Early Real-World Liver Biomarker Changes Among Resmetirom-Treated MASH Patients, With and Without T2DM: A Descriptive Cohort Study

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INTRODUCTION

- Metabolic dysfunction-associated steatohepatitis (MASH) is a progressive form of fatty liver disease that often arises in the setting of metabolic disorders, including type 2 diabetes mellitus (T2DM).[1,2]
- Resmetirom (Rezdiffra™), a THR-β agonist, has received conditional FDA approval for the treatment of noncirrhotic MASH with moderate-to-advanced fibrosis,[3] and in the Phase III MAESTRO-NASH trial demonstrated greater efficacy than placebo in achieving MASH resolution and improving liver fibrosis.[4]
- However, it remains unclear whether the effectiveness of resmetirom differs between patients with and without T2DM in a real-world setting.

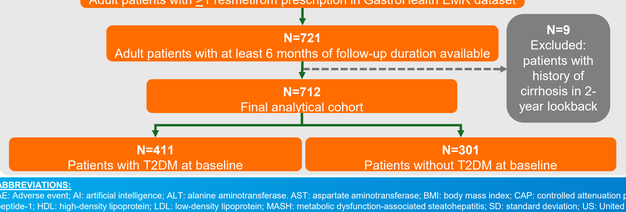
AIM

The aim of this study was to descriptively evaluate changes in liver biomarkers, clinical measures and responder rates among resmetirom-treated adults, stratified by T2DM status, over a ≥6-month follow up period.

METHODS

- **Study design & data source:** Single arm, retrospective cohort study using the Latica real-world data, which compiles de-identified EMR data from Gastro Health.
- **Population:** Eligible patients were adults with ≥1 prescription for resmetirom between April 2024 and April 2025 with a minimum of 6 months of follow-up since their first prescription during this period (**FIGURE 1**). Patients with a documented history of compensated or decompensated cirrhosis within the 2-year lookback period before resmetirom initiation were excluded using a validated algorithm of diagnostic codes.[5] Patients were stratified by baseline T2DM status.
- The **index date** was defined as the date of the patient's first resmetirom prescription. The **baseline period** encompassed the 12 months prior to index, during which clinical, laboratory and medication history were assessed. The **follow-up** period was defined as ≥ 6 months after initiation of resmetirom. Participants with at least one healthcare interaction during this timeframe were considered to have had a follow-up interaction.
- **Outcomes:**
  - **Clinical characteristics:** demographics, cardiometabolic conditions, GLP-1 use.
  - **Laboratory measures:** LDL, HDL, cholesterol, ALT, AST, kPa, CAP, and FAST at baseline and follow-up, stratified by T2DM status, when available.
    - Proportion of patients achieving threshold responses for ALT, FAST, and VCTE, as defined by literature.[6,7,8]
    - **Cardiometabolic conditions:** metabolic syndrome, hypertension, dyslipidemia, and obesity.

FIGURE 1. Study flow diagram



RESULTS

- Of the 1,278 who initiated resmetirom, 721 (56.4%) had at least 6 months of follow-up duration available. After excluding those with a history of cirrhosis in the 2-year look-back period, 712 patients comprised the final analytic cohort (**FIGURE 1**).
- 411(57.7%) patients had comorbid T2DM at baseline. Obesity was more common in patients with T2DM than those without T2DM (76.9% vs 63.5%; **TABLE 1**).

