AASLD The Liver Meeting®

# EVALUATING THE EARLY REAL-WORLD IMPACT OF RESMETIROM IN PATIENTS WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOHEPATITIS (MASH): A UNITED STATES COHORT STUDY USING ELECTRONIC MEDICAL RECORDS


Y. Kim[1], J. O'Donnell[1], R. Fakhraei[2], K. Johnston[2], R. Sun[2], M. Bather[2], Y. Silberberg[3], K. Keren[3], R. Mustafa[2], M. Charlton[1], R. Eisdorfer[3], S. Balter[3], R. Chadalavada[4], N. Alkhouri[5], P. Bekal[4]

1. Madrigal Pharmaceuticals, Inc., West Conshohocken, PA, USA
2. Broadstreet HEOR, Vancouver, BC, Canada
3. Latica, Palo Alto, CA, USA
4. Gastro Health, Cincinnati, OH, USA
5. Arizona Liver Health, Phoenix, AZ, USA


Madrigal Pharmaceuticals

## INTRODUCTION

- Metabolic dysfunction–associated steatohepatitis (MASH) is a progressive liver disease characterized by excess hepatic fat, inflammation, and ongoing tissue injury. [1]
- Over time, this process can drive fibrosis and cirrhosis, increasing the risk of liver failure and cardiovascular disease. [2,3]
- Resmetirom (Rezdiffra™), an oral thyroid hormone receptor-β selective agonist, was granted conditional FDA approval on March 14, 2024, supported by the results from the Phase 3 MAESTRO-NASH trial. The approval covers U.S. patients with noncirrhotic NASH and moderate to advanced fibrosis (stages F2/F3). [2]
- While pivotal trials established the efficacy of resmetirom, real-world data are needed to characterize patients receiving treatment in practice and to evaluate its effectiveness outside the controlled trial setting.

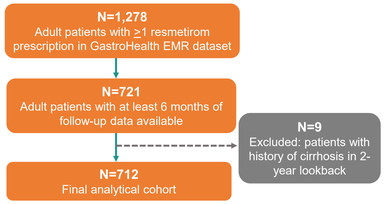
## AIM

This study aimed to characterize patients treated with resmetirom in routine gastroenterology practice and evaluate its 6-month real-world effectiveness, as measured by changes in blood-based biomarkers.

## METHODS

- **Study design & data source:** Single arm, retrospective cohort study using real-world data from the GastroHealth electronic medical records (EMR) system. Data were accessed via the Latica AI platform, which compiles de-identified EMR data from participating health systems.
- **Population:** Adults with ≥1 prescription for resmetirom between April 2024–Apr 2025 and ≥6 months of follow-up data available. Patients with a documented history of compensated or decompensated cirrhosis within the two years preceding resmetirom initiation were excluded, based on validated diagnostic codes as defined by Khalifa et al. [4].
- The **index date** was the first resmetirom prescription.
- **Baseline characteristics** were assessed in the 12 months prior to the index date.
- Outcomes:
  - **Clinical characteristics:** demographics, comorbidities, medication use.
  - **Laboratory measures:** AST, ALT, platelet count, FIB-4 (baseline and 6-month follow-up, when available).
  - **Cardiometabolic risk factors:** metabolic syndrome, hypertension, dyslipidemia, obesity, type 2 diabetes.
  - **Safety profiles:** Treatment-related adverse events documented in clinical notes, including, fatigue, arthralgia, diarrhea, nausea, pruritus, urinary tract infection (UTI), vomiting.

**Figure 1.** Study flow diagram




## RESULTS

- Of the 1,278 who initiated resmetirom, 721 (56.4%) had ≥6 months of follow-up data available. After excluding those with a history of cirrhosis in the 2 years before resmetirom initiation (n=9; 1.25%), 712 patients comprised the final analytic cohort (**Figure 1**). The mean age was 59.0 years (SD: 12.9) (**Table 1**)
- The median duration of pre-treatment data was 5.9 years (IQR: 1.3–11.7 years).

