter, authors made comments on the study of Houot et al. and published their local experience (Mount Sinai, New York, USA) with FibroTest performed on hepatitis C patients from 2015 compared to APRI and FIB-4.

Authors concluded that APRI and FIB-4 show only a marginal correlation with FibroTest and therefore cannot be used reliably in place of FibroTest for the evaluation of liver fibrosis. APRI and Fib-4 are not sufficiently accurate to use them as a follow-up tool for patients.

Poynard 2016
FibroTest
2D SWE
TE

Applicability of 2D-SWE versus TE and FibroTest

Real-Time Shear Wave versus Transient Elastography for predicting fibrosis: applicability, and impact of inflammation and steatosis. A non-invasive comparison.

Poynard T, Pham T, Perazzo H, et al.; FIBROFRANCE-HECAM. PLoS One. 2016 Oct; 11:e0163276.

Authors aimed to compare several criteria of applicability of the real-time shear wave elastography (2D-SWE) to the standard reference, transient elastography (TE), and to assess inflammation and steatosis impact on real-time shear wave elastography (2DSWE).

FibroTest was taken as the fibrosis reference and ActiTest and SteatoTest as quantitative estimates of inflammation and steatosis.

The applicability of 2D-SWE (95%CI) 89.6% (88.2-90.8), was significantly higher than that of TE, 85.6% (84.0-87.0; P<0.0001).

2D-SWE had results less impacted by inflammation and steatosis than TE especially in patients with non-advanced fibrosis, as presumed by FibroTest.

Bignulin 2016
FibroTest
Liver Transplantation

New validation of FibroTest in liver transplanted

Usefulness of acoustic radiation force impulse and FibroTest in liver fibrosis assessment after liver transplant.

Bignulin S, Falleti E, Cmet S, et al. Ann Hepatol. 2016;15:200-6.

This study assessed the accuracy of ARFI and FibroTest in 51 HCV positive liver transplanted patients who consecutively underwent to annual liver biopsy concomitantly with ARFI and blood chemistry. ARFI and FibroTest had similar performances (AUROC 0.885 and 0.848, respectively) and their combination did not improve each marker alone in discriminating between patients with or without significant fibrosis (Ishak score 0-2 vs. 3-6).

Both FibroTest and ARFI seemed accurate non-invasive tools for identifying patients with a benign course of HCV recurrence after liver transplantation.

Matta 2016
FibroTest
HIV

Review of studies that validated FibroTest in HIV co-infected

Use of non-invasive testing to stage liver fibrosis in patients with HIV

Matta B, Lee TH, Patel K. Curr HIV/AIDS Rep 2016;13:279–288

Authors reviewed the non-invasive modalities of liver fibrosis assessment in HIV mono and co-infected patients and listed the studies that developed these methods in an attempt to avoid liver biopsy and allow for repeated testing.

For FibroTest, the performances for advanced fibrosis in HIV-HCV co-infection were as follows as per AUROC (Number of patients, Author-Year): 0.856 (N=130, Myers 2003), 0.81 (N=272, Cacoub-2008), 0.778 (N=444, Cales-2010), 0.85 (N=116, Castera-2014), 0.75 (N=101, Schmid-2015) and 0.84 for cirrhosis (N=101, Schmid-2015).

For FibroTest, the performances for advanced fibrosis in HIV-HBV co-infection for advanced fibrosis/cirrhosis were as follows: 0.77 / 0.87 (N=108, Bottero-2008) and 0.86 / 0.93 (N=59 Miaihes-2011)

Authors concluded that non-invasive test results should be considered in conjunction with available clinical, laboratory, and other imaging data to evaluate fibrosis in HIV co-infected patients.

Natarajan 2017
FibroTest
Prognostic

Impact of comorbidities on mortality of HCV patients with cirrhosis as per FibroTest

Role of non-hepatic medical comorbidity and functional limitations in predicting mortality in patients with HCV

Natarajan Y, White DL, El-Serag HB. Dig Dis Sci 2017; 62:76–83.

In a cohort of 1 052 patients with HCV infection, authors proposed to determine the effect of comorbidities and functional status variables (as per Schonberg Index (SI) based on age, gender, medical comorbidities), on survival after adjusting for liver disease severity as per FibroTest and MELD score. Cirrhosis was defined with the FibroTest test (F3/4–F4). Comorbidities and functional limitations as per SI predict higher mortality in patients with HCV, independently of cirrhosis. Baseline cirrhosis as per FibroTest had the highest hazard ratio for mortality in HCV patients higher than congestive heart failure or alcohol ingestion suggesting that FibroTest is a real marker of severity of the disease. However, comorbidities as per SI should be taken into account for predicting cirrhosis.

FibroTest Scientific Publications
Key Publications for 2017

Stasi 2016
FibroTest
TE

Short review on FibroTest and TE

Non-invasive assessment of liver fibrosis: Between prediction/prevention of outcomes and cost-effectiveness

Stasi C, Milani S. World J Gastroenterol 2016;22: 1711-1720.

This short review addressed the interest of the most validated non-invasive markers of fibrosis, mainly FibroTest and transient elastography (TE). The authors stressed that combinations of non-invasive may improve accuracy, particularly when they include FibroTest and TE, as for Elasto-FibroTest (EFT). For the detection of cirrhosis EFT performed better than TE or FibroTest alone, but for advanced fibrosis FibroTest alone performed as well as the EFT, contrarily to TE. The cost effectiveness study that assessed FibroTest against liver biopsy when using the new interferon-free therapy, FibroTest only was cost-effective.

Finally, authors admitted that only FibroTest demonstrated its effectiveness in screening programs.

