

Noninvasive initiation and monitoring of the therapy with TNR-beta agonist Resmetirom (RT) using LIVERFAS^t, FIB-4 and Vibration-controlled transient elastography (VCTE, Fibroscan) in patients with MASH.

Jeevin Singh Sandhu¹, Shaheen Mehrara¹, Mona Munteanu², Mangesh Pagadala¹, Ashwini Mehta¹, John Lee², Obinna Okolo¹, Parker Woods¹, Parvez Mantry¹

(1) Methodist Dallas Medical Center, Division of Hepatology, Internal Medicine*, Dallas Texas, USA

(2) Fibronostics, US Inc., New Orleans, LA, USA.

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, Florida, 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

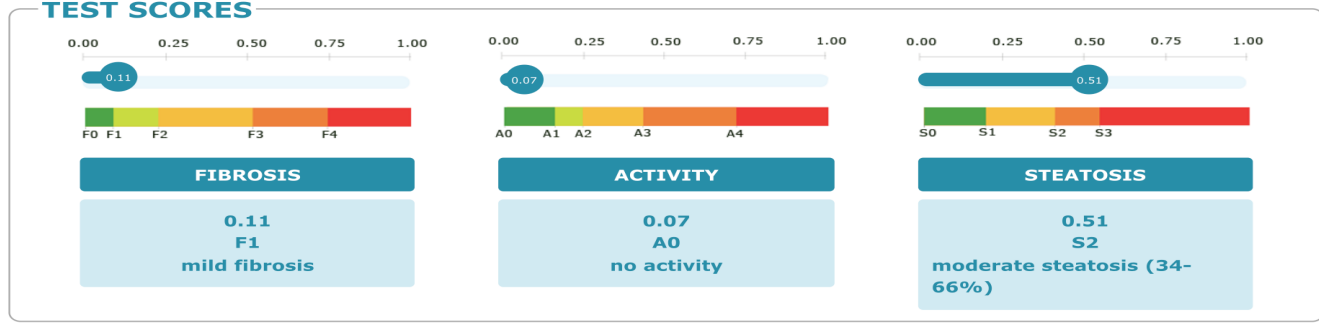
1/ To assess the dynamic of LIVERFAST, FIB-4 and VCTE during longitudinal monitoring of patients ongoing Resmetirom therapy. 2/ To estimate the fibrosis progression rate (PR) from baseline to repeated NIT. Between baseline and repeated measurements in the overall population and according to the RT dose 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, US)

Blood-based test, generates scores (0.00-1.00) proportional to the severity of fibrosis, activity, and steatosis.



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

METHODS

All patients have been included retrospectively.

N= 86 patients have been eligible with baseline LIVERFAST without RT discontinuation (62% 80mg-dose).

NITs had baseline and repeated testing: 67 had FIB-4, 44 LIVERFAST and 30 VCTE

Vibration Controlled Transient Elastography (VCTE)

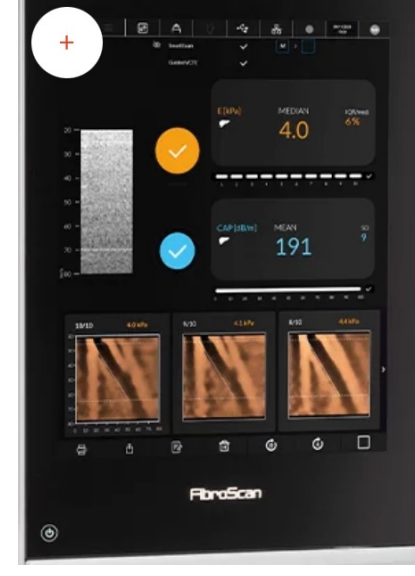
(Echosens, France)

Liver stiffness measurement (LSM)

< 30% IQR/median ratio included

10 valid measurements

No applicability criteria has been used for CAP



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).

