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Using FibroScan in NASH/MASH drug trials

- Céline Fournier, PhD – Chief Medical Officer
- Paris NASH meeting – September 8th, 2023

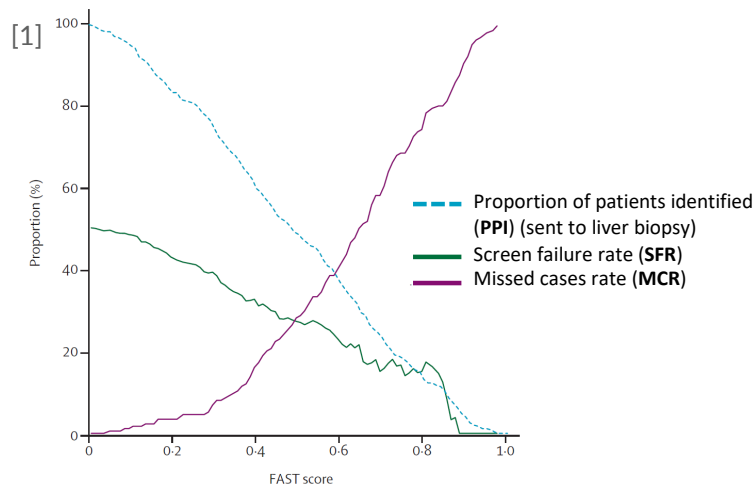
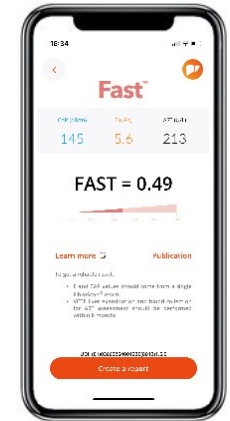
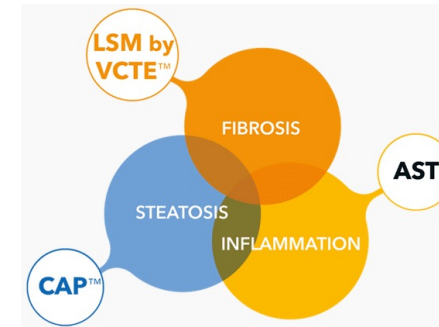
Context

- ◉ 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

Reduction of screen failure rate with Fast

Fast¹

- 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



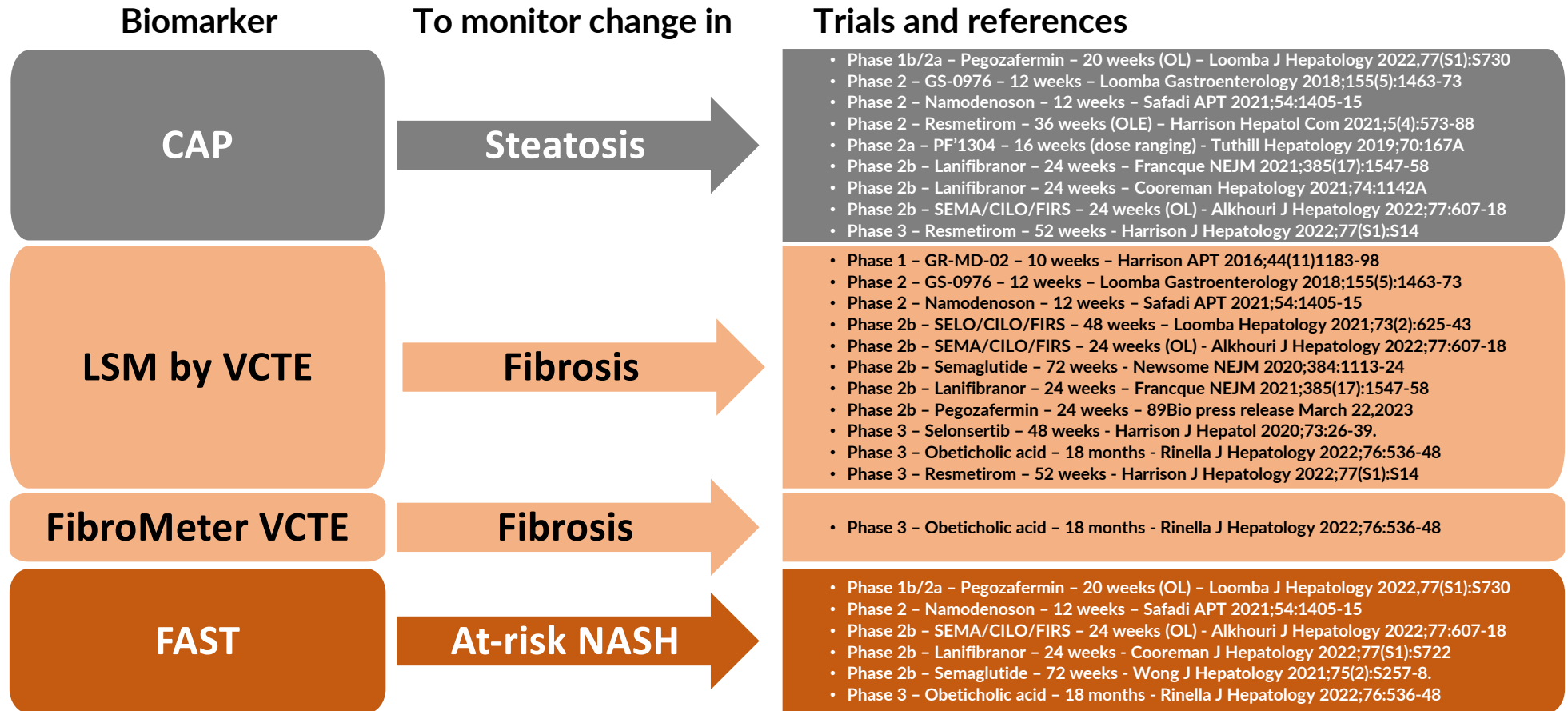
Meta-analysis [2] (n=5836 pts)	Rule-out	Rule-in
At-risk NASH prevalence	28% (95%CI 21%-34%)	
Summary AUROC	0.79 (0.77-0.81)	
Cut-off	≤ 0.35	≥ 0.67
Combined Sensitivity	0.89 (0.82-0.93)	0.46 (0.37-0.55)
Combined Specificity	0.56 (0.43-0.67)	0.89 (0.83-0.94)
LR-	0.2 (0.15-0.27)	0.61 (0.54-0.68)
LR+	2.0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



