

Twelve-month changes in liver function enzymes, lipids, and vibration-controlled transient elastography measures in patients receiving resmetirom

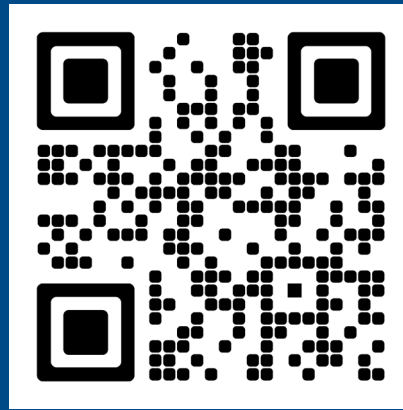
Christina M. Parrinello,¹ Sean Stern,² Setareh A. Williams,² Yestle Kim,¹ John O'Donnell,¹ Anthony Martinez³

¹Madrigal Pharmaceuticals, Inc., West Conshohocken, PA, USA; ²Star Biopharma Consulting, LLC, Malvern, PA, USA;

³Department of Medicine, Jacobs School of Medicine & Biomedical Sciences, University at Buffalo, Buffalo, NY, USA

Anthony Martinez
adm35@buffalo.edu

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Introduction

- Metabolic dysfunction–associated steatohepatitis (MASH) is a complex condition that frequently coexists with metabolic comorbidities, including type 2 diabetes (T2D), obesity, and dyslipidaemia¹
- Resmetirom is an oral thyroid hormone beta–selective agonist that received accelerated approval in the United States in March 2024 for the treatment of adults with noncirrhotic MASH and moderate to advanced fibrosis (consistent with stages F2–F3)²
- Studies evaluating the real-world effectiveness of resmetirom are limited

Aim

- To evaluate 12-month changes in liver function enzymes, lipids, and vibration-controlled transient elastography (VCTE) measurements amongst patients initiating resmetirom overall and stratified by baseline T2D, obesity, glucagon-like peptide 1 (GLP-1) use, and statin use

Methods

Study design and data source

- This retrospective cohort study used de-identified electronic health record (EHR) data linked to third-party medication dispensing data within Truveta, a collaborative health data platform representing 30 health systems across the US, including hospitals, ambulatory care centers, imaging centers, clinics, and medical offices

Study population

- Adults aged ≥18 years initiating resmetirom on or after 14 March 2024 were included and followed through 17 October 2025
- Patients were required to have had ≥1 healthcare encounter per year during the 24-month period prior to index date (date of first resmetirom dispensing), no evidence of other causes of liver disease (eg, excess alcohol use) or advanced liver disease (eg, cirrhosis), and ≥9 months of follow-up

Baseline characteristics

- Sociodemographic characteristics and clinical characteristics were defined as the value closest to the index date from within the previous 365 days
- T2D, obesity, hypertension, dyslipidaemia, and Elixhauser Comorbidity Index score were identified using a combination of International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) codes, laboratory values, vital signs, and medication use, as appropriate

Outcomes

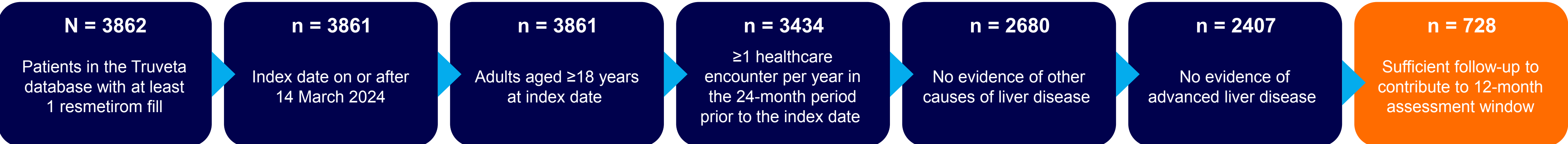
- Outcomes included blood biomarkers (alanine aminotransferase [ALT], aspartate aminotransferase [AST], and low-density lipoprotein cholesterol [LDL-C]), obtained from structured EHR data, and noninvasive markers of liver disease (Fibrosis-4 Index [FIB-4] and VCTE measures, including liver stiffness measurement [LSM] and controlled attenuation parameter [CAP]), with VCTE results extracted from unstructured data from patients with available documentation using natural language processing
- Laboratory markers were assessed at baseline using the closest value within –90 to +45 days from index and at 12 months using the closest value within ±90 days
- VCTE was assessed at baseline using the closest value within –360 to +45 days from index and at 12 months using the closest value within ±180 days
- Mean (SD) values were calculated at baseline and follow-up, absolute and percentage changes from baseline were derived, and statistical significance was assessed using paired *t* tests