Description of the included population

N=86	Overall	Group on 80mg dose (62%)	Group on 100mg dose (38%)
Age	62.4 (1.3)	60.8 (1.5)	63.8 (2)
Male	39%	39%	50%
BMI	33.7 (1.3)	29.9 (0.6)	39.7 (2.7)
Type 2 Diabetes	55%	46%	63%
GLP-1RA	46%	40%	57%
ALT	44 (4)	49 (5)	38 (5)
FIB-4	1.79 (0.14)	1.86 (0.21)	1.64 (0.12)
Baseline prevalence of F2F3 stages			
Using VCTE	44%	46%	40%
Using LIVERFAST	61%	58%	65%
Median (max) delay, months baseline-to- repeated testing			
Using VCTE	7.6 (3.1)	6.9 (4.4)	8.0 (4.5)
Using LIVERFAST	3.3 (0.3)	3.0 (0.4)	3.9 (0.6)
Using FIB-4	6.7 (0.5)	6.3 (0.6)	7.4 (0.8)

Biomarker	Mean (SE)		Probability Level*
	Baseline assessment	Re-assessment	
LIVERFAST N=44			
LIVERFAST Fibrosis (0-1)	0.48 (0.02)	0.38 (0.02)	<0.001
LIVERFAST Steatosis (0-1)	0.50 (0.02)	0.42 (0.02)	<0.05
LIVERFAST Activity (0-1)	0.45 (0.02)	0.42 (0.02)	NS
GGT, IU/l	68 (5)	41 (5)	<0.001
Total bilirubin,mg/dl	0.68 (0.03)	0.58 (0.03)	<0.05
Alpha2 Macroglobulin, mg/dl	274 (4)	258 (4)	<0.01
Apolipoprotein A1, mg/dl	131 (2.5)	146 (2.5)	<0.001
Haptoglobin, mg/dl	137 (3)	147 (3)	<0.05
ALT, IU/l	53 (4)	40 (4)	<0.05
AST, IU/l	44 (3)	36 (3)	NS
Triglycerides, mg/dl	144 (5)	108 (5)	<0.0001
Total cholesterol, mg/dl	168 (2.4)	146 (2.4)	<0.0001
Blood glucose, mg/dl	108 (2)	112 (2)	NS
BMI	33.4 (0.2)	33.3 (0.2)	NS

Fibroscan N=30			
Liver Stiffness Measurement (VCTE), KPa	10.7 (0.8)	10.1 (0.8)	NS
Controlled Attenuation parameter (CAP), dB/m	301 (7)	299 (7)	NS
FIB-4 N=67			
Platelet count	230 (3)	224 (3)	NS
FIB-4	1.85 (0.13)	2.02 (0.13)	NS

