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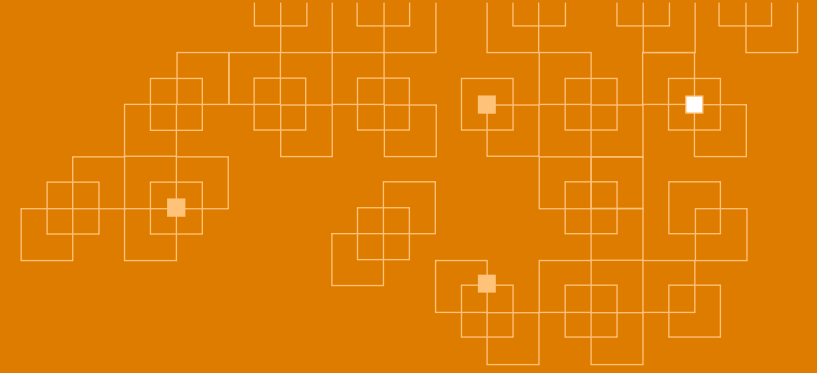
Liver Forum 15

September 6, 2023

Institut Pasteur

Veronica Miller, PhD
Director

Berkeley Public
Health



Session IV: Moving Forward with NITs

Moderators:

Laurent Castera, Université Paris Cite Hôpital Beaujon

Meena Bansal, Mount Sinai Hospital, NY



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Brief Overview of Liver Forum Work in NITs

Veronica Miller, Forum for Collaborative Research

Baseline Parameters in Clinical Trials for Nonalcoholic Steatohepatitis: Recommendations From the Liver Forum



regulatory agencies, the pharmaceutical and medical diagnostics industries, and patient advocacy organizations to develop consensus recommendations for standardized baseline parameters for NASH-related clinical trials.

Methods

A working group of the Liver Forum assessed the state of the science in clinical trials for NASH and made specific recommendations for the categories of data to

NAFLD fibrosis p morbid condition ular disease.⁷ Ag include decrease and mitochondr and ethnicity, oft known genetic considered impc capture for proof phase II trials, an essential compor als. These are t given the curren

Gastroenterology 2017;153:621–625

Table 1. Metabolic Panel

	Early Phase Trials	Late Phase Trials
Fasting glucose	E	E
Fasting insulin	E	E
Hemoglobin A1c	E	E
HOMA	C	C
Glucose clamp	C	NR
OGTT	C	C

C, consider; E, essential; HOMA, homeostasis model assessment; NR, not recommended; OGTT, oral glucose tolerance test.

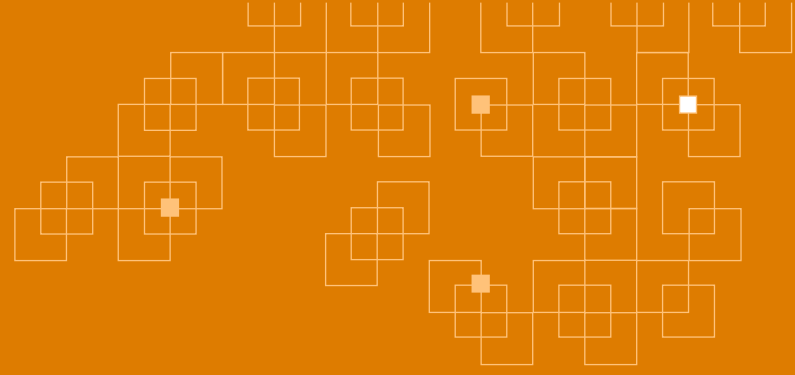
Table 2. Laboratory Tests

	Early Phase Trials	Late Phase Trials
ALT	E	E
AST	E	E
ALP	E	E
Total bilirubin	E	E
Direct bilirubin	E	E
GGT	E	E
Albumin	E	E
Prothrombin time or INR	E	E
Total cholesterol	E	E
LDL-C	E	E
HDL-C	E	E
TSH	E	E
Triglycerides	E	E
Hemoglobin	E	E
Hematocrit	E	E
Platelets	E	E
BUN	E	E
Creatinine	E	E
Urine microalbumin	C	C
Ferritin	I	I

Supplementary Materials

- Comorbidities & Surgical History
- Anthropometrics
- Specialized Biomarkers
- Health Related Quality of Life

- LF12
 - Review diagnostic and prognostic NITs
- LF14
 - Review treatment response NITs



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FDA NIT Workshop: Open Invitation

Abbas Bandukwala, US Food and Drug Administration*



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Proposal to the Liver Forum

Quentin Anstee, Newcastle University*

Meta-Thoughts on Response Biomarkers in NASH Drug Development



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1. Rapidly attaining a NIT 'response threshold' is not a guarantee of early efficacy.

2. Interpret changes in 'Simple Panels' (APRI, FIB4, NFS) with caution.

3. In the absence of a single 'gold standard' biomarker, undertake a wholistic assessment of biomarker response and demonstrate change *at the patient level*.

4. We should agree and define a common set of biomarkers that will be measured *and reported* in all future clinical trials.

Quentin Anstee LF12

Trial Phase		Phase IIa/IIb																							
Year		2018	2020	2021	2021	2022	2019	2019	2021	2021	2020	2020	2021	2021	2022	2020	2016	2020	2020	2021	2015	2020	2021	2018	2020
Duration		12	12	12	12	12	12/36	16	16	16	24	24	24	24	24/48	48	52	52	52	52	72	72	72	96	104
		Aldafermin	Aldafermin	TVB-2640 (FASCINATE 1)	Tern-101 (LIFT)	EDP-305 (ARGON-1)	Resmetrom (MGL-3196-05)	Pegbelfermin (FGF21)	Efruxifermin (BALANCED)	Saroglitazar (EVIDENCES IV)	Clofevor	Combination (ATLAS)	Lanifibranor (NATIVE)	Aldafermin (ALPINE 2/3)	Pegbelfermin (FALCON 1/2)	Tropifexor (FLIGHT-FXR)	Elaftibranor (GOLDEN-505)	Seladelpar	MSDC-0602K (EMMINENCE)	Aramchol (ARREST)	OCA (FLINT)	Emricasin	Semaglutide	Simtuzumab	CVC (CENTAUR)
Clinical Chemistry	ALT & AST	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	APRI								✓	✓				✓				✓							✓
Simple Scores Indirect Biomarkers	NFS					✓								✓					✓					✓	
	FIB4					✓				✓		✓		✓					✓	✓					✓
	CK18			✓			✓		✓	✓	✓	✓						✓	✓			✓	✓		
	ELF	✓	✓	?			✓		✓	✓	✓	✓	✓	✓	✓				✓	✓				✓	✓
Direct Biomarkers	Fibrotest									✓							✓		✓					✓	
	PRO-C3	✓	✓	✓			✓	✓	✓				✓	✓	✓										✓
	VCTE								✓	✓	✓	✓			✓									✓	
Fibroscan	FAST										✓												✓		
	MR-PDFF	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓		✓		✓					
MR	MR-ct1		✓		✓																				
	MRE							✓			✓	✓			✓										
Liver Biopsy	Histology		✓	✓			✓		✓				✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

Panel Discussion

Panelists:

- Manal Abdelmalek*, Mayo Clinic
- Vlad Ratziu, Sorbonne Université
- Claudia Filozof, Fortrea
- Corinna Schoelch, Boehringer Ingelheim
- Michael Betel, Fatty Liver Alliance
- Michael Middleton, UC San Diego