**Table 1.** Baseline characteristics of cohort (n=712)

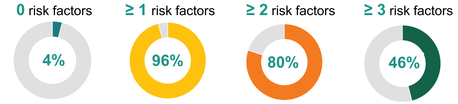
| Characteristic | n(%) or mean ± SD |
|---|---|
| ***Age at index (years)*** | 59.0 ± 12.9 |
| 18-44 | 107 (15.0%) |
| 45-64 | 340 (47.8%) |
| ≥65 | 265 (37.2%) |
| ***Sex*** | |
| Female | 406 (57.0%) |
| Male | 306 (43.0%) |
| ***Race/ethnicity*** | |
| White | 280 (39.3%) |
| Multiple | 113 (15.9%) |
| 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**** | |
| Medicare | 301 (42.3%) |
| Medicaid | 15 (2.1%) |
| Any commercial insurance† | 712 (100.0%) |
| ***State*** | |
| Florida | 436 (61.2%) |
| Ohio | 117 (16.4%) |
| Alabama | 41 (5.8%) |
| Other | 118 (16.6%) |
| ***Body mass index*** | |
| ≥30 | 495 (69.5%) |
| 25 to <30 | 170 (23.9%) |
| <25 | 43 (6.0%) |
| Unknown | 4 (0.6%) |
| ***Cardiovascular disease*** | 28 (4.0%) |
| ***Weighted Elixhauser Comorbidity Index*** | 8.9 ± 4.6 |
| ***Cardiometabolic risk factors**** | |
| Metabolic syndrome | 29 (4.1%) |
| Hypertension | 549 (77.1%) |
| Dyslipidemia | 167 (23.5%) |
| Obesity | 507 (71.2%) |
| Type 2 diabetes mellitus (T2DM) | 411 (57.7%) |

Abbreviations: SD, standard deviation *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. Additional detail by coverage entity available.

### Comorbidity profile

- The mean weighted Elixhauser Comorbidity Index score was 8.9 (SD: 4.6).
- Around 96% of the cohort had one or more cardiometabolic risk factors (**Figure 2**), which included hypertension (77%), obesity (71%), dyslipidemia (24%), type 2 diabetes mellitus (58%) and metabolic syndrome (4%).
- Cardiovascular disease (CVD) was uncommon, with 28 patients (4.0%) having a prior CVD diagnosis at baseline (**Table 1**).
- Changes in ALT and AST varied by the number of comorbidities, with a general trend of better improvement in these measures, in individuals with fewer comorbidities.

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




* Metabolic syndrome, hypertension, dyslipidemia, T2DM, and obesity

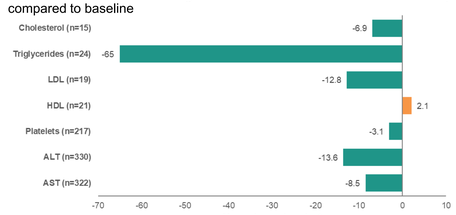
### Concomitant medication use

- **Statins:** Statin use was observed in 32.6% (232/712) of patients on resmetirom during follow-up, while 67.4% (480/712) had no evidence of statin use. Among statin users (n=232), moderate-intensity statins were most common (59.5%, 138/232).
  - During follow-up, both statin users and non-users demonstrated improvements in ALT and AST.
  - Similar trends were observed in both cohorts for LDL and total cholesterol, although the number of patients with follow-up data for these measures was limited.
- **GLP-1RAs:** During follow-up, 19.5% (139/712) of patients received a GLP-1RA concurrently with resmetirom, while the remaining 80.5% (573/712) had no evidence of GLP-1RA use.
  - Among patients with GLP-1RA use during follow-up (n=139), semaglutide was the most commonly prescribed agent (49.6%, 69/139).

### Biomarker responses at 6-month follow-up

- At 6 months, patients showed improvements in key blood biomarkers. Mean AST decreased by 8.5 U/L and ALT decreased by 13.6 U/L, indicating reductions in liver injury markers. LDL-C declined by 12.8 mg/dL, suggesting additional cardiometabolic benefit (**Figure 3**).

