Early real-world effectiveness of resmetirom in adults with metabolic dysfunction associated steatohepatitis and moderate-to-advanced fibrosis

POSTER #FRI-141

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INTRODUCTION

- Metabolic dysfunction-associated steatohepatitis (MASH) is a form of fatty liver disease that develops due to one or more metabolic disorders,[1,2] often leading to prolonged inflammation and liver fibrosis that can progress to cirrhosis.[3]
- Resmetirom (Rezdiffra™), an oral thyroid hormone receptor β-selective agonist, received accelerated approval from the United States (US) Food and Drug Administration in March 2024 for the treatment of moderate to advanced fibrosis among noncirrhotic patients with MASH.[4]
- The recent Phase III MAESTRO-NASH trial demonstrated that resmetirom was more effective than placebo in achieving MASH resolution and improving liver fibrosis.[5]
- However, the real-world prescribing practices and clinical effectiveness of resmetirom remain unclear.

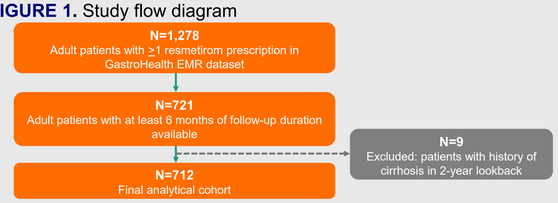
AIMS

This study descriptively assessed early real-world effectiveness of resmetirom in a US gastroenterology practice, focusing on changes in blood biomarkers and clinical measures.

METHODS

- **Study design & data source:** Single arm, retrospective cohort study using the Latica real-world data repository, which compiles de-identified electronic medical records (EMR) data from Gastro Health.
- **Population:** Eligible patients were adults with ≥1 resmetirom prescription 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.[6]
- 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, comorbidities, medication use.
  - **Laboratory measures:** LDL, HDL, cholesterol, ALT, AST, kPa (from Vibration-Controlled Transient Elastography), CAP, and FAST at baseline and follow-up, when available.
    - Proportion of patients achieving threshold responses for ALT, FAST, and VCTE, as defined by literature [7,8,9]
  - **Cardiometabolic risk factors:** metabolic syndrome, hypertension, dyslipidemia, obesity, type 2 diabetes mellitus.
  - **Safety profile:** treatment related adverse events.

FIGURE 1. Study flow diagram



RESULTS

- Of the 1,278 who initiated resmetirom, 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**).
- The mean age was 59.0 years (SD: 12.9) (**TABLE 1**).

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

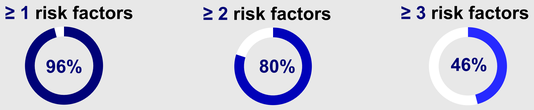
Characteristic		Estimate
Mean age at index in years (SD)		59.0 (12.9)
Female, n(%)		406 (57.0%)
Follow-up data (months)*	Mean (SD)	9.1 (5.6)
	Median [IQR]	9.0 [5.3, 12.3]
Race/ethnicity, n(%)	White	280 (39.3%)
	Mixed	113 (15.9%)
	Hispanic	52 (7.3%)
	Asian	15 (2.1%)
	Black or African American	28 (3.9%)
	Other	13 (1.8%)
	Unknown	211 (29.6%)
Insurance coverage†, n(%)	Medicare	301 (42.3%)
	Medicaid	15 (2.1%)
	Commercial††	522 (73.3%)
	Other/Unknown	1 (0.1%)
State, n(%)	Florida	437 (61.4%)
	Ohio	117 (16.4%)
	Virginia	49 (6.9)%
	Other	109 (15.3%)
Body mass index category, n(%)	≥30	495 (69.5%)
	25 to <30	170 (23.9%)
	<25	43 (6.0%)
	Unknown	4 (0.6%)

Abbreviations: IQR, Interquartile range; SD, standard deviation
Notes: *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

Comorbidity profile

- ~80% of the cohort had ≥2 cardiometabolic risk factors, while ~46% had ≥3 cardiometabolic risk factors, including hypertension (77%), obesity (71%), type 2 diabetes mellitus (58%), dyslipidemia (24%), and metabolic syndrome (4%) (**FIGURE 2**).

FIGURE 2. Burden of cardiometabolic risk factors among patients treated with resmetirom (n=712)‡



‡Cardiometabolic conditions include metabolic syndrome, dyslipidemia, hypertension, obesity, and/or T2DM.

Follow-up data distributions

- The mean time from index to most recent follow up test was 9.1 months (**TABLE 1**).
- Time to follow-up test varied depending on the type of biomarker (**TABLE 2**).

Biomarker responses at follow-up

- At follow-up (mean 9.1 months), most biomarkers improved with notable reductions in LDL (-12.8 mg/dL), cholesterol (-6.9 mg/dL), liver enzymes (ALT -13.8 U/L, AST -8.6 U/L), kPa (-2.2), CAP (-56.0 dB/m), and FAST scores (-0.2), suggesting overall metabolic and hepatic improvement.
- HDL levels in this group showed modest improvements over follow up (+2.1 mg/dL), indicating a favorable shift in lipid profile
- Similarly, BMI and body weight decreased over follow up (-0.68 and -2.3 kgs, respectively) (**TABLE 2**).

