AASLD The Liver Meeting® 2026

A 12-MONTH REAL-WORLD ASSESSMENT OF CLINICAL CHARACTERISTICS AND BIOMARKER CHANGES FOLLOWING RESMETIROM INITIATION IN PATIENTS WITH MASH: A DESCRIPTIVE COHORT STUDY USING ELECTRONIC MEDICAL RECORDS IN THE UNITED STATES

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

INTRODUCTION

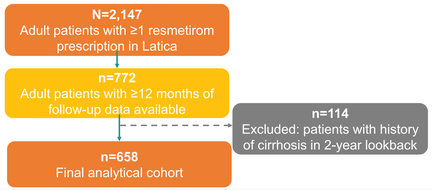
- Metabolic dysfunction-associated steatohepatitis (MASH) is a form of fatty liver disease that develops due to one or more metabolic disorders,[1,2] often leading to prolonged inflammation and liver fibrosis that can progress to cirrhosis.[3]
- Resmetirom (Rezdiffra™), an oral thyroid hormone receptor 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.

This study aimed to descriptively assess real-world clinical characteristics and early changes in liver and metabolic biomarkers after at least 12 months of follow-up following resmetirom initiation.

METHODS

- **Study design & data source:** Single arm, retrospective cohort study using the Latica real-world data repository, which compiles de-identified electronic medical record data from Gastro Health. Gastro Health includes more than 403 affiliated physicians operating across 152 clinical locations in 7 US states.
- **Population:** Eligible patients were adults with ≥1 resmetirom prescription between April 2024 and April 2025, with a minimum of one encounter ≥12 months since their index date (first prescription). Patients with a documented history of compensated or decompensated cirrhosis within the 2-year lookback period before resmetirom initiation were excluded using validated algorithm of diagnostic codes by Khalifa *et al.*[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 and medication history were assessed.
- The **follow-up period** was defined as the time from resmetirom initiation through at least 12 months post-initiation.
- **Outcomes:**
  - **Baseline characteristics:** demographics, BMI, cardiometabolic risk factors (hypertension, dyslipidemia, obesity, T2DM, metabolic syndrome).
  - **Laboratory measures**: ALT, AST, FIB-4, BMI, weight, kPa (VCTE), CAP, and FAST at baseline and follow-up.
  - **Responder thresholds:** Proportion of patients achieving threshold responses for FAST, ALT, CAP and VCTE LSM, as defined by literature.[7-11]
  - **Concomitant medication use**: Pioglitazone, SGLT2i, statins, GLP-1 use at follow-up.

FIGURE 1. Study flow diagram



RESULTS

Baseline characteristics

- Of 2,147 patients who initiated resmetirom, 772 (36%) had ≥12 months of follow-up data available. After excluding those with coding related to cirrhosis in the 2 years prior to resmetirom initiation (n=114, 5.3%), 658 patients comprised the final analytic cohort (**Figure 1**).
- Patients were a mean (standard deviation [SD]) age of 58.6 (12.9) years and were primarily female (56.4%, **Table 1**).
- The mean time from index to most recent follow-up encounter was 14 months (SD: 7 months).

TABLE 1. Baseline characteristics of cohort (n=658)

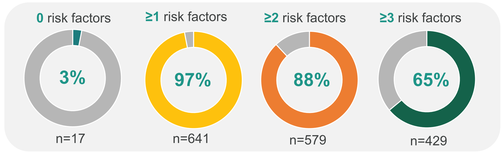
Characteristic		Estimate
		Mean (SD)
Age at index in years		58.6 (12.9)
Follow-up data in months*		14.0 (7.0)
Weighted Elixhauser Comorbidity Index		8.8 (4.6)
		n (%)
Female		371 (56.4)
Race/ethnicity	White	246 (37.4)
	Mixed	109 (16.6)
	Hispanic	49 (7.4)
	Black	28 (4.3)
	Asian	13 (2.0)
	Other	11 (1.7)
	Unknown	202 (30.7)
Insurance coverage†	Medicare	178 (27.1)
	Medicaid	13 (2.0)
	Commercial‡	466 (70.8)
	Other/Unknown	1 (0.2)
State	Florida	405 (61.6)
	Ohio	101 (15.3)
	Virginia	52 (7.9)
	Alabama	35 (5.3)
	Other	65 (9.9)
Body mass index (BMI) category	≥30 kg/m^2	450 (68.4)
	≥25 to <30 kg/m^2	167 (25.4)
	<25 kg/m^2	36 (5.5)
	Unknown	5 (0.8)
Cardiometabolic risk factors§	Hypertension	501 (76.1)
	Dyslipidemia	465 (70.7)
	Obesity	462 (70.2)
	T2DM	402 (61.1)

Notes: *Follow-up data were defined using the most recent available measurement after 12-months post-index 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. §Categories are not mutually exclusive.

