Twelve-month changes in laboratory- and imaging-based biomarkers in patients who have initiated resmetirom: a real-world retrospective cohort analysis using electronic health records

POSTER 3477

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INTRODUCTION

- MASH is a complex condition that frequently occurs with cardiometabolic comorbidities, including T2D, obesity, dyslipidemia, and cardiovascular disease[1]
- Resmetirom is an oral thyroid hormone β-selective agonist that is conditionally approved in the US for the treatment of adults with noncirrhotic MASH with moderate-to-advanced fibrosis (consistent with stage F2 to F3 fibrosis) in conjunction with diet and exercise[2]
- Emerging real-world data have shown improvements in laboratory- and imaging-based biomarkers[3]; however, follow-up durations and sample sizes remain limited

AIM

- This retrospective cohort study aimed to evaluate real-world changes in blood- and imaging-based biomarkers and composite noninvasive risk scores 12 months after resmetirom initiation

METHODS

Study design and data source

- Truveta Data, including de-identified electronic health record (EHR) data from a collective of 30 US healthcare systems and medication dispensing data (via e-prescribing)

Study population

- Eligible patients (**FIGURE 1**) were indexed at first resmetirom fill on or after March 14, 2024 and followed through June 6, 2026

Baseline characteristics

- Sociodemographic and clinical characteristics were defined as the value on index or closest to index within the previous 365 days

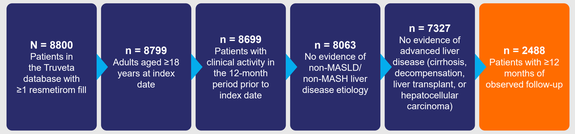
Outcomes

- Changes in biomarkers
  - Hepatic: ALT, AST, liver stiffness measurement (LSM) and controlled attenuation parameter (CAP) measured by vibration-controlled transient elastography [VCTE], and composite noninvasive risk scores (FibroScan-AST [FAST] and steatosis-associated fibrosis estimator [SAFE])
  - Cardiometabolic: LDL-C, HDL-C, total cholesterol (TC), triglycerides (TGs), and TG/HDL-C ratio

Statistical analysis

- Mean (SD) was calculated at baseline and follow-up; mean change (SD), mean percent change (SD) and median change (Q1, Q3) from baseline to follow-up (12 ± 3 months) were calculated
- Statistical significance was evaluated using paired *t* tests

FIGURE 1. Study population attrition.



The index date is the date of first resmetirom dispensing.

RESULTS

Patient characteristics

- Of 2488 patients, the mean age was 58.5 years, 62.5% were female, 77.0% were White, and 49.8% were from Southern states, with a median follow-up of 16.6 months (**FIGURE 1**)
- Metabolic comorbidities were common in the overall cohort (**TABLE 1**)
  - The proportions of patients receiving concomitant statin and GLP-1 therapy (defined as any post-index use) were 57.4% and 52.7%, respectively

TABLE 1. Clinical characteristics at baseline.

Characteristic, n (%)	Overall cohort N = 2488
Charlson Comorbidity Index category	
0	708 (28.5)
1-2	973 (39.1)
3-4	531 (21.3)
≥5	276 (11.1)
Obesity	1486 (59.7)
T2D	1192 (47.9)
Dyslipidemia	1863 (74.9)
Hypertension	1522 (61.2)
Any concomitant GLP-1 RA use[a]	1,311 (52.7)
Any concomitant statin use[a]	1,427 (57.4)

[a]Concomitant use is defined as any use of a GLP-1 RA or statin post-index
GLP-1 RA, glucagon-like peptide 1 receptor agonist; T2D, type 2 diabetes.