Jullian-Desayes 2016
FibroMax
NAFLD
OSA

FibroMax panel for the screening of NAFLD in obstructive sleep apnea (OSA)

Impact of effective versus sham continuous positive airway pressure on liver injury in obstructive sleep apnea: Data from randomized trials

Jullian-Desayes I, Tamisier R, Zarski JP, et al.. Respirology. 2016;21:378-85

OSA patients have high risk of NAFLD. This randomized study on 103 OSA patients proposed to study the prevalence of liver injury estimated by the FibroMax panel and the impact on liver injury of 6 to 12 weeks of treatment with positive effective pressure (CPAP).

The prevalence of NAFLD among OSA patients seems very high: 43.7% severe steatosis as per SteatoTest, 49.5% NASH or borderline NASH as per NashTest and 3.7% fibrosis as per FibroTest.

The FibroMax helped to identify previously undiagnosed NAFLD among OSA patients with normal liver enzymes.

Olivares-Gazca 2016
FibroMax
NAFLD

FibroMax identified NAFLD as a cause of mild thrombopenia without cirrhosis

More on the thrombocytopenia of the non-alcoholic fatty liver disease

Olivares-Gazca JC, Nunez-Cortes AK, Mendez-Huerta MA. Hematology 2016;14:1-4.

Authors are hematologists and proposed to study the cause of mild thrombopenia in a prospective cohort of patients. FibroMax along with transient elastography were used to exclude cirrhosis. After exclusion of other causes of thrombopenia, authors identified by using FibroMax that NAFLD should be considered as a cause of mild thrombocytopenia that was associated with overweight.

Parikh 2017
FibroTest
HBV
FIB-4
TE

Review article on treatment for hepatitis B

Fibrosis assessment in patients with chronic hepatitis B virus (HBV) infection

Parikh P, Ryan JD, Tsochatzis EA. Ann Transl Med 2017;5:40

Authors admit that the detection and quantification of liver fibrosis is a key factor for chronic hepatitis B management and prognostication. They stressed that reliance on invasive liver biopsy to stage disease is diminishing with the advent non-invasive algorithms. These algorithms can reliably stage disease and are now incorporated into International guidelines for HBV management.

Authors remind that in a meta-analysis of 71 studies APRI had lower performances than FIB-4, transient elastography (TE) and FibroTest in both HBV and HCV patients. FibroTest was identified to rule out cirrhosis as per recent meta-analysis.

Gines 2016
FibroTest
Screening
TE

Review of the screening studies with FibroTest and TE

Screening for liver fibrosis in the general population: a call for action

Screening for liver fibrosis in the general population: a call for action

Authors alert about the lack of strategies for detection of liver fibrosis at early stages, while liver cirrhosis is one of the main causes of death and disability worldwide.

The authors review the screening studies in the general population, using non-invasive methods, FibroTest or TE.

Authors remind the screening done using FibroTest on 7463 French subjects over 40 years or more that revealed a prevalence of unknown advanced fibrosis of 2.8% and of unknown cirrhosis of 0.3%. Most of the cases from the general population with unknown liver disease and fibrosis were associated with non-alcoholic fatty liver disease.

The prevalence of increased liver stiffness as per TE was about 17% suggesting a possible overestimation of fibrosis by elastography mainly due to the presence of steatosis (see below Poynard and AL. Response letter).

Authors concluded that these data suggest that programs of screening for liver fibrosis in the general population should be assessed.

Poynard 2016
FibroTest
Screening diabetics

FibroTest more accurate for early stages of fibrosis screening

FibroTest more accurate for early stages of fibrosis screening

Poynard T, Peta V, Pollo-Flores P et al. Correspondence http://dx.doi.org/10.1016/S2468-1253(16)30081-4

Authors wrote this letter to Gines et al. review to stress three points:

First, that a prospective screening of 696 type 2 diabetes with FibroTest was missing from the review.

Two direct head-to-head comparisons of non-invasive tests, already exist and there is a higher prevalence of significant fibrosis presumed by TE than by FibroTest. These differences could be related to a lower performance of TE than FibroTest as a fibrosis marker of early fibrosis stages.

Authors suggest that screening studies in very low-risk patients such as blood donors and healthy volunteers, may improve detection of false-positive and therefore the appropriate cutoff for screening.

Harris 2017
FibroTest Screening

FibroTest proposed for the screening of unknown liver diseases in the general population

Prevalence of clinically significant liver disease within the general population, as defined by non-invasive markers of liver fibrosis: a systematic review

Harris R, Harman DJ, Card TR et al. Lancet Gastroenterol Hepatol 2017 Published Online http://dx.doi.org/10.1016/ S2468-1253(16)30205-9

Authors proposed to review 19 studies of fibrosis screening, among which 11 used non-invasive tests. Only TE and FibroTest were compared with histological endpoints. The prevalence of advanced liver fibrosis was 0.9–2.0% and of cirrhosis 0.1–1.7%. Higher prevalence of advanced liver fibrosis (0–27.9%) and cirrhosis (2.4–4.0%) than in the general population were reported in targeted patients with risk factors of liver disease, such as non-alcoholic fatty liver disease, hazardous alcohol use, or type 2 diabetes.

FibroTest was considered as the most validated for liver fibrosis screening and to consistently detect otherwise unrecognized liver disease in the general population. (Poynard et al. 2010, Zelber-Sagi et al 2012 and Grattagliano et al. 2013)

Authors concluded that only the use of validated specific markers like FibroTest can consistently detect disease that would have otherwise been missed by current referral pathways based on abnormal liver function tests.

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