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Using FibroScan in NASH/MASH drug trials

- Céline Fournier, PhD – Chief Medical Officer

- Paris NASH meeting – September 8th, 2023

Context

- Histology-based endpoints are currently the only surrogate endpoints accepted by regulators for drug development in non-cirrhotic MASH patient but is associated with many challenges/limitations.
- FibroScan-based biomarkers are widely used in routine clinical practice globally since more than 20 years with more than 4,200+ peer-reviewed publications and 180+ guidelines.
- FibroScan-based biomarkers are also used in the vast majority of MASH drug phase 2/3 trials to :
  - To reduce the number unnecessary biopsies and the associated screen failure rate
  - As an exploratory endpoint to assess treatment response
- Like for any other procedures, FibroScan use in clinical trials requires specific guidance and supervision.
- In this talk we will present
  - Some of the clinical evidence on the use of FibroScan-based biomarkers in MASH trials
  - The services and tools developed to support sponsors/CROs in collecting standardized and consistent data from FibroScan

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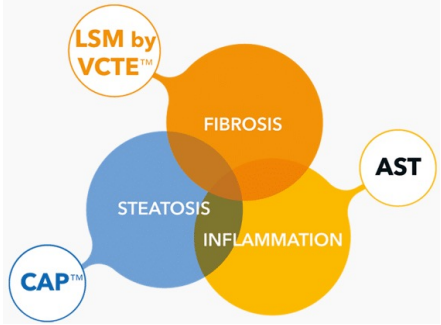
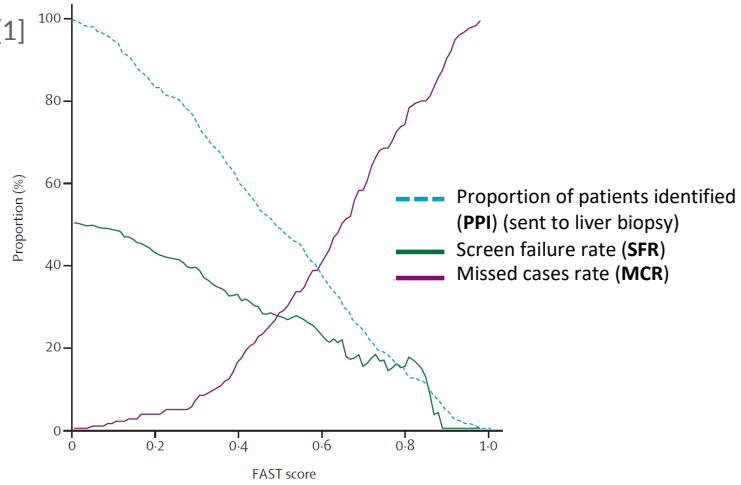
Reduction of screen failure rate with Fast

- Fast[1]
  - Combines LSM by VCTE, CAP and AST
  - Provides the probability of having at-risk NASH (NAS ≥ 4, with at least one in each component and F≥ 2)
  - Free calculator available on app and website



[1]



Meta-analysis [2] (n=5836 pts)	Rule-out	Rule-in
At-risk NASH prevalence	28% (95%CI 21%-34%)	
Summary AUROC	0.79 (0.77-0.81)	
Cut-off	≤0.35	≥ 0.67
Combined Sensitivity	0.89 (0.82-0.93)	0.46 (0.37-0.55)
Combined Specificity	0.56 (0.43-0.67)	0.89 (0.83-0.94)
LR-	0.2 (0.15-0.27)	0.61 (0.54-0.68)
LR+	2.0 (1.6-2.4)	4.3 (3.1-5.9)