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

- At 12 months after resmetirom initiation, ALT, LSM, CAP, FAST score, and SAFE score were significantly decreased relative to baseline ($P < 0.001$ for all; **TABLE 2**)
- Most patients shifted toward lower LSM categories or were stable at 12 months (**FIGURE 2A**)
  - The number of patients with LSM <8 kPa increased at 12 months and the number of patients in the 10 to <15 kPa category decreased
  - Of 150 patients with paired measurements, 100 (66.7%) had ≥1 category improvement in LSM category at 12 months
- In a responder analysis, most patients (~93%) had reductions (≥25% or ≥30%) or stabilization (<25% or <30% increase) in LSM at 12 months; conversely, 10 (6.7%) had an increase in liver stiffness of ≥25% and 9 (6.0%) had an increase of ≥30% (**FIGURE 2B**)

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

- At 12 months after resmetirom initiation, the cardiometabolic biomarkers LDL-C, TC, TG, and TG/HDL-C ratio were statistically significantly decreased relative to baseline ($P < 0.001$ for all; **TABLE 2**)
  - Conversely, mean HDL-C was statistically significantly increased at 12 months after resmetirom initiation relative to baseline ($P = 0.0014$)

Shift into lower LDL-C threshold categories

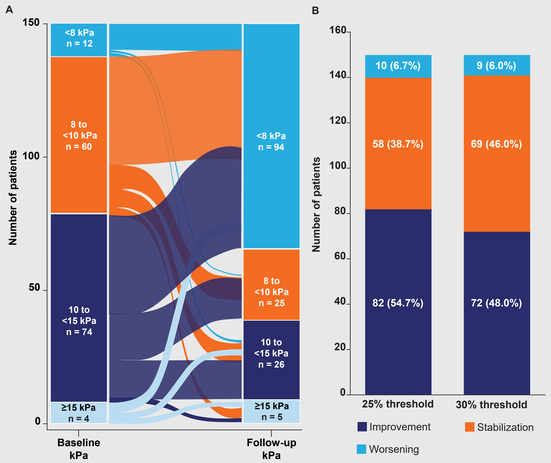
- Among patients with elevated baseline LDL-C, a substantial proportion shifted into lower guideline-defined LDL-C threshold categories 12 months after resmetirom initiation (**TABLE 3**)
- Similar patterns were observed regardless of concomitant statin use

TABLE 2. Hepatic and cardiometabolic biomarkers at baseline and 12 months after resmetirom initiation.

	N	Baseline mean (SD)	Follow-up mean (SD)	Mean change (SD)	Median change (Q1, Q3)	Mean % change (SD)	*P* value
Hepatic biomarkers							
ALT, U/L	1161	55.0 (44.9)	38.8 (29.0)	−16.2 (42.4)	−7.0 (−26.0, 3.0)	−9.4 (59.5)	**<0.001**
LSM, kPa	150	10.3 (2.2)	7.8 (3.0)	−2.5 (3.3)	−2.8 (−4.5, −0.8)	−22.1 (31.8)	**<0.001**
CAP, dB/m	125	305.8 (44.4)	261.4 (54.5)	−44.5 (61.7)	−36.0 (−88.0, −1.0)	−13.2 (20.4)	**<0.001**
FAST score	95	0.43 (0.22)	0.23 (0.14)	−0.20 (0.19)	−0.19 (−0.35, −0.06)	–	**<0.001**
SAFE score	527	126.3 (103.1)	100.0 (105.4)	−26.2 (79.8)	−20.9 (−74.9, 23.1)	–	**<0.001**
Cardiometabolic biomarkers							
LDL-C, mg/dL	635	91.6 (36.6)	76.1 (32.9)	−15.5 (32.8)	−13.0 (−31.1, 2.9)	−11.4 (39.1)	**<0.001**
HDL-C, mg/dL	639	45.6 (12.1)	46.7 (11.5)	1.1 (9.0)	1.0 (−4.0, 6.0)	5.1 (22.2)	**0.0014**
TC, mg/dL	653	167.5 (43.3)	146.1 (40.5)	−21.4 (39.1)	−17.0 (−41.0, 1.0)	−10.7 (21.0)	**<0.001**
TG, mg/dL	656	169.2 (106.2)	128.2 (78.0)	−41.0 (86.5)	−30.7 (−72.0, 4.2)	−16.9 (38.4)	**<0.001**
TG/HDL-C ratio	632	4.2 (4.1)	3.1 (2.7)	−1.2 (3.2)	−0.8 (−1.8, 0.1)	−16.2 (46.9)	**<0.001**