Bonferroni (All-Pairwise) Multiple Comparison Test

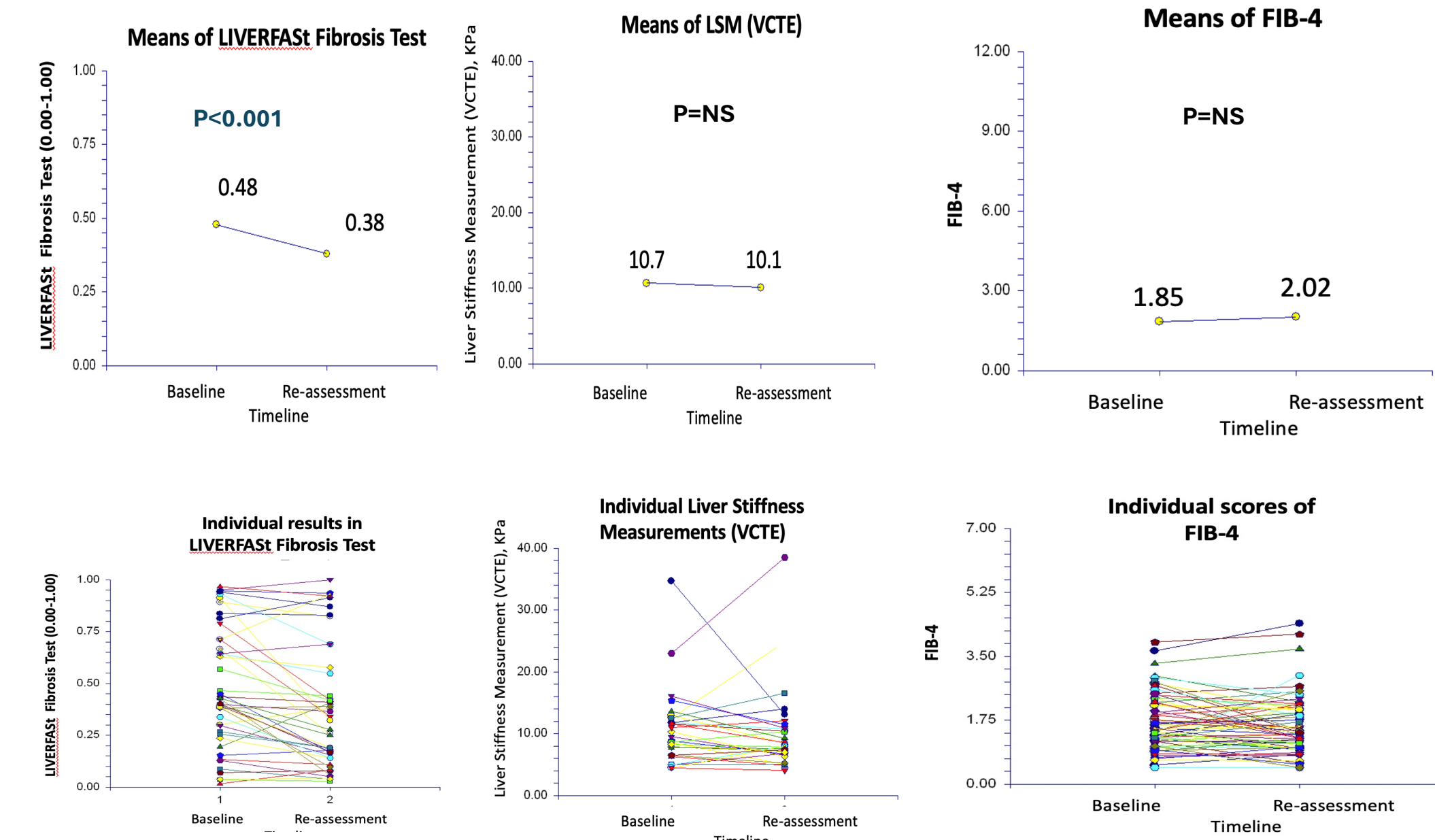
Non-invasive tests	Mean (SE)		
	Baseline assessment	Re-assessment	Probability Level*
LIVERFasT N=44			
LIVERFasT Fibrosis (0-1)			
80 mg, n=27	0.49 (0.02)	0.35 (0.02)	<0.001
100 mg, n=17	0.46 (0.03)	0.42 (0.03)	NS
LIVERFasT Steatosis (0-1)			
80 mg, n=27	0.49 (0.03)	0.38 (0.03)	<0.05
100 mg, n=17	0.51 (0.04)	0.48 (0.04)	NS
LIVERFasT Activity (0-1)			
80 mg, n=27	0.46 (0.03)	0.39 (0.03)	NS
100 mg, n=17	0.43 (0.04)	0.48 (0.04)	NS
Fibroscan N=30			
Liver Stiffness			
Measurement	9.2 (1.2)	8.2 (1.2)	NS
80 mg, n=14	12 (1.1)	11.8 (1.1)	NS
100 mg, n=16			
CAP by Fibroscan, dB/m			
80 mg, n=14	280 (10)	267 (10)	NS
100 mg, n=16	318 (9)	326 (9)	NS
FIB-4 N=67			
FIB-4			
80 mg, n=39	2.03 (0.17)	2.09 (0.17)	NS
100 mg, n=28	1.59 (0.20)	1.93 (0.20)	NS