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

3 [1] Newsome LGH 2020;5:362-73
[2] Ravaoli Gut 2023;72:1399-409

Assessing treatment response - Overview



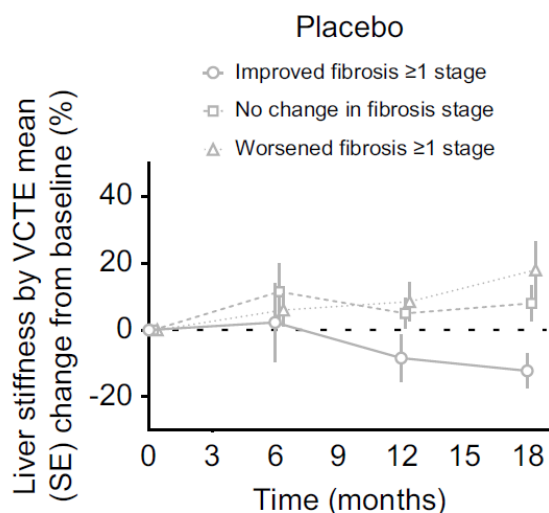
OL: open label; OLE: open label extension

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

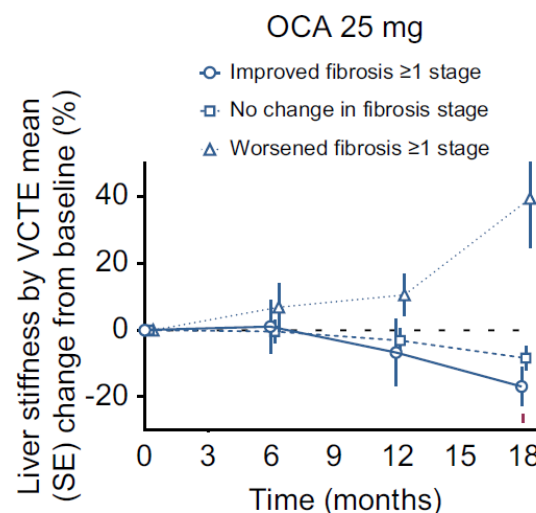
Assessing change in fibrosis with LSM by VCTE