	Without FAST	Fast > 0.35
PPI (%)	100	54
SFR (%)	72	48
MCR (%)	0	11

[1] Newsome LGH 2020;5:362-73
[2] Ravaioli Gut 2023;72:1399-409

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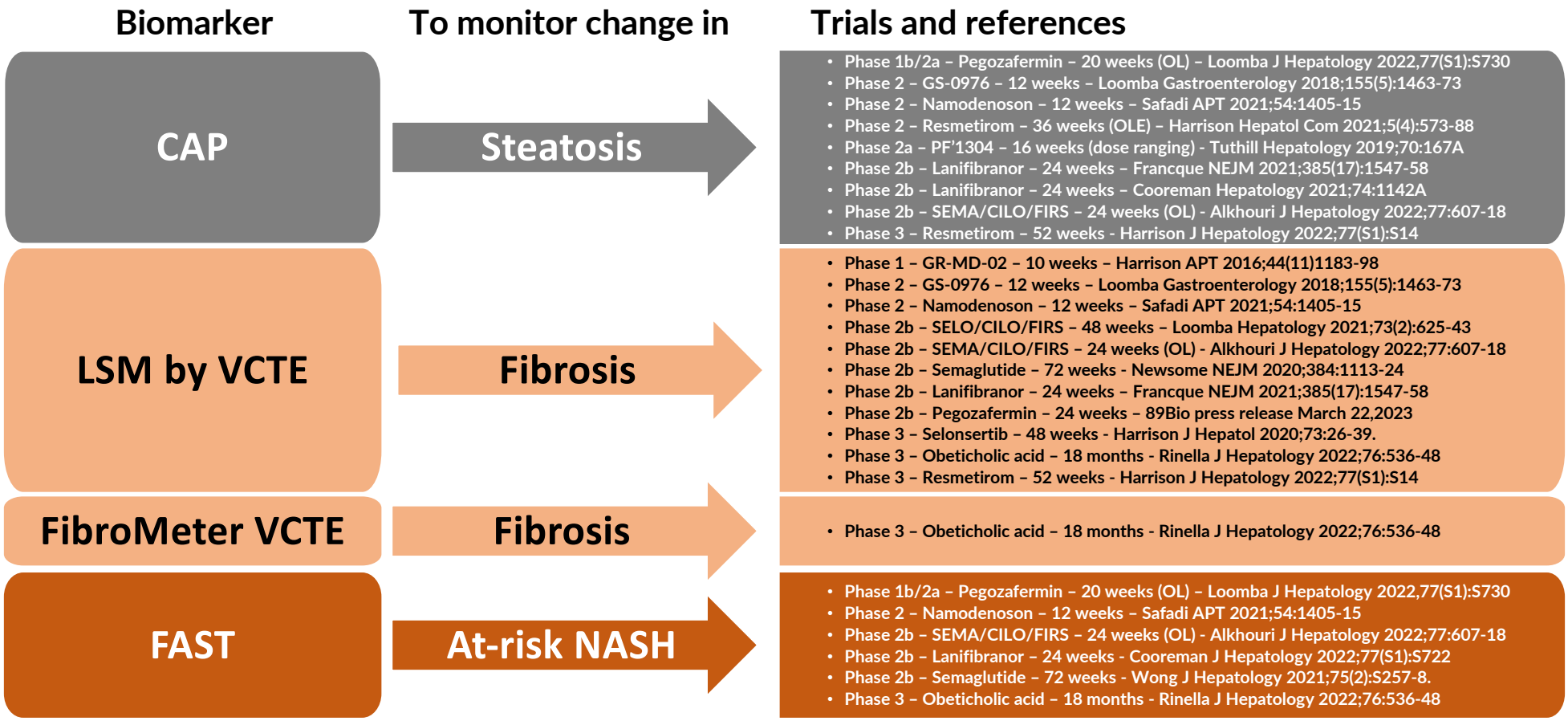
Assessing treatment response - Overview



OL: open label; OLE: open label extension

More detailed presentation on Liver Forum website https://forumresearch.org/liver-forum/liver-forum-meetings/1799-liver-forum-14

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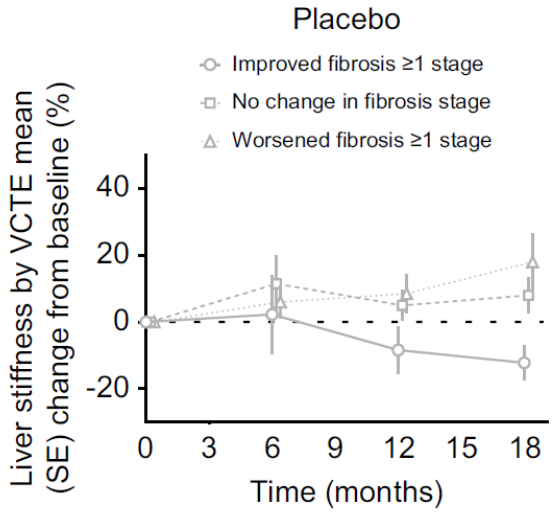
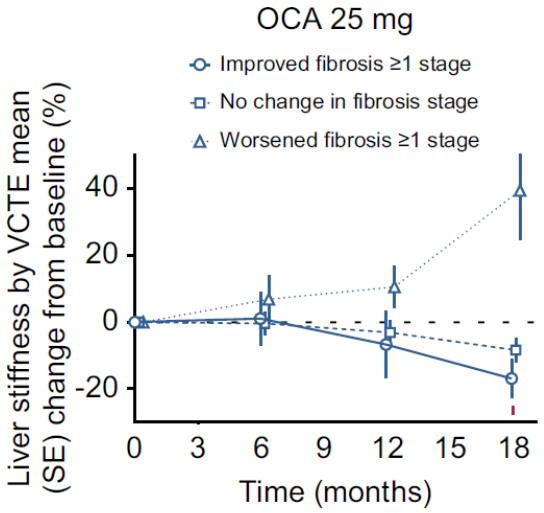
Assessing change in fibrosis with LSM by VCTE