Bonferroni (All-Pairwise) Multiple Comparison Test

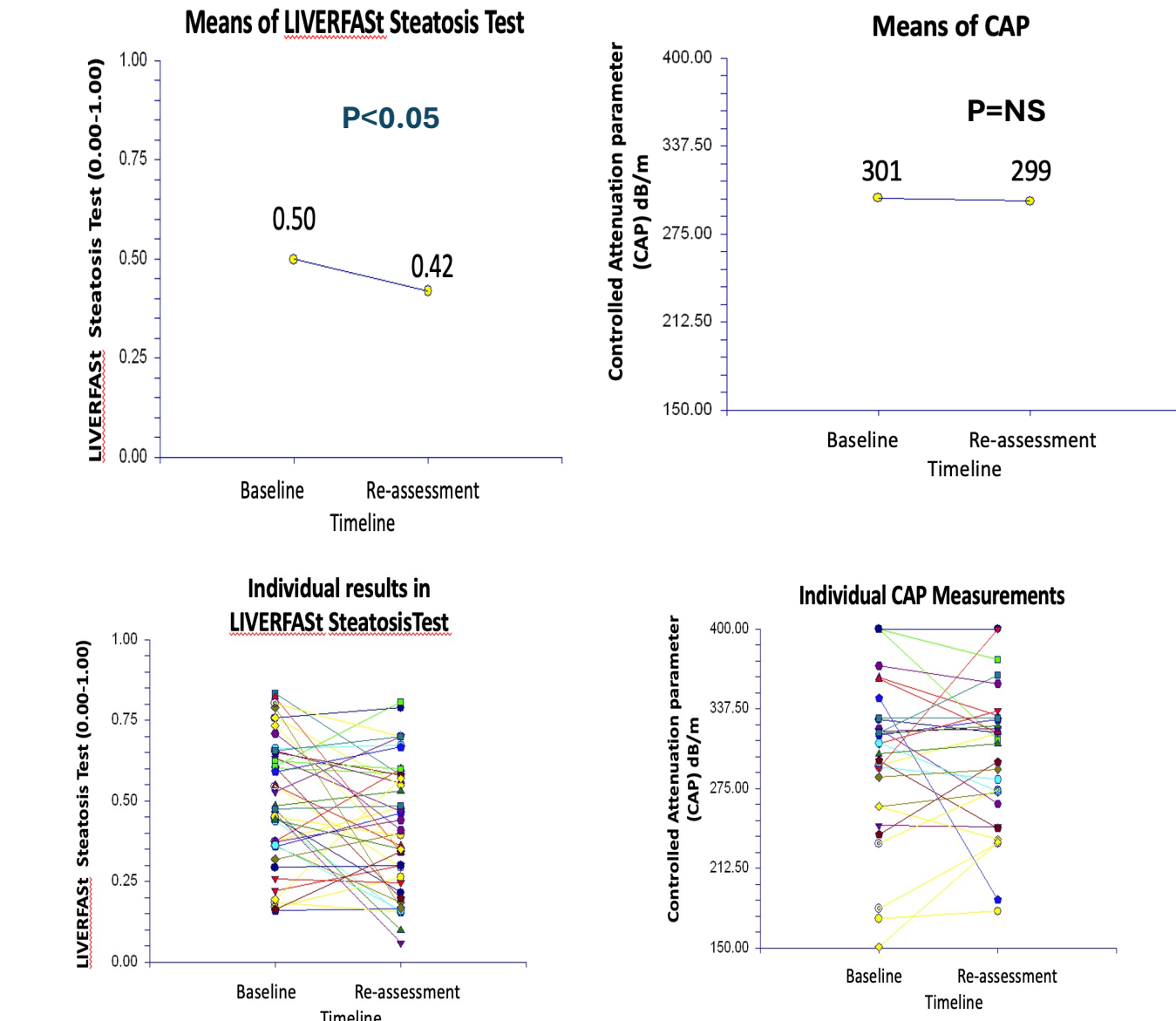
Non-invasive tests	Mean (SE)		P Level*
	Baseline assessment	Re-assessment	
LIVERFASt N=44			
LIVERFASt Fibrosis (0-1)			
Resmetirom alone, n=23	0.43 (0.02)	0.34 (0.02)	<0.05
GLP1 RA + Resmetirom, n=21	0.53 (0.03)	0.43 (0.03)	<0.05
LIVERFASt Steatosis Test (0-1)			
Resmetirom alone, n=23	0.55 (0.03)	0.44 (0.03)	<0.05
GLP1 RA + Resmetirom, n=21	0.44 (0.03)	0.40 (0.03)	NS
LIVERFASt Activity Test (0-1)			
Resmetirom alone, n=23	0.47 (0.03)	0.41 (0.03)	NS
GLP1 RA + Resmetirom, n=21	0.43 (0.03)	0.43 (0.03)	NS
Fibroscan N=30			
Liver Stiffness Measurement			
Resmetirom alone, n=16	8.7 (1.1)	8.3 (1.1)	NS
GLP1 RA + Resmetirom, n=14	12.9 (2.1)	12.2 (2.4)	NS
CAP by Fibroscan, dB/m			
Resmetirom alone, n=16	280 (9)	290 (9)	NS
GLP1 RA + Resmetirom, n=14	324 (9)	307 (9)	NS
FIB-4 N=67			
FIB-4			
Resmetirom alone, n=37	1.85 (0.18)	2.22 (0.18)	NS
GLP1 RA + Resmetirom, n=30	1.85 (0.20)	1.78 (0.20)	NS
Bonferroni (All-Pairwise) Multiple Comparison Test			

