Twelve-month changes in laboratory- and imaging-based biomarkers following resmetirom initiation: a real-world analysis across cardiometabolic and concomitant medication subgroups

POSTER 3433

Anthony Martinez,[1,2] Susan Thapa,[2] Christina M. Parrinello,[2] Yestle Kim,[2] John C. O'Donnell[2]

[1]Jacobs School of Medicine & Biomedical Sciences, University at Buffalo, Buffalo, NY; [2]Madrigal Pharmaceuticals, Inc., West Conshohocken, PA

INTRODUCTION

- Resmetirom is an oral thyroid hormone receptor β–selective agonist conditionally approved in the United States for the treatment of adults with noncirrhotic MASH with moderate to advanced fibrosis (consistent with stage F2-F3 fibrosis) in conjunction with diet and exercise[1]
- Patients with MASH have high prevalence of T2D and obesity and commonly receive concomitant medications, including GLP-1 RAs and statins[2]
  - Real-world studies describing changes in hepatic and cardiometabolic biomarkers across these subgroups are limited

AIM

- This retrospective cohort study aimed to evaluate real-world changes in blood- and imaging-based hepatic and cardiometabolic biomarkers 12 months after resmetirom initiation in clinically relevant patient subgroups

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

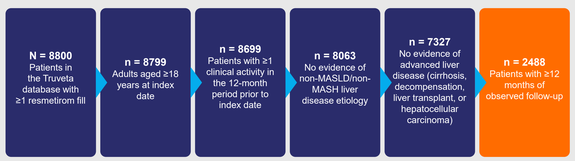
Outcomes

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

Statistical analysis

- Mean (SD) was calculated at baseline and follow-up; mean 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 across predefined subgroups of patients stratified by baseline obesity status, T2D status, and concomitant use of GLP-1 RAs and statins

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
- 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 overall and by key subgroups.

Characteristic, n (%)	Overall cohort N = 2488	T2D		Obesity		Concomitant statin use		Concomitant GLP-1 RA use	
		Yes n = 1192	No n = 1296	Yes n = 1486	No n = 1002	Yes n = 1427	No n = 1061	Yes n = 1311	No n = 1177
Charlson Comorbidity Index category									
0	708 (28.5)	228 (19.1)	480 (37.0)	225 (15.1)	483 (48.2)	384 (26.9)	324 (30.5)	344 (26.2)	364 (30.9)
1-2	973 (39.1)	446 (37.4)	527 (40.7)	668 (45.0)	305 (30.4)	534 (37.4)	439 (41.4)	505 (38.5)	468 (39.8)
3-4	531 (21.3)	343 (28.8)	188 (14.5)	386 (26.0)	145 (14.5)	324 (22.7)	207 (19.5)	315 (24.0)	216 (18.4)
≥5	276 (11.1)	175 (14.7)	101 (7.8)	207 (13.9)	69 (6.9)	185 (13.0)	91 (8.6)	147 (11.2)	129 (11.0)
Hypertension	1522 (61.2)	903 (75.8)	619 (47.8)	1101 (74.1)	421 (42.0)	943 (66.1)	579 (54.6)	856 (65.3)	666 (56.6)
Dyslipidemia	1863 (74.9)	1037 (87.0)	826 (63.7)	1206 (81.2)	657 (65.6)	1321 (92.6)	542 (51.1)	1021 (77.9)	842 (71.5)
T2D	1192 (47.9)	1192 (100)	0	810 (54.5)	382 (38.1)	846 (59.3)	346 (32.6)	833 (63.5)	359 (30.5)
Obesity	1486 (59.7)	810 (68.0)	676 (52.2)	1486 (100)	0	859 (60.2)	627 (59.1)	879 (67.0)	607 (51.6)
Any concomitant GLP-1 RA use*	1,311 (52.7)	833 (69.9)	478 (36.9)	879 (59.2)	432 (43.1)	834 (58.4)	477 (45.0)	1311 (100)	0
Any concomitant statin use*	1,427 (57.4)	846 (71.0)	581 (44.8)	859 (57.8)	568 (56.7)	1427 (100)	0	834 (63.6)	593 (50.4)