N represents patients with measurements at baseline and 12 months after resmetirom initiation.
The outcome measurement window was between Months 9 and 15.
P values are derived from paired *t* tests.
Mean (SD) days from baseline to follow-up values: ALT, 359.7 (41.7); LSM by VCTE, 353.8 (40.7); CAP by VCTE, 353.3 (40.1); LDL-C, 359.2 (46.7); HDL-C, 359.6 (46.6); TC, 359.6 (46.1);
TG, 359.6 (46.1); TG/HDL-C ratio, 359.4 (46.5).
ALT, alanine aminotransferase; CAP, controlled attenuation parameter; FAST, FibroScan-aspartate aminotransferase; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LSM, liver stiffness measurement; Q1, quartile 1; Q3, quartile 3; SAFE, steatosis-associated fibrosis estimator; TC, total cholesterol; TG, triglycerides.

FIGURE 2. Patient (A) flow across LSM (kPa) by risk categories from baseline to 12 months and (B) proportion achieving 25% and 30% threshold in LSM at 12 months.



kPa, kilopascals; LSM, liver stiffness measurement.

TABLE 3. Changes in LDL-C threshold category from baseline to 12 months, overall and by concomitant statin use.

Group	N	LDL-C ≥70 mg/dL at baseline, n (%)	LDL-C ≥70 mg/dL at 12 months, n (%)	Change from LDL-C ≥70 mg/dL to <70 mg/dL, n (%)	LDL-C ≥100 mg/dL at baseline, n (%)	LDL-C ≥100 mg/dL at 12 months, n (%)	Change from LDL-C ≥100 mg/dL to <100 mg/dL, n (%)
Overall	635	446 (70.2)	334 (52.6)	150 (33.6)	236 (37.2)	130 (20.5)	138 (58.5)
Concomitant statin	399	240 (60.2)	167 (41.9)	104 (43.3)	105 (26.3)	53 (13.3)	71 (67.6)
No concomitant statin	236	206 (87.3)	167 (70.8)	46 (22.3)	131 (55.5)	77 (32.6)	67 (51.1)

Follow-up window: 9-15 months post-index date.
Denominator is patients with baseline LDL-C at or above the respective threshold.
LDL-C, low-density lipoprotein cholesterol.

Limitations

- As this was a descriptive retrospective study using real-world data, the findings may be affected by missing or inaccurately recorded information, as well as limitations in the ability of structured EHR data to fully represent patients' healthcare journeys
- No comparator was used and certain data are affected by missing values

CONCLUSIONS

- **In this descriptive analysis, 12-month improvements in hepatic and cardiometabolic biomarkers were observed in patients who initiated resmetirom**
  - **Changes in LSM by VCTE were, on average, consistent with a shift into a lower fibrosis risk category**
- **These findings add to the emerging real-world evidence on outcomes following resmetirom initiation but should not be interpreted as demonstrating a causal treatment effect**
- **Continued follow-up in larger populations with more complete longitudinal measurements will be important to assess the durability of these changes and longer-term liver-related and cardiovascular outcomes**

REFERENCES

1. Sandireddy R et al. *Front Cell Dev Biol*. 2024;12:1433857.
2. Rezdiffra (resmetirom) tablets, for oral use. Prescribing information. United States: Madrigal Pharmaceuticals, Inc.; March 2025.
3. Harrison SA et al. *Nat Med*. 2003;29(11):2919-2928.

DISCLOSURES

ST, **CMP**, **YK**, and **JCO** are employees and shareholders of Madrigal Pharmaceuticals, Inc.
AM reports consulting/advisory/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, and Sirtex and board membership for Liver Education Advocates.

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