Cardiometabolic risk factors

- Among the entire cohort (n=658), 97% had ≥1 cardiometabolic risk factor, followed by 88% with ≥2 and 65% with ≥3 risk factors (**Figure 2**).

FIGURE 2. Cardiometabolic risk factors* (n=658)



Notes: *Cardiometabolic risk factors include metabolic syndrome, hypertension, dyslipidemia, obesity, and T2DM. Denominator is the total cohort (n=658).

Changes in biomarkers from baseline to follow-up

- Among patients with both baseline and follow-up values, statistically significant mean reductions (p-value <0.05) were observed for ALT, AST, FIB-4, BMI, body weight, kPa (VCTE), CAP, and FAST score.

TABLE 2. Mean and median changes in biomarkers from baseline to follow-up

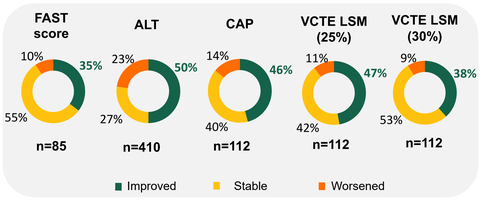
Biomarker (unit)	Time to FU in months, mean (SD)	n	Mean BL value (SD)	Mean FU value (SD)	Mean difference (SD)	Median difference (Q1, Q3)
ALT (U/L)	11.9 (5.4)	410	57.6 (49.8)	40.3 (29.4)	**-17.3 (46.3)**	**-6.5 (-28.0, 4.8)**
AST (U/L)	11.9 (5.5)	409	44.7 (36.2)	34.4 (25.9)	**-10.2 (37.9)**	**-4.0 (-18.0, 4.0)**
FIB-4*	11.9 (5.3)	290	1.7 (1.1)	1.6 (1.1)	**-0.1 (0.8)**	**-0.1 (-0.4, 0.2)**
BMI (kg/m^2)	11.8 (5.1)	525	33.9 (6.6)	32.9 (6.5)	**-1.0 (2.8)**	**-0.6 (-2.0, 0.4)**
Weight (kg)	11.8 (5.1)	526	96.2 (22.0)	93.4 (21.6)	**-2.7 (8.6)**	**-1.8 (-5.4, 1.2)**
kPa (VCTE)	13.3 (4.4)	112	10.0 (2.6)	8.8 (7.1)	**-1.2 (7.6)**	**-2.2 (-3.8, -0.2)**
CAP (dB/m)	13.3 (4.4)	112	321.0 (51.6)	285.2 (62.1)	**-35.8 (77.0)**	**-30.0 (-79.8, 20.5)**
FAST score†	13.6 (3.8)	85	0.4 (0.2)	0.3 (0.2)	**-0.1 (0.2)**	**-0.1 (-0.3, 0.0)**

Notes: Sample sizes (n) reported reflect patients with baseline and follow-up measurements of each corresponding biomarker; biomarkers with n=<5% of total cohort are not presented; p-values were determined by paired Wilcoxon signed-rank test to circumvent potential issues with small sample sizes and high variability in the data; **bolded values indicate p<0.05**; *In cases where FIB-4 was manually calculated, time to follow-up was determined by averaging the test dates for ALT, AST, and platelets to create a FIB-4 proxy test date. †FAST score proxy test dates were determined by averaging the test dates for kPa, CAP, and AST.

Responder thresholds

- At follow-up, rates of improvement ranged between 35%-50% across responder endpoints for FAST, ALT, CAP, VCTE LSM as defined by the literature (**Figure 3**).[7-10]
- Among those with both baseline and follow-up CAP values, 46% (51/112) saw reductions of >40 dB/m[10] (**Figure 3**).
- At follow-up, 12% (61/525) and 11% (60/526) of patients saw reductions (≥10%)[11] in BMI and weight, respectively.

FIGURE 3. Responder thresholds for FAST, ALT, CAP, VCTE LSM

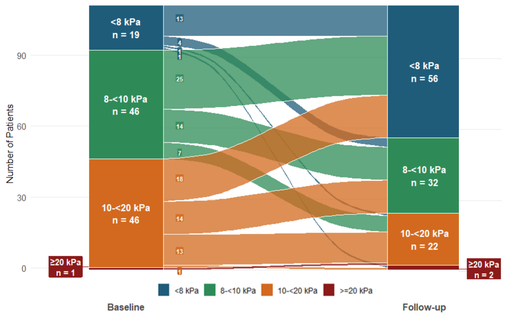


Definitions: Improvement thresholds were defined as ALT ≥17-unit reduction or ≥20% reduction from baseline[7]; FAST score ≥0.22-point reduction from baseline[8]; VCTE (FibroScan) LSM (kPa), ≥30% reduction from baseline[8]; VCTE (FibroScan) LSM (kPa), ≥25% reduction from baseline[9]; CAP >40 dB/m reduction from baseline[10]; Worsened was defined as the inverse of the corresponding improvement threshold, while stable was defined as any change between the improvement and worsened thresholds.
Notes: Sample sizes (n) reported reflect patients with baseline and follow-up measurements for each corresponding biomarker (i.e., denominator for each response).