TABLE 1. Baseline characteristics of cohort by T2DM status (n=712)

Characteristics		With T2DM (n=411)	Without T2DM (n=301)
Mean age at index in years (SD)		59.5 (12.6)	58.2 (13.2)
Female, n(%)		260 (63.3)	146 (48.5)
Follow-up data in months*	Mean (SD)	9.5 (5.6)	8.5 (5.5)
	Median (IQR)	9.4 (6.2,12.6)	8.5 (4.4,12.0)
Race, n(%)	White	176 (42.8)	104 (34.6)
	Asian	11 (2.7)	4 (1.3)
	Black or African American	18 (4.4)	10 (3.3)
	Hispanic	25 (6.1)	27 (9.0)
	Mixed	60 (14.6)	53 (17.6)
	Other	11 (2.7)	2 (0.7)
	Unknown	110 (26.8)	101 (33.6)
Insurance†, n(%)	Medicare	177 (43.1)	124 (41.2)
	Medicaid	11 (2.7)	4 (1.3)
	Commercial‡	290 (70.6)	232 (77.1)
	Unknown	0 (0.0)	1 (0.3)
State, n(%)	Florida	242 (58.9)	195 (64.8)
	Ohio	77 (18.7)	40 (13.3)
	Virginia	29 (7.1)	20 (6.6)
	Other	63 (15.3)	46 (15.3)
Cardiometabolic conditions, n(%)	Metabolic syndrome	19 (4.6)	10 (3.3)
	Hypertension	333 (81.0)	216 (71.8)
	Dyslipidemia	99 (24.1)	68 (22.6)
	Obesity	316 (76.9)	191 (63.5)
	≥2 cardiometabolic conditions‡	290 (70.6)	173 (57.5)

Abbreviations: IQR, Interquartile range; SD, standard deviation; T2DM, type 2 diabetes mellitus
*Follow-up data were defined using the most recent available post-index measurement across all encounters; † Insurance categories are not mutually exclusive, patients may have had multiple coverage types during the study period (e.g., dual eligibility or plan switching); ‡Includes employer-sponsored and individually purchased private insurance plans; ‡Cardiometabolic conditions include metabolic syndrome, dyslipidemia, hypertension, and/or obesity (excluding T2DM).

Follow-up data distributions

- The mean time from index to the most recent available follow-up measurement across all encounters was longer among patients with T2DM than among those without T2DM (9.5 vs. 8.5 months; **TABLE 1**).

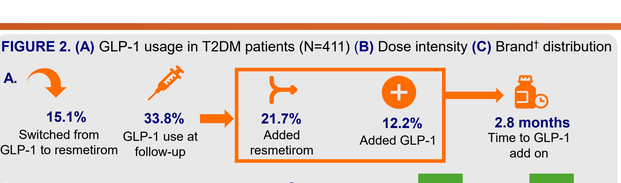
GLP-1 use from baseline to follow-up

- Among the 411 patients with T2DM, 151 (36.7%) were receiving a GLP-1 at baseline and 139 (33.8%) during follow-up. All patients with GLP-1 use at baseline (151/151) and/or follow-up (139/139) had T2DM. By resmetirom initiation (index), 62/411 (15.1%) patients with T2DM had discontinued baseline GLP-1 use and switched to resmetirom only, with no GLP-1 use during follow-up **(FIGURE 2A).**
- Among patients who initiated a GLP-1 after index, the mean time to GLP-1 initiation was 2.8 months **(FIGURE 2A).** Of the 139 patients receiving a GLP-1 during follow-up, 33 (23.7%) received a high-dose GLP-1 regimen* **(FIGURE 2B).** Ozempic (semaglutide) was the most commonly used GLP-1 at both time points, used by 69/151 patients (45.7%) at baseline and 60/139 (43.2%) at follow-up **(FIGURE 2C).**

Changes in BMI and body weight by T2DM status

- Patients with T2DM experienced greater reductions in BMI and body weight over follow-up than those without T2DM (-0.8 vs -0.5 kg/m² and -2.5 vs -1.8 kg, respectively; **TABLE 2**).

FIGURE 2. (A) GLP-1 usage in T2DM patients (N=411) **(B)** Dose intensity **(C)** Brand† distribution



Notes: The denominator for Figure 2A is n=411 (T2DM group); **Abbreviations:** N/A, not available; *High-dose GLP-1 cutoffs vary by drug: Mounjaro/Zepbound (≥12.5 mg); Saxenda/Trulicity (≥3 mg); Wegovy (≥2.4 mg); Ozempic (≥2 mg); Victoza (≥1.8 mg); and Rybelsus (≥7 mg); †Brand categories are not mutually exclusive; patients may have received multiple GLP-1 prescriptions during the study period.

