DYNAMICS OF NONINVASIVE TESTS (NITS) - LIVERFAST, FIB-4 AND VIBRATION-CONTROLLED TRANSIENT ELASTOGRAPHY (VCTE, FIBROSCAN), DURING MONITORING THERAPY WITH TNR-BETA AGONIST RESMETIROM (RT) IN PATIENTS WITH MASH- UPDATE

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INTRODUCTION

Resmetirom therapy (RT) was recently approved by the FDA for non-cirrhotic MASH with fibrosis. The impact of RT on NITs has not been assessed in real-life patients.

LIVERFASt (Fibronostics, New Orleans, US) is a new blood-based AI-test that assesses **liver fibrosis, activity, and steatosis**, potentially useful in initiating and monitoring patients during Resmetirom therapy.

AIMS

1/ To assess he dynamic of LIVERFAST, FIB-4 and VCTE during longitudinal monitoring of patients ongoing Resmetirom therapy.

2/ To estimate the fibrosis progression rate (PR) between baseline and repeated NITs measurements in the overall population according to the RT dose and concomitant therapy with GLP-1 Receptor Agonist (GLP1RA).

METHODS

Patients on RT with baseline and repeated LIVERFASt, VCTE and FIB4 have been included retrospectively

LIVERFASt (Fibronostics New Orleans, US): Blood-based test, generates scores (0.00-1.00) proportional to the severity of fibrosis, activity, and steatosis. (www.fibronostics.com)

Serum biomarkers : alpha-2 macroglobulin, haptoglobin, apolipoprotein A1, total bilirubin, GGT, ALT, AST, glucose, total cholesterol, triglycerides, age, sex, height, and weight

FIB-4 Index: calculated using ALT, AST , platelet count and age

Vibration Controlled Transient Elastography (VCTE)

(Echosens Paris, France)

- Quqlity criteria: Liver stiffness measurement (LSM)

< 30% IQR/median ratio included, 10 valid measuremets

Statistics

NITs dynamics have been assessed using Kaplan Meier non-parametric statistics censored at -10% PR occurrence from t0, Tukey-Kramer Multiple-Comparison Test (repeated measurements ANOVA), descriptive and subgroup analysis (dose and GLP-1 receptor agonists (GLP-1RA) analysis.

RESULTS

Description of the included population

N=96	Overall
Age	61.8 (1.2)
Male	39%
BMI	33.1 (1.0)
Type 2 Diabetes	48.7%
GLP-1RA	37.5%
ALT	45 (3)
FIB-4	1.80 (0.12)

RESULTS

NITs had baseline and repeated testing:

- N=88 FIB-4,
- N=41 VCTE/CAP and
- N=96 LIVERFASt and, among them, 30 had repeated VCTE/CAP and 60 repeated FIB-4

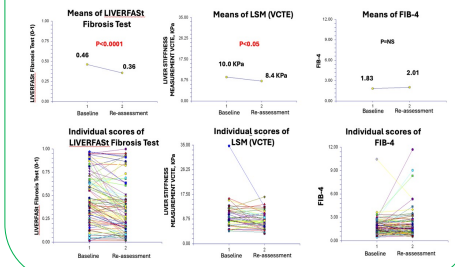
Median (max) delay, months baseline-to- repeated testing

Using VCTE	7.6 (3.1)
Using LIVERFASt	6.0 (0.6)
Using FIB-4	7.3 (0.5)

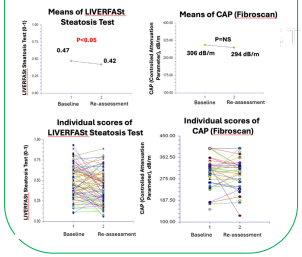
Biomarker	Mean (SE) Baseline assessment	Re-assessment	Probability Level*
Repeated LIVERFASt N=95			
LIVERFASt Fibrosis (0-1)	0.46 (0.03)	0.35 (0.03)	**<0.0001**
LIVERFASt Steatosis (0-1)	0.47 (0.02)	0.42 (0.02)	**<0.05**
LIVERFASt Activity (0-1)	0.40 (0.02)	0.40 (0.02)	ns
GGT, IU/l	61 (7)	45 (5)	<0.001
Total bilirubin, mg/dl	0.63 (0.03)	0.57 (0.03)	<0.05
Alpha2 Macroglobulin, mg/dl	267 (8)	243 (7)	<0.001
Apolipoprotein A1, mg/dl	135 (3)	141 (3)	<0.05
Haptoglobin, mg/dl	138 (6)	141 (7)	ns
ALT, IU/l	45 (3)	44 (3)	ns
AST, IU/l	38 (2)	38 (2)	ns
Triglycerides, mg/dl	153 (9)	120 (9)	<0.001
Total cholesterol, mg/dl	171 (5)	148 (4)	<0.001
Blood glucose, mg/dl	112 (4)	115 (4)	ns
BMI	33.1 (1.1)	31.9 (0.7)	<0.001
Repeated Fibroscan N=41			
Liver Stiffness Measurement (VCTE), KPa	10.1 (0.8)	**8.3 (0.5)**	**<0.05**
Controlled Attenuation parameter (CAP), dB/m	307 (10)	293 (10)	ns
Repeated FIB-4 N=88			
Platelet count	229 (8)	219 (7)	ns
FIB-4	1.83 (0.13)	2.01 (0.19)	ns