Phase 3 – Obeticholic acid - REGNERATE– 18 months

Change from baseline over time by treatment group and histological fibrosis improvement status





Improved, n =	40	38	38	37
No change, n =	111	100	104	100
Worsened, n =	42	41	40	39

Improved, n =	66	63	59	57
No change, n =	92	90	87	82
Worsened, n =	26	25	26	25

- In both PBO and OCA 25 mg arms, LSM by VCTE :
  - Increases in patients with worsening of fibrosis by histology
  - Decreases in patients with improvement of fibrosis by histology
- Among patient with stable fibrosis by histology, LSM by VCTE improved in patients receiving OCA 25 mg vs PBO

Mean (SE) percentage change for patients assessed at sites with FibroScan® equipment available. SE: standard error of the mean.

Rinella J Hepatology 2022;76:536-48.

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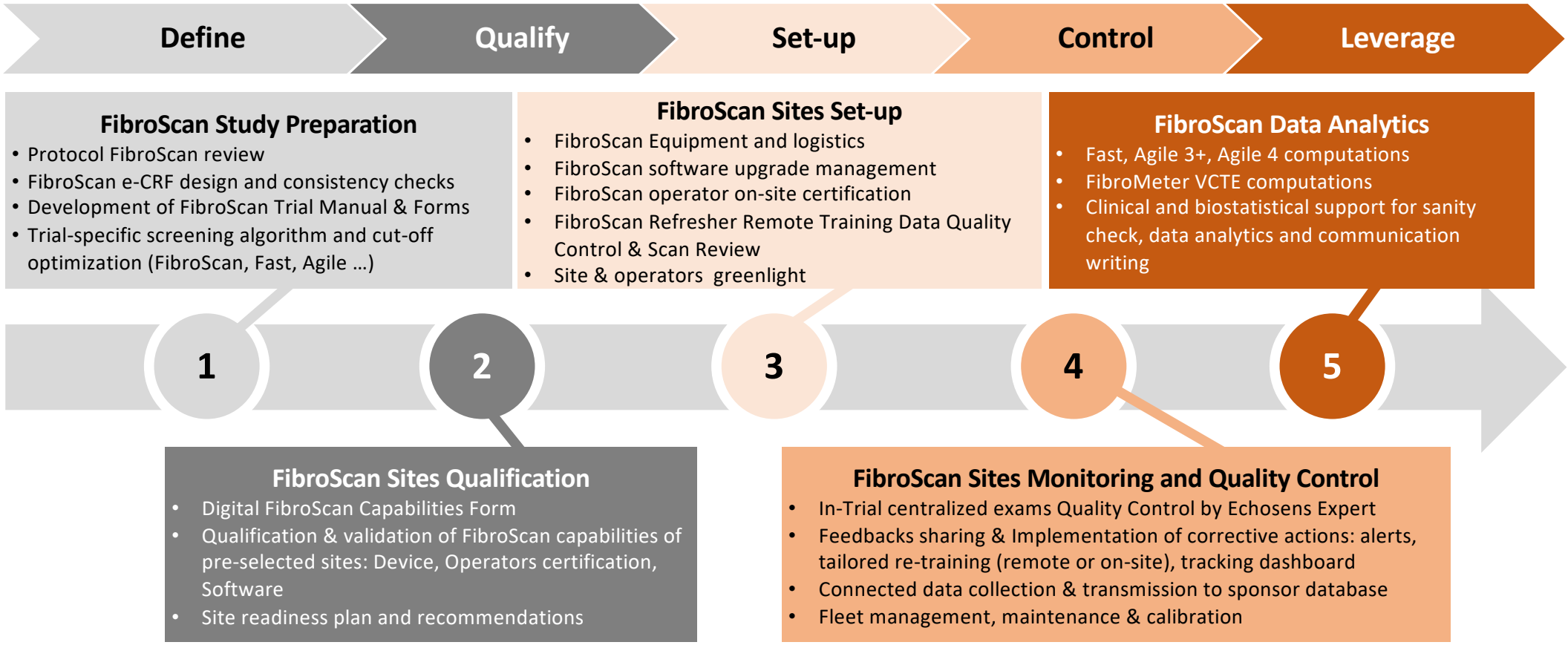
De-risk trial execution & ensure data quality and consistency