TABLE 2. Mean change in BMI and body weight by T2DM status

Outcome	With T2DM (n=411)					Without T2DM (n=301)				
	Time to FU assessment (months), mean (SD)	n*	BL value	FU value	Mean change (SD)	Time to FU assessment (months), mean (SD)	n*	BL value	FU value	Mean change (SD)
BMI (kg/m²)	7.4 (3.7)	306	34.6	33.8	**-0.8 (3.0)**	7.2 (3.8)	197	32.8	32.3	**-0.5 (2.7)**
Weight (kg)	7.4 (3.7)	307	97.6	95	**-2.5 (10.2)**	7.2 (3.8)	197	94.9	92.6	**-1.8 (6.8)**

Abbreviations: BMI, body mass index; BL, baseline; FU, follow up; GLP-1, glucagon-like peptide-1; SD, standard deviation; T2DM, type 2 diabetes mellitus. **Notes:** Bolded values indicate p<0.05. *sample sizes (n) reported reflect patients with baseline and follow up measurements of each corresponding assessment.

Mean changes in biomarkers from baseline to follow-up by T2DM status

- Based on mean change from baseline to follow-up, individuals without T2DM showed numerically greater reductions in ALT (-14.0 vs -13.7), AST (-9.0 vs -8.3), cholesterol (-25.5 vs +5.4), CAP (-59.9 vs -54.3), and FAST score (-0.3 vs -0.2) than those with T2DM.
- Individuals with T2DM had greater improvement in HDL (+5.3 vs -2.0) and larger reductions in VCTE LSM (-2.4 vs -1.8 kPa) and LDL (-14.5 vs -10.9; **TABLE 3**) than those without T2DM.

TABLE 3. Mean change in biomarkers and time follow up test stratified by T2DM status

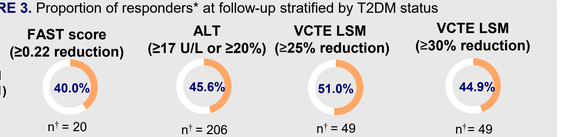
Biomarker (unit)	With T2DM (n=411)					Without T2DM (n=301)				
	Time to FU test months, mean (SD)	n*	BL value	FU value	Mean change (SD)	Time to FU test months, mean (SD)	n*	BL value	FU value	Mean change (SD)
LDL (mg/dL)	9.6 (4.6)	10	78.8	64.3	-14.5 (48.5)	8.7 (3.3)	9	116.7	105.8	-10.9 (34.1)
HDL (mg/dL)	9.9 (5.2)	12	38.7	43.9	5.3 (8.5)	8.7 (3.3)	9	40.7	38.7	-2.0 (6.2)
Cholesterol (mg/dL)	10.2 (6.3)	9	138.9	144.3	5.4 (35.8)	8.2 (2.1)	6	200.0	174.5	**-25.5 (35.8)**
ALT (U/L)	9.1 (4.5)	206	54.7	41.0	**-13.7 (36.6)**	8.8 (4.7)	124	53.8	39.8	**-14.0 (37.4)**
AST (U/L)	9.1 (4.5)	199	43.3	35.0	**-8.3 (31)**	8.8 (4.6)	123	43.9	34.9	**-9.0 (38.1)**
kPa†	10.3 (4.3)	49	11.5	9.1	**-2.4 (4.8)**	9.7 (3.2)	21	10.9	9.0	-1.8 (4.2)
CAP (dB/m)	11 (4.2)	31	334.4	280.1	**-54.3 (75.6)**	10.5 (3.8)	14	315.9	256.1	**-59.9 (61.7)**
FAST‡	NA	20	0.4	0.2	**-0.2 (0.2)**	NA	8	0.6	0.3	**-0.3 (0.2)**

Abbreviations: BL, baseline; FU, follow up; NA, not available; SD, standard deviation; T2DM, type 2 diabetes mellitus. **Notes:** Bolded values indicate p<0.05. *sample sizes (n) reported reflect patients with BL and FU measurements of each corresponding biomarker; †kPa values derived from vibration-controlled transient elastography; ‡FAST scores are derived from multiple biomarker measurements that may occur at different FU intervals.