Results

Patient characteristics

- A total of 728 patients who initiated resmetirom met the eligibility criteria and had sufficient follow-up (≥9 months, median 385 days) to contribute to the 12-month assessment window (**Figure 1**); mean (SD) age was 57.5 (12.8) years, 64.0% were female, 76.9% were White, and 79.3% were not Hispanic or Latino
 - Census region for the overall cohort was: 38.6% South, 26.0% Midwest, 13.9% West, 8.5% Northeast, and 13.0% unknown
- A high burden of metabolic comorbidities was observed in the overall cohort, including dyslipidaemia (79.7%), obesity (64.0%), hypertension (62.0%), and T2D (51.8%), with 30.2% of patients receiving GLP-1 therapy during the baseline period
- Patients with T2D, obesity, baseline GLP-1 use, and baseline statin use generally had a numerically greater metabolic disease burden than their respective comparison groups (**Table 1**)

Figure 1. Study population attrition



The index date is the date of first resmetirom dispensing.

Table 1. Baseline clinical characteristics overall and by key subgroups (T2D, obesity, baseline GLP-1 use, and baseline statin use)

		T2D		Obesity		Baseline GLP-1 use		Baseline statin use	
Characteristic	Overall cohort	Yes	No	Yes	No	Yes	No	Yes	No
	N = 728	n = 377	n = 351	n = 466	n = 262	n = 220	n = 508	n = 390	n = 338
Elixhauser Comorbidity Index score, ^a mean (SD)	10.0 (9.0)	11.1 (8.8)	8.7 (9.0)	10.3 (8.8)	9.4 (9.3)	10.3 (8.7)	9.8 (9.2)	10.8 (9.0)	9.0 (9.0)
Obesity, n (%)	466 (64.0)	260 (69.0)	206 (58.7)	466 (100)	0 (0)	155 (70.5)	311 (61.2)	256 (65.6)	210 (62.1)
T2D, n (%)	377 (51.8)	377 (100)	0 (0)	260 (55.8)	117 (44.7)	178 (80.9)	199 (39.2)	246 (63.1)	131 (38.8)
Dyslipidemia, n (%)	580 (79.7)	336 (89.1)	244 (69.5)	385 (82.6)	195 (74.4)	182 (82.7)	398 (78.3)	390 (100)	190 (56.2)
Hypertension, n (%)	451 (62.0)	258 (68.4)	193 (55.0)	334 (71.7)	117 (44.7)	147 (66.8)	304 (59.8)	263 (67.4)	188 (55.6)
Baseline statin use, n (%)	390 (53.6)	246 (65.3)	144 (41.0)	256 (54.9)	134 (51.1)	140 (63.6)	250 (49.2)	390 (100)	0 (0)
Baseline GLP-1 use, n (%)	220 (30.2)	178 (47.2)	42 (12.0)	155 (33.3)	65 (24.8)	220 (100)	0 (0)	140 (35.9)	80 (23.7)

^aThe Elixhauser Comorbidity Index score (refined for ICD-10-CM) is a measure that quantifies the presence of 38 different preexisting comorbid conditions using binary indicators based on ICD-10-CM codes to predict risk of in-hospital mortality and 30-day, all-cause hospital readmission. A higher score indicates greater comorbidity burden and higher risk.
GLP-1, glucagon-like peptide 1 receptor agonist; ICD-10-CM, International Classification of Diseases, 10th Revision, Clinical Modification; T2D, type 2 diabetes.

Changes in blood biomarkers in patients with baseline and 12-month measurements

- Statistically significant reductions in ALT and AST over 12 months (*p* < 0.001) were observed in the overall cohort of patients receiving resmetirom; these reductions in liver enzymes were consistent across all subgroups, irrespective of baseline T2D status, obesity, baseline GLP-1 use, and baseline statin use (**Table 2**)
- LDL-C levels showed a statistically significant decrease over 12 months in the overall cohort (*p* = 0.035); reductions across subgroups were generally modest and of similar magnitude to the overall cohort, although larger numerical decreases were observed in patients without obesity and smaller numerical decreases were observed amongst patients receiving GLP-1 therapy at baseline (**Table 2**)

Table 2. Change in ALT, AST, and LDL-C in the overall cohort and by key subgroups