Changes in kPa from baseline to follow-up

- Overall, the distribution of patients with a baseline and follow-up kPa measure (n=112) shifted towards a lower VCTE LSM category at follow-up (**Figure 4**).
- Most notably, 70% (32/46) who started in the 10-<20 kPa category moved to a category below 10 kPa at follow-up.
- At follow-up, approximately 52% (58/112) moved to a lower kPa category, 36% (40/112) remained in the same category, and 12% (14/112) moved to a higher category.

FIGURE 4. Changes in kPa over time – all patients with kPa results at baseline and follow-up (n=112)



Concomitant medication use during follow-up

TABLE 3. Concomitant medication use and dosage strength during follow-up

Medication	Follow-up n (%)
Pioglitazone*	**10 (1.5)**
SGLT2i*	**61 (9.3)**
Statins†	**335 (50.9)**
Low intensity‡	22 (6.6)
Moderate intensity‡	179 (53.4)
High intensity‡	110 (32.8)
Unknown‡	24 (7.2)
GLP-1s†	**235 (35.7)**
Low intensity‡	105 (44.7)
High intensity‡	48 (20.4)
Unknown‡	19 (8.1)

- Statin use was observed in 51% (335/658) of patients on resmetirom during follow-up. Among statin users (n=335), moderate intensity dose statins were most common (53%,179/335) followed by high intensity dose statins (33%,110/335).
- GLP-1 use was observed in 36% (235/658) of patients on resmetirom during follow-up. Among GLP-1 users (n=235), 20.4% were on high intensity dose GLP-1s (48/235).
- At follow-up, pioglitazone and SGLT2i use was very low at <2% and <10%, respectively.

Notes: *Pioglitazone and SGLT2i doses were not reported. †For GLP-1s and statins, dose category reflects the highest dose recorded during baseline or follow-up and is based on the minimum and maximum recommended doses in each medication's product monograph. High intensity dose GLP-1 cutoffs: Mounjaro ≥12.5 mg; Ozempic ≥2 mg; Rybelsus ≥7 mg; Saxenda ≥3 mg; Trulicity ≥3 mg; Victoza ≥1.8 mg; Wegovy ≥2.4 mg; Zepbound ≥12.5 mg. No high-dose cutoff was specified for Bydureon. ‡For statin and GLP-1 use, n (%) denominators are the total users at baseline and follow-up, respectively; for overall medication use, the denominator is the total cohort (N=658). Concomitant medication use was defined as any post-index use.

Treatment-related adverse events

- Adverse events were infrequently reported among patients on resmetirom (**Figure 5**), with 10.6% (n=70) of patients experiencing ≥1 adverse event.
- The most frequently reported events were diarrhea (7.3%), nausea (4.0%).

FIGURE 5. Prevalence of most common treatment-related adverse events reported among resmetirom patients



Notes: Categories are not mutually exclusive (i.e., patients could have reported more than one adverse event). Denominator is the total cohort (n=658).

Limitations include missing outcome data for laboratory and imaging measures, variability in coding, potential care received outside the database network, inability to confirm treatment adherence, and limited generalizability given data were derived from a single healthcare system.

Key takeaways

- Resmetirom use was associated with clinically meaningful improvements in laboratory and non-invasive clinical measures over follow-up.
- Approximately 9 out of 10 patients remained stable or improved in VCTE LSM during follow-up.
- The proportion of patients with VCTE LSM >8.0 kPa decreased from 83% at baseline to 50% at follow-up, reflecting a shift toward lower liver stiffness.
- During follow-up, approximately one-third of patients used concomitant GLP-1s and one-half of patients used concomitant statins.
- Cardiometabolic risk factors were highly prevalent, underscoring the high-risk profile of this population.
- Treatment was generally well-tolerated, with very few treatment-related adverse events reported.

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ABBREVIATIONS
ALT, alanine aminotransferase; AST, aspartate aminotransferase; BL, baseline; BMI, body mass index; CAP, controlled attenuation parameter; FIB-4, fibrosis-4 index; FAST, FibroScan-AST score; FU, follow-up; GLP-1, glucagon-like peptide-1; LSM, liver stiffness measurement; SD, standard deviation; SGLT2i, sodium-glucose co-transporter 2 inhibitor; T2DM, type 2 diabetes mellitus; US, United States; VCTE, vibration-controlled transient elastography.

CONCLUSION

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 14 months, 70% who started in the 10 - <20 kPa category moved to a category below 10 kPa at follow-up and 35%–50% met predefined responder thresholds across endpoints, suggesting early effectiveness consistent with the 52-week results from the MAESTRO-NASH trial.[5] Larger studies with longer follow-up are needed to confirm these results.

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