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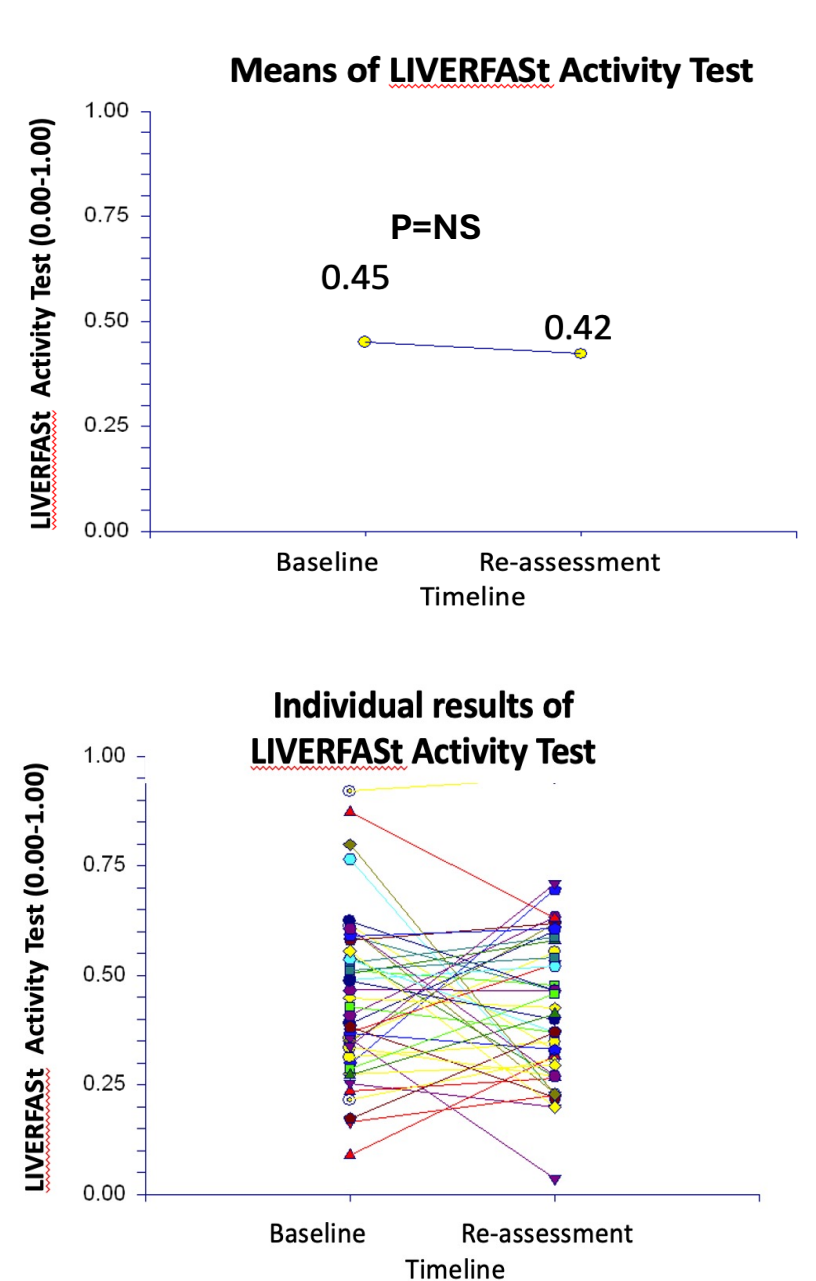
Dynamics of LIVERFAST Fibrosis test, VCTE and FIB-4 scores between baseline and re-assessment during Resmetirom therapy (RT)