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

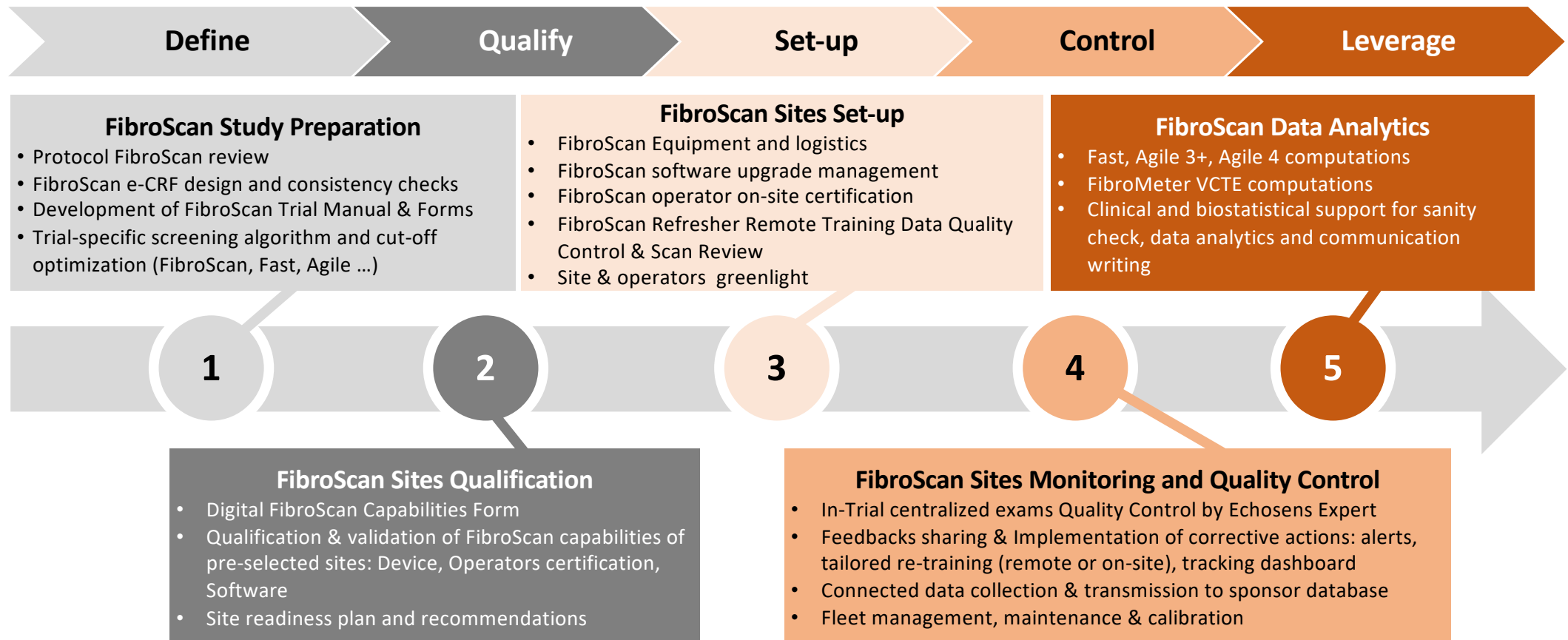


Improved, n =	66	63	59	57
No change, n =	92	90	87	82
Worsened, n =	26	25	26	25

- 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.

De-risk trial execution & ensure data quality and consistency



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

Guidance for the Use of FibroScan® Solutions in Drug Development Clinical Trials



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FibroScan e-CRF design

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Electronic Data Capture (EDC) Data Collection

Recommended solution for drug development clinical trials

Use this for anything not applicable, do not leave blank

For any questions on this survey, please contact sales@echosens.com

* Required

Site information

1. PI Full Name *

Enter your answer

2. PI phone number

Enter your answer

3. PI email *

Enter your answer

FibroScan Model *

Select correct value

Serial Number / FibroScan ID with XXXXXXX *

FibroScan Operator *

Enter your answer

Digital FibroScan Technical Requirements Form

FibroScan

FibroScan Technical Requirements Form

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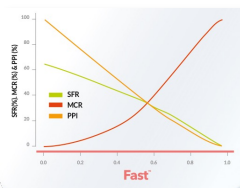
FibroScan model, software and operator greenlight

FibroScan® model recommendations for use in drug trials

Revision 3 - March 2022

Model	Software	Operator	Recommendation
FibroScan M	Yes	Yes	Recommended
FibroScan M	Yes	No	Not recommended
FibroScan M	No	Yes	Not recommended
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FibroScan M	No	No	Not recommended
FibroScan M	Yes	Yes	Recommended
FibroScan M	Yes	No	Not recommended
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Trial-specific screening algorithm & cut-off



Whitepaper



The Role of FibroScan® and Associated Solutions in NASH Clinical Trials

As understanding drug development, the role of FibroScan and associated solutions in NASH clinical trials is becoming increasingly important.

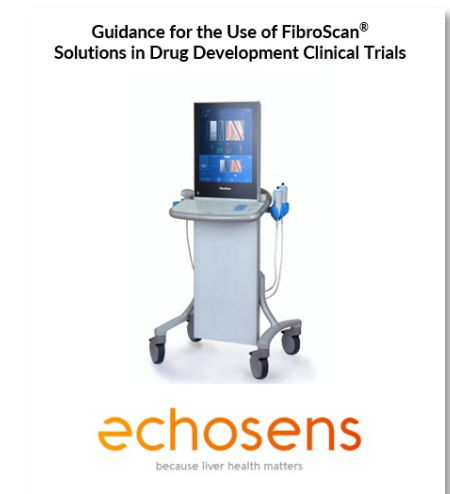
FibroScan

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

FibroScan Qualification Process				FibroScan Set-up and QC			
FibroScan Device	FibroScan Software	FibroScan Operator	FibroScan Device	FibroScan Software	FibroScan Operator	FibroScan Device	FibroScan Software
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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.



The background of the image is a photograph of the interior of Antelope Canyon. The walls of the canyon are composed of smooth, undulating sandstone that has been eroded into flowing, wave-like patterns. The lighting is warm and directional, coming from the right side, which creates a gradient of colors from deep reds and oranges on the left to bright, almost white highlights on the right. The overall effect is one of organic, sculptural beauty.

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because liver health matters