*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 and cardiometabolic biomarkers across clinically relevant subgroups

- There were statistically significant reductions in AST and SAFE 12 months after resmetirom initiation across all subgroups ($P < 0.05$ for all; **TABLE 2**)
- At 12 months, LDL-C and TG were statistically significantly decreased from baseline in the overall population and across all patient subgroups ($P < 0.001$ for all; **TABLE 2**)
- Mean HDL-C increased relative to baseline; the difference was statistically significant overall and in most subgroups (**TABLE 2**)
- Mean LSM was significantly reduced at 12 months after resmetirom initiation compared with baseline across all patient subgroups ($P < 0.001$ for all); similarly, mean CAP was significantly decreased 12 months following resmetirom initiation across all patient subgroups ($P < 0.001$ for all)

Responder analyses stratified by patient subgroup

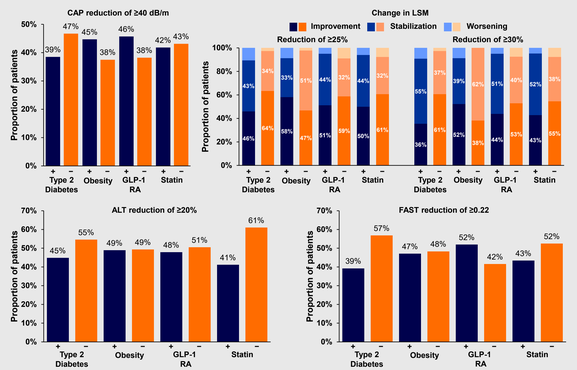
- Across subgroups, substantial proportions of patients achieved responder outcomes, including CAP reductions of ≥40 dB/m, LSM reductions of ≥25% or ≥30%, ALT reductions of ≥20%, and FAST reduction of ≥0.22 (**FIGURE 2**)
  - Subgroup mean changes in LSM ranged from −1.8 to −3.2 kPa

TABLE 2. Changes from baseline to 12 months in hepatic and cardiometabolic biomarkers across patient subgroups.