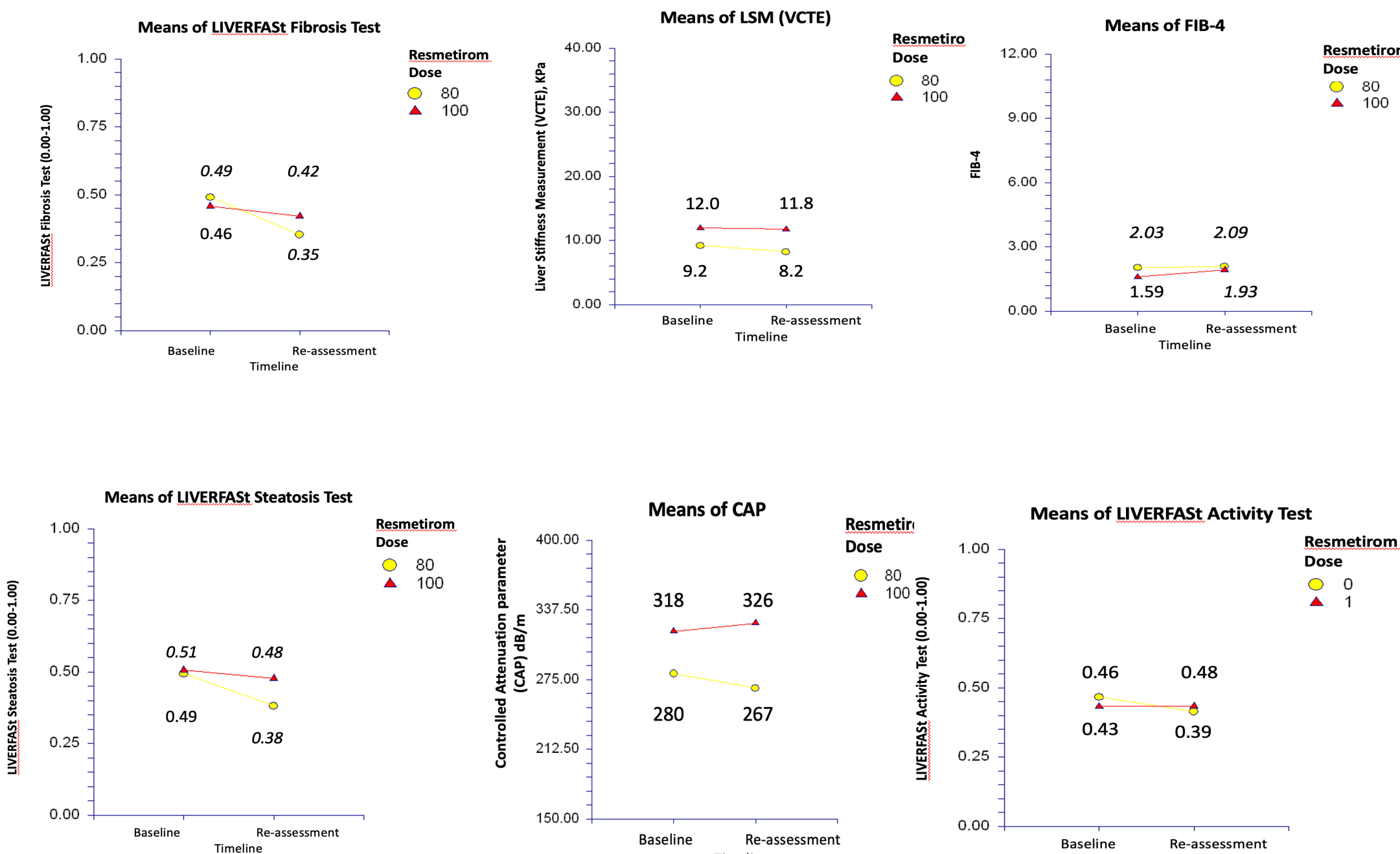
Dynamics of LIVERFAST Steatosis test and CAP (Fibroscan) scores between baseline and re-assessment during RT