	T2D			Obesity		Baseline GLP-1 use		Baseline statin use	
	Overall	Yes	No	Yes	No	Yes	No	Yes	No
	N = 728	n = 377	n = 351	n = 466	n = 262	n = 220	n = 508	n = 390	n = 338
ALT, U/L									
n (%) with both measurements	222 (30.5)	138 (36.6)	84 (23.9)	164 (35.2)	58 (22.1)	70 (31.8)	152 (29.9)	124 (31.8)	98 (29.0)
Baseline mean (SD)	64.5 (47.5)	59.5 (37.4)	72.9 (59.8)	66.1 (50.5)	60.0 (37.4)	61.0 (41.5)	66.2 (50.0)	61.8 (43.8)	68.0 (51.7)
12-month mean (SD)	43.1 (32.0)	41.5 (24.0)	45.5 (42.1)	43.4 (33.3)	42.1 (28.3)	39.9 (25.7)	44.5 (34.5)	44.4 (25.4)	41.4 (38.9)
Mean change (SD)	-21.5 (42.2)	-17.9 (35.7)	-27.3 (50.7)	-22.7 (41.6)	-17.9 (43.8)	-21.1 (39.0)	-21.6 (43.7)	-17.4 (39.2)	-26.6 (45.4)
Mean % change	-18.5	-17.5	-20.1	-21.1	-11.2	-20.3	-17.7	-12.2	-26.5
p value	<0.001	<0.001	<0.001	<0.001	0.003	<0.001	<0.001	<0.001	<0.001
≥17 U/L decrease from baseline, n (%)	99 (44.6)	56 (40.6)	43 (51.2)	73 (44.5)	26 (44.8)	31 (44.3)	68 (44.7)	49 (39.5)	50 (51.0)
AST, U/L									
n (%) with both measurements	222 (30.5)	138 (36.6)	84 (23.9)	164 (35.2)	58 (22.1)	70 (31.8)	152 (29.9)	124 (31.8)	98 (29.0)
Baseline mean (SD)	50.1 (35.5)	50.5 (35.5)	49.5 (35.6)	50.9 (38.3)	47.8 (26.1)	51.1 (41.9)	49.7 (32.2)	49.9 (37.9)	50.4 (32.3)
12-month mean (SD)	35.4 (20.4)	35.7 (18.9)	34.9 (22.9)	34.7 (19.5)	37.6 (23.0)	33.8 (19.7)	36.2 (20.8)	36.5 (18.1)	34.0 (23.1)
Mean change (SD)	-14.7 (33.9)	-14.8 (32.0)	-14.6 (36.9)	-16.3 (34.5)	-10.2 (31.8)	-17.3 (36.6)	-13.5 (32.6)	-13.4 (33.9)	-16.3 (33.9)
Mean % change	-13.9	-15.8	-10.7	-17.0	-5.1	-17.8	-12.0	-11.1	-17.4
p value	<0.001	<0.001	<0.001	<0.001	0.017	<0.001	<0.001	<0.001	<0.001
LDL-C, mg/dL									
n (%) with both measurements	85 (11.7)	53 (14.1)	32 (9.1)	63 (13.5)	22 (8.4)	27 (12.3)	58 (11.4)	44 (11.3)	41 (12.1)
Baseline mean (SD)	93.9 (33.4)	87.7 (34.1)	104.1 (29.8)	92.7 (33.2)	97.1 (34.5)	86.9 (32.2)	97.1 (33.7)	83.1 (29.4)	105.4 (33.8)
12-month mean (SD)	85.4 (34.1)	79.9 (34.7)	94.7 (31.4)	86.9 (32.0)	81.3 (40.0)	85.9 (32.5)	85.2 (35.1)	78.7 (32.6)	92.7 (34.5)
Mean change (SD)	-8.5 (36.4)	-7.9 (41.4)	-9.4 (26.6)	-5.9 (33.2)	-15.8 (44.3)	-1.0 (45.6)	-11.9 (31.0)	-4.5 (40.3)	-12.7 (31.5)
Mean % change	-2.1	0.9	-7.0	0	-8	14	-9.6	4.5	-9.2
p value	0.035	0.173	0.053	0.165	0.108	0.911	0.005	0.467	0.013