Bonferroni (All-Pairwise) Multiple Comparison Test

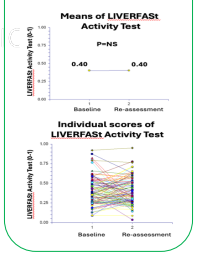
Dynamics of LIVERFASt FIBROSIS test, VCTE and FIB-4 scores between baseline and re-assessment during Resmetirom therapy (RT)



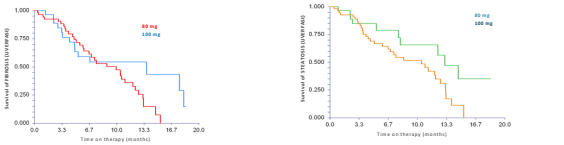
Dynamics of LIVERFASt STEATOSIS test and CAP (Fibroscan) scores between baseline and re-assessment during RT



Dynamics of LIVERFASt ACTIVITY test during RT



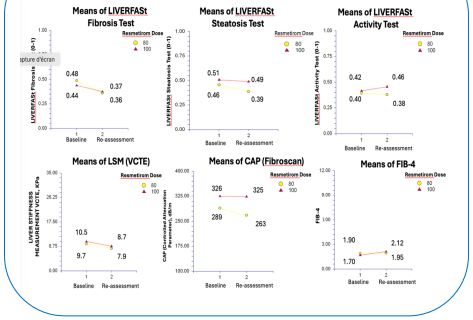
Cumulative incidence of 10% reduction in LIVERFASt Fibrosis and LIVERFASt Steatosis Tests according to the time from starting RT



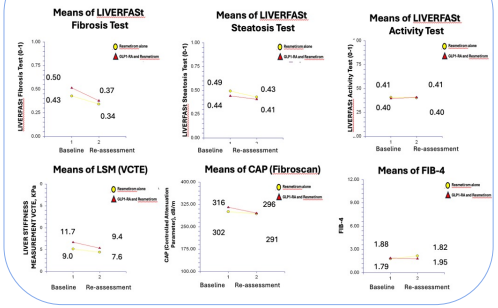
Resmetirom dose group	Cumulative incidence of 10% improvement of fibrosis according to LIVERFASt				P value
	3 months	6 months	9 months	12 months	
80mg group	10.7%	33.4%	49.8%	67.3%	ns
100mg group	15.4%	41.1%	45.6%	45.6%	

Resmetirom dose group	Cumulative incidence of 10% improvement of steatosis according to LIVERFASt				p value
	3 months	6 months	9 months	12 month	
80mg group	12.1%	33.1%	49.3%	61.6%	<0.05
100mg group	15.1%	21.2%	34.3%	34.4%	

Dynamics of LIVERFASt , VCTE and FIB-4 during therapy according to Resmetirom DOSE



Dynamics of LIVERFASt, VCTE and FIB-4 according to the association of RT with GLP-1 Receptor Agonists



CONCLUSIONS

- **Initiation of resmetirom therapy based on the assessment of MASH using LIVERFASt, FIB4 or VCTE is efficient and allows further non-invasive monitoring.**
- **LIVERFASt is an efficient in monitoring fibrosis and steatosis and reflects histology remodeling by providing earlier insights into disease regression during resmetirom therapy.**
- **Significant improvement, higher than 10% in LIVERFASt scores being observed since 3rd month of resmetirom therapy without difference between the 80mg and 100 mg groups**
- **FIB-4 and LSM (VCTE) scores showed lower change at reassessment, suggesting limited ability to detect early fibrosis or steatosis improvement.**

REFERENCES

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DISCLOSURES

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