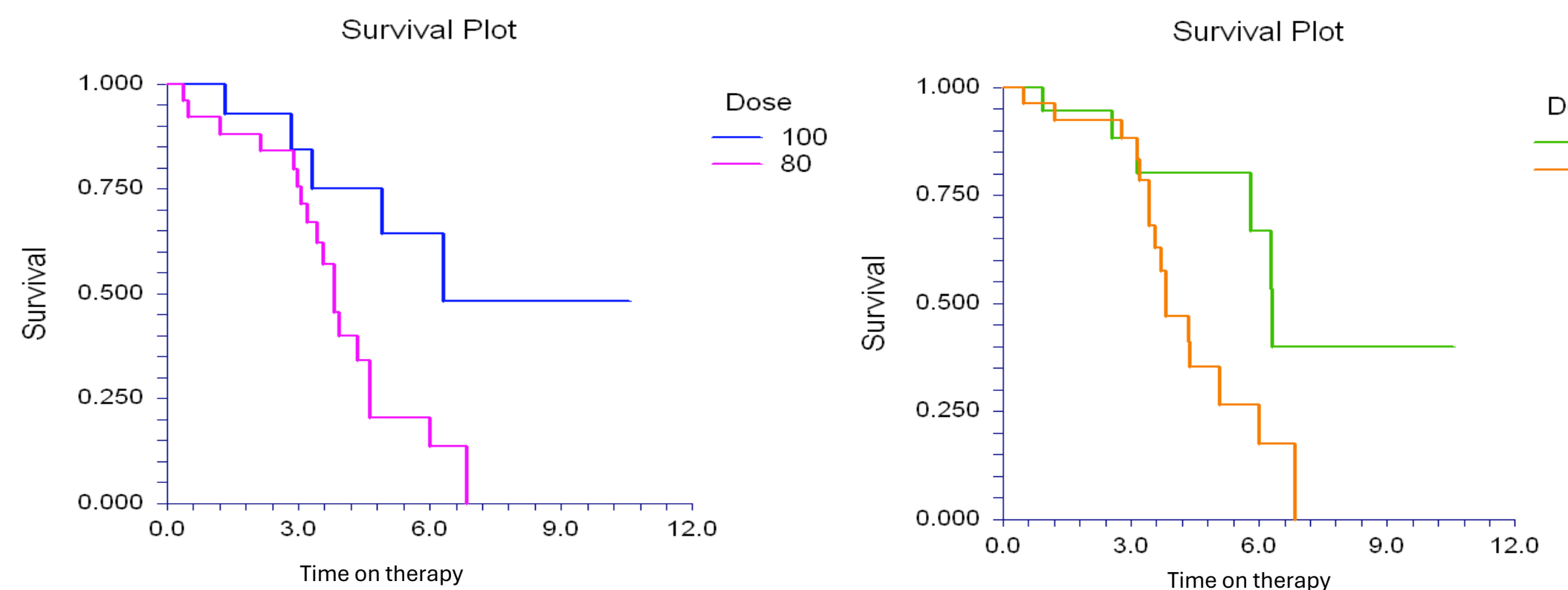
Dynamics of LIVERFAST Activity test during RT