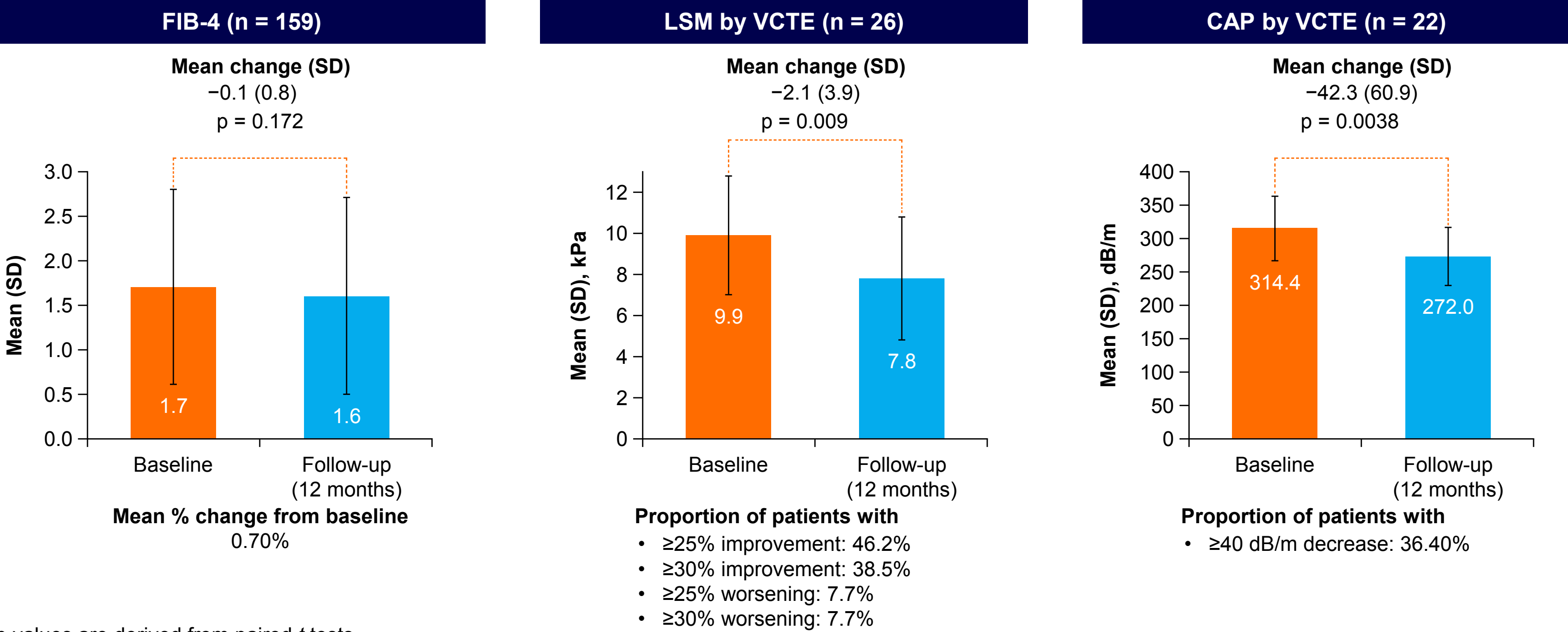
p values are derived from paired *t* tests. Statistically significant values and corresponding mean change (SD) are in bold.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; GLP-1, glucagon-like peptide 1 receptor agonist; LDL-C, low-density lipoprotein cholesterol; T2D, type 2 diabetes.

Changes in noninvasive markers of liver disease

- In the overall cohort, mean FIB-4 remained stable over 12 months, with no statistically significant change during this period (**Figure 2**); a statistically significant decrease in FIB-4 was observed in patients with obesity (*p* = 0.018) but not in other subgroups (data not shown)
- LSM and CAP by VCTE decreased significantly over 12 months in the overall cohort (**Figure 2**); similar trends were observed across subgroups, though statistical significance was not consistently achieved, likely reflecting limited sample sizes (data not shown)

Figure 2. Mean change in FIB-4 scores, LSM by VCTE, and CAP by VCTE in the overall cohort



p values are derived from paired *t* tests.

CAP, controlled attenuation parameter; FIB-4, Fibrosis-4 Index; LSM, liver stiffness measurement; VCTE, vibration-controlled transient elastography.

References

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Disclosures

CMP, YK, and JOD are employees and shareholders of Madrigal Pharmaceuticals, Inc. **SS** and **SAW** are consultants for Madrigal Pharmaceuticals, Inc. and employees of Star Biopharma Consulting, LLC, which received funding from Madrigal Pharmaceuticals, Inc. to participate in this research. **AM** reports consulting/advisor/other roles and/or support for travel relationships with Madrigal Pharmaceuticals, Inc., AbbVie, Altimmune, Arbutus, Arrowhead, Atea, Braeburn, Cepheid, Gilead, Inventiva, Ipsen, Merck, New York State Department of Health, Novo Nordisk, Roche, Sirtex; and board membership for Liver Education Advocates.

Conclusions

- In this descriptive study of patients treated with resmetirom, mean liver function tests showed significant improvement over 12 months, irrespective of baseline T2D status, obesity status, GLP-1 use, or statin use
- LDL-C levels decreased significantly in the overall cohort and showed directional reductions across all subgroups, although statistical significance was not consistently observed
- Statistically significant improvements in LSM and CAP by VCTE were observed in the overall cohort; findings were generally consistent across subgroups, although interpretation is limited by smaller sample sizes
- Mean liver stiffness declined from 9.9 to 7.8 kPa over 12 months among patients receiving resmetirom, crossing a common threshold and shifting, on average, into a lower fibrosis risk category (approximately F1)¹
- Limitations of the analysis included incomplete data, small sample sizes and no comparator
- These findings provide early real-world evidence supporting the effectiveness of resmetirom on liver-related biomarkers, LDL-C, liver stiffness, and steatosis, highlighting the importance of further research to evaluate longer-term outcomes, including sustained changes across multiple timepoints and additional noninvasive measures of disease progression

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