Biomarker	Subgroup		N	Baseline, mean (SD)	Follow-up, mean (SD)	Mean change (SD)	Median change (Q1, Q3)
Hepatic biomarkers							
AST (U/L)	**Overall**		1158	43.3 (34.9)	33.7 (23.7)	**−9.6 (36.3)**	−4.0 (−17.0, 4.0)
	Type 2 diabetes	Yes	655	40.2 (29.4)	33.4 (25.0)	**−6.8 (30.7)**	−3.0 (−15.0, 5.0)
		No	503	47.2 (40.7)	34.1 (22.0)	**−13.2 (42.3)**	−5.0 (−21.0, 4.0)
	Obesity	Yes	861	42.2 (36.6)	33.0 (24.7)	**−9.2 (38.7)**	−3.0 (−16.0, 4.0)
		No	297	46.5 (29.4)	35.8 (20.3)	**−10.8 (28.4)**	−6.0 (−20.0, 5.0)
	Concomitant statin use	Yes	698	39.8 (29.2)	33.3 (18.7)	**−6.5 (27.7)**	−2.0 (−13.0, 6.0)
		No	460	48.6 (41.6)	34.4 (29.7)	**−14.2 (46.1)**	−7.0 (−23.0, 3.0)
	Concomitant GLP-1 RA use	Yes	640	41.9 (38.5)	32.8 (23.7)	**−9.1 (39.7)**	−3.0 (−15.2, 5.0)
		No	518	45.0 (29.9)	34.8 (23.6)	**−10.2 (31.7)**	−5.0 (−20.0, 4.0)
SAFE score	**Overall**		527	126.3 (103.1)	100.0 (105.4)	**−26.2 (79.8)**	−20.9 (−74.9, 23.1)
	Type 2 diabetes	Yes	305	151.3 (98.0)	127.6 (98.9)	**−23.7 (72.4)**	−20.7 (−73.0, 24.1)
		No	222	91.9 (100.1)	62.2 (102.5)	**−29.6 (89.0)**	−22.0 (−80.3, 22.5)
	Obesity	Yes	409	131.6 (104.1)	105.0 (103.6)	**−26.7 (80.4)**	−20.8 (−75.3, 22.5)
		No	118	107.6 (97.4)	82.9 (110.0)	**−24.6 (78.0)**	−21.5 (−74.1, 26.2)
	Concomitant statin use	Yes	319	132.4 (93.6)	113.1 (96.6)	**−19.4 (72.2)**	−15.2 (−67.3, 31.2)
		No	208	116.8 (115.7)	80.1 (115.0)	**−36.7 (89.4)**	−29.9 (−85.5, 12.9)
	Concomitant GLP-1 RA use	Yes	309	133.2 (95.3)	104.6 (98.1)	**−28.5 (79.8)**	−24.0 (−75.4, 21.8)
		No	218	116.4 (112.6)	93.5 (114.8)	**−22.9 (79.8)**	−13.9 (−73.1, 24.8)
Cardiometabolic biomarkers							
LDL-C, mg/dL	**Overall**		635	91.6 (36.6)	76.1 (32.9)	**−15.5 (32.8)**	−13.0 (−31.1, 2.9)
	Type 2 diabetes	Yes	398	84.8 (34.7)	71.2 (32.0)	**−13.6 (31.6)**	−12.0 (−28.0, 3.0)
		No	237	103.0 (36.9)	84.3 (32.7)	**−18.8 (34.5)**	−15.5 (−34.0, 1.0)
	Obesity	Yes	473	92.2 (35.9)	77.5 (33.1)	**−14.7 (31.2)**	−12.0 (−28.0, 2.0)
		No	162	89.9 (38.6)	72.1 (32.0)	**−17.9 (37.1)**	−15.8 (−36.8, 3.8)
	Concomitant statin use	Yes	399	84.0 (37.1)	68.4 (32.1)	**−15.6 (35.5)**	−12.0 (−29.8, 2.9)
		No	236	104.5 (31.8)	89.0 (30.0)	**−15.4 (27.7)**	−15.0 (−32.0, 2.2)
	Concomitant GLP-1 RA use	Yes	368	87.6 (36.8)	71.1 (31.4)	**−16.5 (33.5)**	−14.0 (−30.1, 1.0)
		No	267	97.1 (35.6)	83.0 (33.7)	**−14.1 (31.8)**	−12.0 (−32.0, 4.0)
HDL-C, mg/dL	**Overall**		639	45.6 (12.1)	46.7 (11.5)	**1.1 (9.0)**	1.0 (−4.0, 6.0)
	Type 2 diabetes	Yes	400	44.3 (11.4)	45.8 (11.5)	**1.6 (8.9)**	1.0 (−3.0, 6.0)
		No	239	47.8 (12.8)	48.2 (11.2)	0.4 (9.1)	0.0 (−5.0, 5.0)
	Obesity	Yes	474	45.2 (11.8)	46.2 (11.4)	**1.0 (8.2)**	1.0 (−4.0, 6.0)
		No	165	46.9 (12.8)	48.3 (11.5)	1.4 (10.9)	1.0 (−4.0, 7.0)
	Concomitant statin use	Yes	398	44.8 (12.3)	45.8 (11.7)	**1.0 (9.3)**	1.0 (−4.0, 6.0)
		No	241	46.8 (11.6)	48.2 (10.9)	**1.4 (8.5)**	1.0 (−4.0, 6.0)
	Concomitant GLP-1 RA use	Yes	368	45.0 (11.5)	46.5 (11.8)	**1.4 (8.6)**	1.0 (−4.0, 6.0)
		No	271	46.3 (12.8)	47.1 (11.0)	0.8 (9.5)	1.0 (−4.0, 6.0)
TG, mg/dL	**Overall**		656	169.2 (106.2)	128.2 (78.0)	**−41.0 (86.5)**	−30.7 (−72.0, 4.2)
	Type 2 diabetes	Yes	411	180.1 (121.1)	133.3 (86.5)	**−46.8 (96.6)**	−33.0 (−80.0, 2.5)
		No	245	150.9 (71.6)	119.6 (60.4)	**−31.3 (65.4)**	−24.0 (−64.0, 7.0)
	Obesity	Yes	486	167.5 (97.0)	131.5 (81.7)	**−36.0 (79.0)**	−29.0 (−67.0, 6.0)
		No	170	174.2 (129.4)	118.8 (65.8)	**−55.3 (104.1)**	−35.0 (−87.0, −2.5)
	Concomitant statin use	Yes	412	175.5 (117.5)	126.8 (75.4)	**−48.8 (92.9)**	−35.0 (−80.0, −2.8)
		No	244	158.6 (83.1)	130.7 (82.3)	**−27.9 (72.8)**	−22.0 (−58.8, 14.2)
	Concomitant GLP-1 RA use	Yes	375	177.9 (107.9)	130.7 (86.9)	**−47.2 (87.6)**	−35.0 (−77.0, −4.0)
		No	281	157.7 (103.1)	124.9 (64.4)	**−32.8 (84.5)**	−23.0 (−66.0, 14.0)