**Figure 3.** Mean absolute changes in blood biomarkers at 6 months follow-up compared to baseline




Abbreviations: LDL, low-density lipoprotein; HDL, high-density lipoprotein; ALT, alanine aminotransferase; AST, aspartate aminotransferase. *Cholesterol, triglycerides, HDL, and LDL were measured in mg/dL. Platelets were measured in x10^9/L (billion per liter). ALT and AST were measured in U/L. Analyses were limited to patients with available measurements at both baseline and 6-month follow-up; sample sizes varied by biomarker (cholesterol n=15, triglycerides n=24, LDL n=19, HDL n=21, platelets n=217, ALT n=330, AST n=322). Mean changes are absolute.

### Trends in non-invasive fibrosis scores

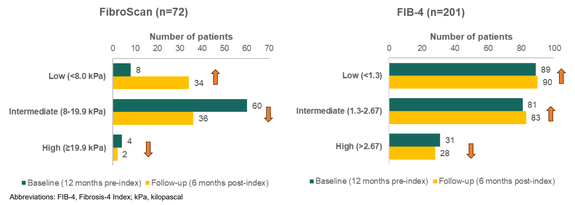
- At 6-month follow-up, mean Fibroscan liver stiffness among patients with paired data declined from 13.0 to 9.0 kPa (Δ –4.0 kPa). The proportion of patients classified as low risk (<8.0 kPa) increased from 8/72 (11.1%) at baseline to 34/72 (47.2%) at follow-up. Those with intermediate fibrosis (8–19.9 kPa) decreased from 60/72 (83.3%) to 36/72 (50.0%), while those in the high-risk group (≥19.9 kPa) declined from 4/72 (5.6%) to 2/72 (2.8%), with median stiffness values decreasing by more than half (**Table 2** and **Figure 4**).
- A ≥25% reduction in FibroScan liver stiffness was observed in 36 of 72 patients (50.0%).
- Similarly, FIB-4 scores decreased (2.3 to 1.9; –0.4). The proportion of patients in the low and intermediate fibrosis risk categories increased (+1 and +2, respectively), while the number of patients classified as high risk declined by 3 (**Table 2** and **Figure 4**).

**Table 2.** Changes in non-invasive fibrosis scores from baseline to 6-month follow-up among patients with available data at both timepoints

| Measure | Baseline (12 months pre-index) | Follow-up (6 months post-index) | Change* |
|---|---|---|---|
| **Overall NIT results** | | | |
| **FibroScan** | | | |
| ***Liver stiffness (n=72)*** | | | |
| Mean kPa (SD) | 13.0 (10.8) | 9.0 (4.1) | -4.0 (11.6) |
| Median kPa (IQR) | 10.4 (8.9, 13.0) | 8.2 (6.1, 11.0) | -2.65 (-4.7, -0.1) |
| ≥ 25% reduction, n (%) | - | - | 36 (50.0%) |
| ***CAP (n=45)*** | | | |
| Mean (SD) | 328.6 (43.5) | 286.0 (95.0) | -42.7 (91.0) |
| Median (IQR) | 330.0 (311.0, 356.0) | 285.0 (235.0, 322.0) | -45.0 (-79.0, -12.0) |
| **FIB-4 (n=201)** | | | |
| Mean (SD) | 2.3 (6.3) | 1.9 (3.1) | -0.4 (6.9) |
| **FibroScan scores by risk category (n=72)†** | | | |
| ***Low (<8.0 kPa), n(%)*** | **8 (11.1%)** | **34 (47.2%)** | +26 |
| Mean (SD) | 7.0 (1.4) | 6.0 (1.4) | -1.0 |
| Median (IQR) | 7.7 (6.9, 7.9) | 6.1 (4.8, 7.2) | -1.6 |
| ***Intermediate (8–19.9 kPa), n(%)*** | **60 (83.3%)** | **36 (50.0%)** | -24 |
| Mean (SD) | 11.5 (2.9) | 11.0 (2.5) | -0.5 |
| Median (IQR) | 10.6 (9.1, 12.9) | 10.7 (8.7, 12.5) | +0.1 |
| ***High (≥19.9 kPa), n(%)*** | **4 (5.5%)** | **2 (2.8%)** | -2 |
| Mean (SD) | 48.0 (28.9) | 24.1 (1.5) | -23.9 |
| Median (IQR) | 48.1 (23.1, 73.0) | 24.1 (23.5, 24.6) | -24.0 |