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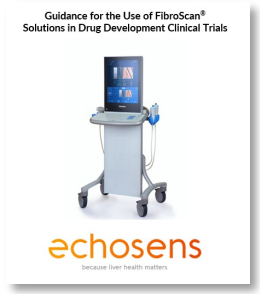
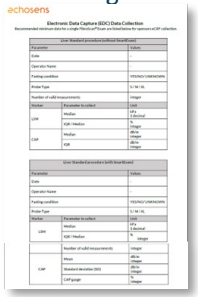
De-risk trial execution & ensure data quality and consistency

Define 1 | **Qualify** 2 | **Set-up** 3 | **Control** 4 | **Leverage** 5

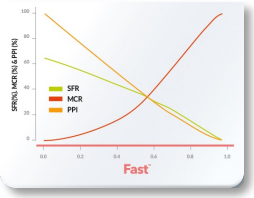
Guidance for the Use of FibroScan Solutions in Trials Protocols



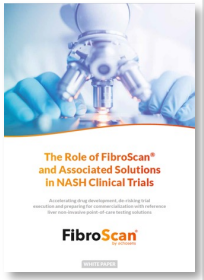
FibroScan e-CRF design



Trial-specific screening algorithm & cut-off

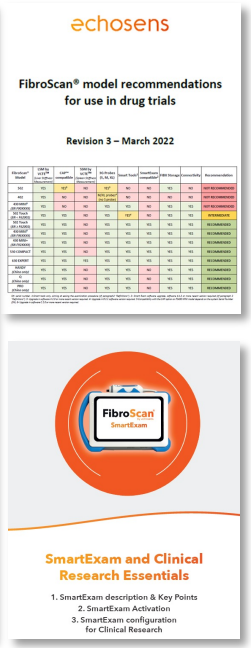


Whitepaper

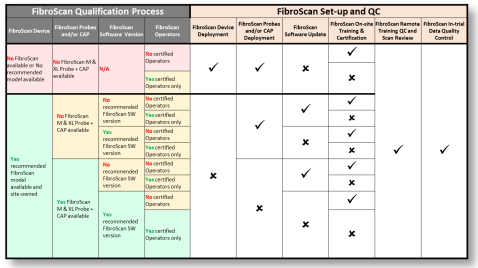


Digital FibroScan Technical Requirements Form

FibroScan model, software and operator greenlight



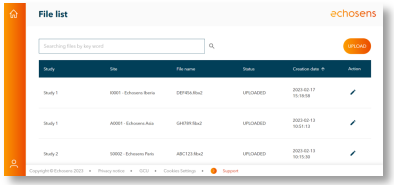
Site Readiness Plan & Set-up (Equipment, Software, On-site certification, Remote training QC…)



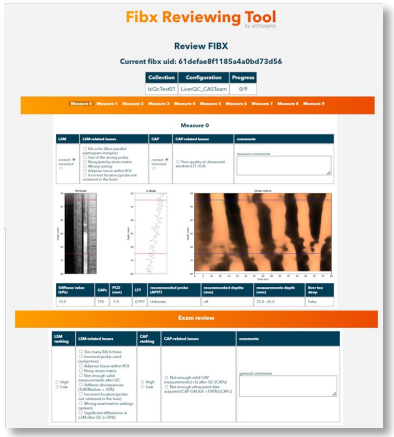
Echosens Academy

FibroScan Trial Manual

Echosens Cloud Portal for FibX exams submission

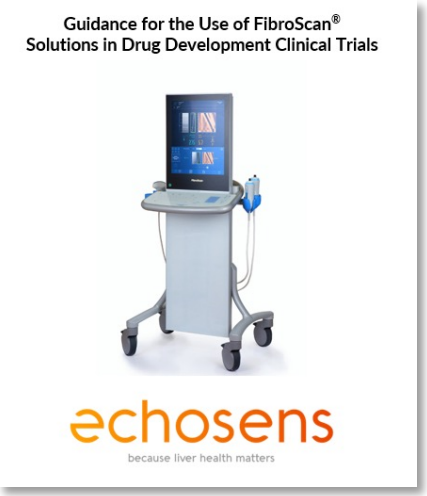


FibroScan Data Quality Control



Takeaways

- Large body of clinical evidence on the usefulness of FibroScan-based biomarkers in diagnosis and assessment of treatment response, but also on prognosis and monitoring contexts of use, with new data regularly published.
- Echosens has set-up a team specifically dedicated to supporting sponsors & CROs using FibroScan in their clinical trials with dedicated services and tools.
- We encourage sponsors & CROs to reach out to us as early as possible when designing trials to benefit from our experience and expertise.
- The Guidance document on the Use of FibroScan Solutions in Drug Development Clinical Trials provides key insights and recommendations.
- We are actively working with LITMUS and NIMBLE for the qualification of FibroScan-based biomarkers as Drug Development Tools.



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