TABLE 2. Mean change in biomarkers at follow-up

Biomarker (unit)	Time to FU test (months), mean (SD)	n*	BL value	FU value	Mean change (SD)
LDL (mg/dL)	9.1 (3.9)	19	96.7	83.9	-12.8 (41.2)
HDL (mg/dL)	9.4 (4.5)	21	39.5	41.7	2.1 (8.3)
Cholesterol (mg/dL)	9.4 (5)	15	163.3	156.4	-6.9 (37.9)
ALT (U/L)	9.0 (4.6)	330	54.4	40.6	**-13.8 (36.8)**
AST (U/L)	9.0 (4.5)	322	43.5	35.0	**-8.6 (33.8)**
kPa†	10.2 (4)	70	11.3	9.1	**-2.2 (4.6)**
CAP (dB/m)	10.8 (4)	45	328.6	272.6	**-56.0 (70.9)**
FAST‡	NA	28	0.5	0.2	**-0.2 (0.2)**
BMI	7.4 (3.7)	503	33.8	33.2	**-0.68 (2.9)**
Body weight (kg)	7.4 (3.7)	504	96.2	93.9	**-2.3 (9.0)**

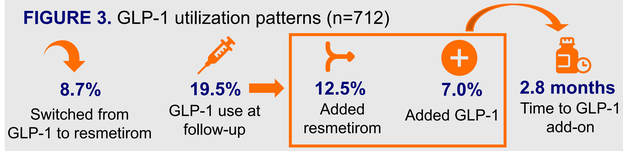
Abbreviations: BL, baseline; FU, follow up; SD, standard deviation; NA, not applicable. **Notes:** Bolded values indicate p<0.05. *sample sizes (n) reported reflect patients with BL and FU measurements of each corresponding biomarker; †kPa values derived from vibration-controlled transient elastography;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

GLP-1 treatment patterns at baseline and follow-up

- At baseline, 62/712 (8.7%) patients had switched to resmetirom by the index date and were no longer using GLP-1s during follow-up **(FIGURE 3).**
- During follow up, 139 (19.5%) patients used GLP-1s:
  - 89/712 (12.5%) patients continued using GLP-1s from baseline through follow-up.
  - 50/712 (7.0%) patients initiated GLP-1 use over the follow-up period, after starting resmetirom.
    - Mean time to GLP-1 add-on was 2.8 months from index
  - Of the patients receiving GLP-1s over follow-up, 33/139 (23.7%) received a high dose GLP-1.*

*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).

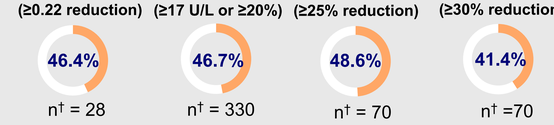
FIGURE 3. GLP-1 utilization patterns (n=712)



Responder rates at follow-up

- At follow-up (mean 9.1 months), response rates ranged between 41-49% across responder endpoints (**FIGURE 4**).

FIGURE 4. Proportion of responders* at follow up among resmetirom-treated patients

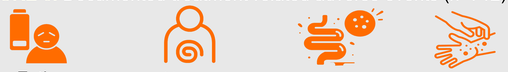


***Responder definitions:** ALT ≥17-unit reduction or ≥20% reduction from baseline[7]; FAST score ≥0.22-point reduction from baseline[8]; VCTE (FibroScan) LSM (kPa), ≥30% reduction from baseline[9]; VCTE (FibroScan) LSM (kPa), ≥25% reduction from baseline[9]
Note: †sample sizes (n) reported reflect patients with baseline and follow up measurements of each corresponding biomarker

Treatment-related adverse events

- Resmetirom was well tolerated, with very few treatment-related adverse events (AEs) reported (**FIGURE 5**). Discontinuation due to these treatment-related AEs was very rare (<1%).

FIGURE 5. Documented treatment-related adverse events (n=712)*



*Categories are not mutually exclusive; patients may have reported more than one adverse event.

DISCUSSION

- In this real-world descriptive analysis, resmetirom use was associated with clinically meaningful improvements in laboratory and non-invasive clinical measures over follow up. With a mean follow-up of approximately 9 months, about 41–49% of patients met predefined responder thresholds across endpoints suggesting early effectiveness consistent with findings from the 52-week MAESTRO-NASH trial.
- Concomitant use of GLP-1s during follow-up was observed in approximately one-fifth of the overall cohort, likely reflecting management of overlapping cardiometabolic conditions. Cardiometabolic risk factors were highly prevalent, underscoring the high-risk profile of this population.
- Treatment was well tolerated, with very few treatment-related adverse events reported.
- Limitations include missing outcome data for laboratory and imaging measures, variability in coding, potential care received outside the database network, and limited generalizability given data were derived from a single healthcare system.

CONCLUSION

These early descriptive findings demonstrate improvements in liver biomarkers and non-invasive clinical measures among resmetirom users; 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.

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