*Change values represent mean differences for overall non-invasive test results, proportions of patients achieving at least a 25% decline from baseline for the "≥ 25% reduction" rows, and absolute differences for FibroScan risk categories.
† For the FibroScan risk categories, mean and median values are calculated among patients classified within that category at each respective timepoint (e.g., the baseline mean of 7.0 kPa is based on the 8 patients in the low-risk group at baseline, while the follow-up mean of 6.0 kPa is based on the 34 patients in the low-risk group at follow-up).
Abbreviations: FIB-4, Fibrosis-4 Index; SD, standard deviation; IQR, interquartile range; NIT, non-invasive test; kPa, kilopascal; n, sample size.

**Figure 4.** Movement of patients across fibrosis risk levels from baseline to follow-up




Abbreviations: FIB-4, Fibrosis-4 Index; kPa, kilopascal

### Treatment-related adverse events

- Adverse events were infrequently reported among patients on resmetirom (**Figure 5**), with 6.2% (n=44) of patients experiencing at least one safety event.
- The most frequently reported events were diarrhea (4.6%), nausea (2.2%), and pruritus (1.3%). Fatigue was rare (0.4%), while no cases of arthralgia or urinary tract infection were reported.

**Figure 5.** Prevalence of most common treatment-related adverse events reported among resmetirom patients (n=712)


### Strengths & Limitations

- Use of Latica electronic health databases enabled characterization of early prescribing patterns and patient profiles at treatment initiation. Integration of unstructured clinician notes allowed extraction of additional real-world insights on treatment outcomes and safety events.
- Six months of follow-up provided an early view of treatment outcomes and trajectories not typically captured in trials.
- Limitations include incomplete or inconsistent data capture, variability in coding, care received outside the database network, inability to confirm medication adherence, and limited generalizability given that data were driven from a single healthcare group, all of which may affect outcome validity.

### Key Takeaways

- In this real-world cohort of adult patients treated with resmetirom, use was associated with **improvements in non-invasive fibrosis scores within 6 months** of initiation.
- Patients also showed **reductions in liver injury markers (ALT, AST) and cardiometabolic biomarkers (LDL, triglycerides)**.
- Treatment was **well tolerated**, with few reported adverse events.
- **Nearly all patients (96%) had ≥1 cardiometabolic risk factor**, and 80% had ≥2, underscoring the high-risk profile of this population.
- **Concomitant use of statins and GLP-1RAs**, observed in roughly one-third and one-fifth of patients respectively, **was common** and reflects treatment of overlapping metabolic conditions.
- Findings support the real-world effectiveness and safety of resmetirom in a population similar to that enrolled in MAESTRO-NASH.

## REFERENCES


1. Ahmed T, Farooq S, Naveed MA, Shahzad A, Rehman W, Haider T, et al. Pathogenesis and treatment of non-alcoholic steatohepatitis and its fibrosis: A systematic review. Cureus. 2025 Aug 13;17(8):e89969. doi: 10.7759/cureus.89969.
2. Younossi ZM, Zelber-Sagi S, Lazarus JV, et al. Global consensus recommendations for metabolic dysfunction-associated steatotic liver disease and steatohepatitis. Gastroenterology. 2025. Apr 11:S0016-5085(25)00632-8. doi: 10.1053/j.gastro.2025.02.044.
3. Steinberg GR, Carpentier AC, Wang D. MASH: the nexus of metabolism, inflammation, and fibrosis. J Clin Invest. 2025 Sep 16;135(18):e186420. doi: 10.1172/JCI186420.
4. Khalifa A, Obeid JS, Gregoski MJ, Rockey DC. Accurate identification of patients with cirrhosis and its complications in the electronic health record. Digestive Diseases and Sciences. 2023 Jun;68(6):2360–2369. doi: 10.1007/s10620-023-07876-7.


## CONCLUSIONS

In this real-world cohort, patients initiating resmetirom showed modest improvements in blood-based biomarkers over the first 6 months, supporting early real-world effectiveness of resmetirom in routine clinical practice. Ongoing follow-up and cohort expansion are needed to confirm long-term effectiveness.

## CONTACT INFORMATION


Dr. Yestle Kim
ykim@madrigalpharma.com