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



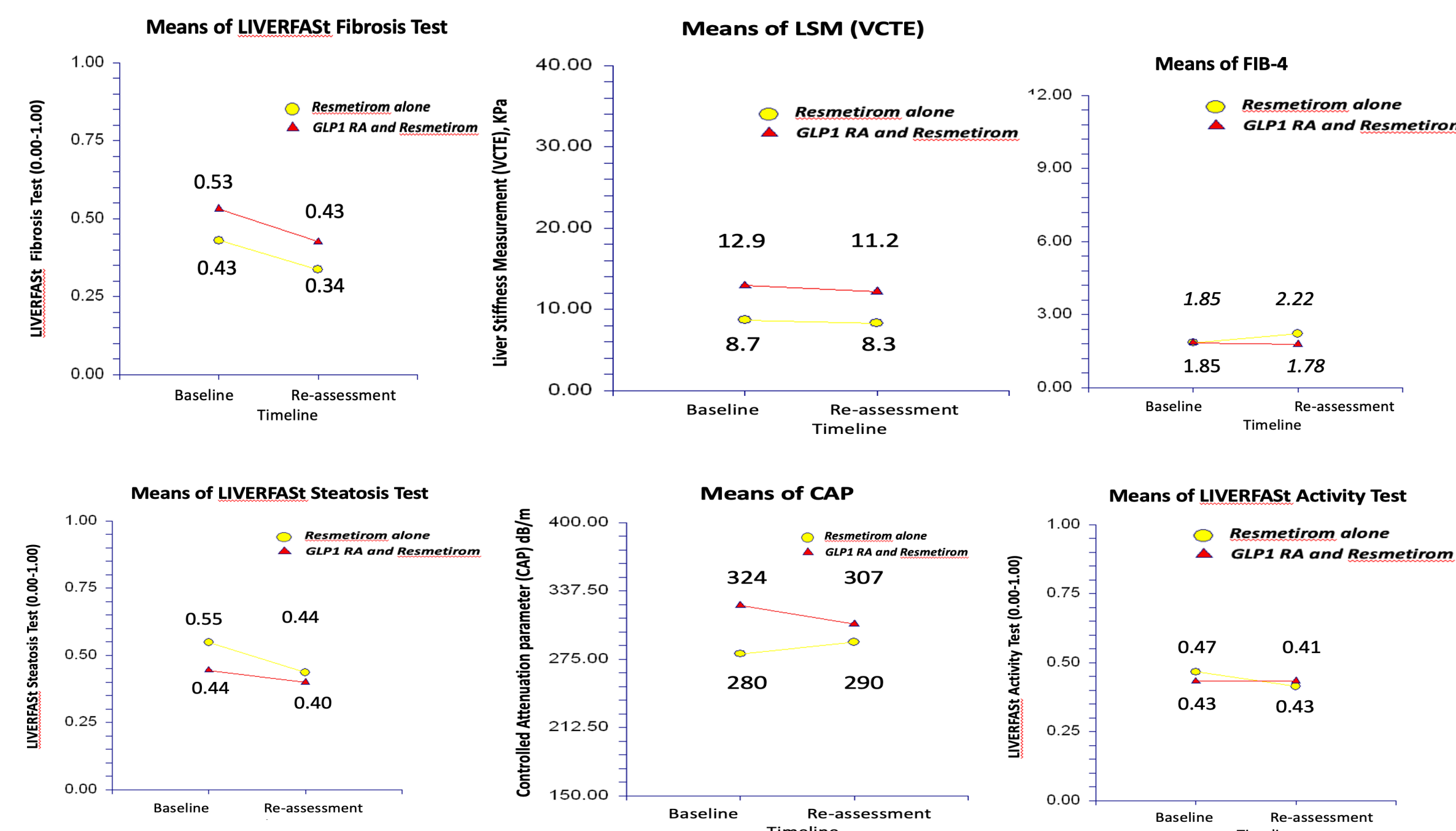
Cumulative incidence of achieving 10% reduction in LIVERFAST Fibrosis and Steatosis Tests



Resmetirom dose group	Cumulative incidence of 10% improvement of fibrosis according to LIVERFAST		P value
	3 months	6 months	
80mg group	23.8%	79.2%	0.02
100mg group	20.7%	37.5%	

Resmetirom dose group	Cumulative incidence of 10% improvement of steatosis according to LIVERFAST		p value
	3 months	6 months	
80mg group	11.7%	73.5%	0.03
100mg group	11.8%	33.3%	

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



CONCLUSION

- Initiation of Resmetirom therapy based on the assessment of MASH using LIVERFAST, FIB4 and VCTE is efficient and allows further non-invasive monitoring.
- LIVERFAST is an efficient monitoring tool of fibrosis and steatosis and significant improvement, higher than 10% in LIVERFAST scores being observed since 3rd month of RT mainly in the 80mg group.
- FIB-4 and LSM (VCTE) scores showed lower change at reassessment, suggesting limited ability to detect early fibrosis or steatosis improvement.

REFERENCES

- Alkhouri N, Mantry P, Gonzalez HC, et al. J Gastrointest Liver Dis 2025; 34(4):437-450.
- Decraecker M, Dutarte D, Hiriart JB, Aliment Pharmacol Ther. 2022 Mar;55(5):580-592.



CONTACT INFORMATION



@JeevinSSandhu
JeevinSandhu@mhd.com



DISCLOSURES

MM, JL: Fibronostics, New Orleans, LA, US