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. Bold values represent $P < 0.05$.
AST, aspartate aminotransferase; FAST, FibroScan-AST; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Q1, quartile 1; Q3, quartile 3; SAFE, steatosis-associated fibrosis estimator; TG, triglycerides.

FIGURE 2. Proportion of patients across subgroups achieving responder outcomes of CAP, LSM, ALT, and FAST.



ALT, alanine aminotransferase; CAP, controlled attenuation parameter; FAST, FibroScan-AST; kPa, kilopascals; LSM, liver stiffness measurement.

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
- Subgroup sample sizes were limited, particularly for imaging measures, and the study was not designed to formally compare treatment response between subgroups
- No comparator was used and certain data are affected by missing values

CONCLUSIONS

- **Among patients initiating resmetirom, improvements in imaging- and blood-based biomarkers as well as composite noninvasive risk scores at 12 months were observed across clinically relevant cardiometabolic and concomitant medication subgroups**
- **Most patients initiating resmetirom had improved or stabilized LSM at 12 months (89-98% across all subgroups)**
- **Future analyses with larger samples and longer follow-up will further characterize biomarker changes across clinically relevant subgroups**

REFERENCES

1. Rezdiffra (resmetirom) tablets, for oral use. Prescribing information. United States: Madrigal Pharmaceuticals, Inc.; March 2025.
2. Tapper EB et al. *BMC Gastroenterology.* 2026;26:301.

CONTACT INFORMATION

Christina Parrinello
cparrinello@madrigalpharma.com

ACKNOWLEDGMENTS

Medical writing and/or editorial assistance was provided by ApotheCom (San Francisco, CA, USA). This assistance was funded by Madrigal Pharmaceuticals, Inc., West Conshohocken, PA, USA. Funding for this research was provided by Madrigal Pharmaceuticals, Inc., West Conshohocken, PA, USA.

DISCLOSURES

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.

ST, **CMP**, **YK**, and **JCO** are employees and shareholders of Madrigal Pharmaceuticals, Inc.

SCAN QR CODE FOR DIGITAL POSTER

Copies of this poster obtained through QR (Quick Response) codes are for personal use only and may not be reproduced without permission from the authors.

RESONANCE Real-World Evidence of Reclassification Advancing Outcomes, Natural History, Assessment, and Clinical Effectiveness

Madrigal

Copyright © 2026 Madrigal Pharmaceuticals, Inc. All rights reserved. Presented at the American Association for the Study of Liver Diseases (AASLD) The Liver Meeting; November 5-9, 2026; Denver, Colorado