Responder rates at follow-up by T2DM status

- At follow-up, patients without T2DM had higher response rates for FAST (62.5% vs. 40%) and ALT (48.4% vs. 45.6%) compared to those with T2DM.
- Patients with T2DM demonstrated higher VCTE response rates, both for ≥25% reduction (51.0% vs. 42.9%) and ≥30% reduction (44.9% vs. 33.3%; **FIGURE 3**).

FIGURE 3. Proportion of responders* at follow-up stratified by T2DM status



***Responder definitions:** ALT ≥17-unit reduction or ≥20% reduction from baseline[6]; FAST score ≥0.22-point reduction from baseline[7]; VCTE (FibroScan) LSM (kPa), ≥30% reduction from baseline[8]; VCTE (FibroScan) LSM (kPa), ≥25% reduction from baseline[8].*
Note: †sample sizes (n) reported reflect patients with baseline and follow up measurements of each corresponding biomarker.

DISCUSSION

- T2DM was common in this resmetirom-treated cohort, with 411/712 patients (57.7%) affected at baseline. Patients with T2DM had a higher prevalence of obesity and a greater burden of multiple metabolic comorbidities at treatment initiation, indicating a more metabolically complex population.
- GLP-1 use was observed only among patients with T2DM, and concomitant use during follow-up was seen in approximately one-fifth of the overall cohort.
- Patients with and without T2DM showed broadly similar favorable changes across several liver-related biomarkers and clinical measures.
- Nearly one half of patients met predefined responder thresholds in less than 10 months, suggesting early improvement following resmetirom initiation in both subgroups.
- Limitations include missing outcome data for laboratory and imaging measures, small sample sizes among patients with both baseline and follow-up biomarker measurements, variability in coding, potential care received outside the database network, inability to confirm medication adherence, short follow-up time, and limited generalizability given data were derived from a single healthcare system.

CONCLUSION

These early descriptive findings suggest improvements in liver biomarkers and non-invasive clinical measures among resmetirom-treated patients regardless of T2DM status, though the pattern and magnitude of response differed by subgroup. Larger studies with longer follow-up are needed to confirm these results.

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ABBREVIATIONS:
AE: Adverse event; AI: artificial intelligence; ALT: alanine aminotransferase. AST: aspartate aminotransferase; BMI: body mass index; CAP: controlled attenuation parameter; EMR: electronic medical record; FAST: FibroScan-AST score; FIB-4: Fibrosis-4 index; GLP-1: glucagon-like peptide-1; HDL: high-density lipoprotein; LDL: low-density lipoprotein; MASH: metabolic dysfunction-associated steatohepatitis; SD: standard deviation; US: United States; VCTE LSM: vibration-controlled transient elastography liver stiffness measurement.

REFERENCES
1. Chan WK, et al. 2023. *J of Obesity & Met Synd.* 32(3):197-213. **2.** Rinella ME, et al. 2023. *Hep.* 78(6):1966-1986. **3.** U.S. Food and Drug Administration. 2024. https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-patients-liver-scarring-due-fatty-liver-disease. **4.** Harrison SA, et al. 2024. *New Engl J of Med.* 390(6):497-509. **5.** Khalifa A, et al. 2023. *Digestive Diseases and Sciences.* Jun;68(6):2360–2369. **6.**Noureddin M et al. *Clin Gastroenterol Hepatol* 2024;22:2367–2377e;7. Wong VW-S et al. *eClinicalMedicine* 2023;66:102310; **8**. Lin H et al. *JAMA* 2024;331:1287–1297