A Real-world Study of Adherence to and Persistence with Resmetirom in Patients with MASH

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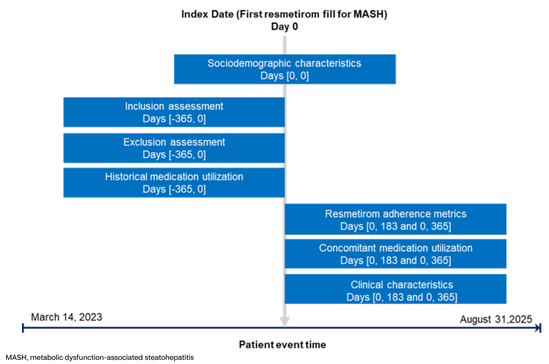
Introduction

- Metabolic dysfunction-associated steatohepatitis (MASH), formerly known as nonalcoholic steatohepatitis/nonalcoholic fatty liver disease (NASH/NAFLD), is a progressive liver disease with limited treatment options.
- In March 2024, the FDA approved resmetirom as the first medication for treatment of MASH and fibrosis stages F2 and F3.[1]
- Resmetirom is a thyroid hormone receptor beta agonist indicated for adults with MASH and moderate to advanced liver fibrosis, to be given along with diet and exercise.[1]
- Clinical trials have shown that resmetirom improves hepatic fibrosis, resolves steatohepatitis, reduces hepatic fat and liver enzymes.[2,3]
- Given the recent approval, understanding the characteristics of MASH patients initiating resmetirom, medication adherence and persistence are essential for optimizing clinical utility and informing management strategies.
- This study examines patient characteristics, resmetirom prescribing patterns, adherence and persistence using a large prescription fill database.

Methods

- This retrospective cohort study used large specialty and retail pharmacy data in the United States (Figure 1).
- The index date was defined as the first resmetirom prescription filled for MASH from March 14, 2024 (resmetirom FDA approval date).
- Inclusion criteria: aged ≥18 years old, with at least 2 fills for resmetirom.
- Patient characteristics included age, gender, region, rural-urban residency, Social Vulnerability Index (SVI identifies communities most at risk from disasters using socioeconomic factors such as poverty, disability, age, and housing conditions),[4] and payer type.
- Clinical characteristics included prescribing physician specialty, practice setting, geography, and academic hospital affiliation. Other clinical variables included proportion of days covered (PDC) and patient Rx-Risk Comorbidity Index,[5] a burden of disease score based on patient prescription history.
- Patients were considered persistent if they were actively filling resmetirom prescriptions at 6- and 12-months post initiation with a permissible 60/90-day fill grace period.
- Adherence was measured using PDC, calculated from the first dispensation for 6 and 12 months. High PDC (indicating good adherence) for resmetirom was defined as PDC ≥ 80%.
- Multivariable logistic regression was used to assess associations between sociodemographic and clinical characteristics and high PDC.



MASH, metabolic dysfunction-associated steatohepatitis

Figure 1. Study design diagram

Results

Patient Sociodemographic Characteristics (Table 1)

- 6-month follow-up: 5,389 patients; 12-month follow-up 1,869 patients.
- The mean age was 56.4 years, 56.8% were female.
- 75.8% of patients had commercial health insurance.
- Patients were geographically dispersed within the South (39.5%), West (22.7%), Northeast (20.4%), and Midwest (16.8%). Patients lived in rural (43.4%), urban (33.4%), and suburban (23.0%) areas.
- The median household income was $60,918; the mean SVI was 0.48.

Prescriber Characteristics

- Resmetirom was mainly prescribed by hepatologists and gastroenterologists (56.4%), with other specialties accounting for 40.4% of new fills.
- Physician practice locations were urban (50.6%), suburban (29.1%), and rural (20.2%); 70.5% were affiliated with an academic hospital.
- Physicians were also geographically dispersed within the South (39.3%), West (21.3%), Northeast (20.8%), and Midwest (17.9%).

Clinical Characteristics

- The average Rx-Risk Index score[5] was 2.4 (SD 4.0).
- Common concomitant prescription fills included cardiovascular (51.6%), dyslipidemia (41.6%), diabetes (33%), and GLP-1 RA medications (23.7%).

Adherence and Persistence

- Proportion of patients with a high PDC: 85.3% (6 months), 75.1% (12 months).
- Persistence (60 days grace): 89.1% (6 months), 71.2% (12 months).
- Discontinuation (45-day gap): 19.2% (6 months), 39.9% (12 months).
- Restart (45-day gap): 26% (6 months), 30.7% (12 months).
- Age, sex, urban-rural area, SVI, and Rx-Risk Index score were associated with high PDC (Table 2).

Differences in Adherence and Persistence between Sexes

- Proportion of patients with high PDC (6 months), Male vs. Female: 86.3% vs. 84.6%.
- Persistence (60 days grace, 6 months), Male vs. Female: 90.4% vs. 88.0%.
- Discontinuation (45-day gap, 6 months), Male vs. Female: 17.6% vs. 20.4%.
- All of the above *p* values <0.01.
- Similar patterns in adherence and persistence observed in 12 months follow-up but didn't reach statistical significance.

Table 1. Patient Sociodemographic Characteristics

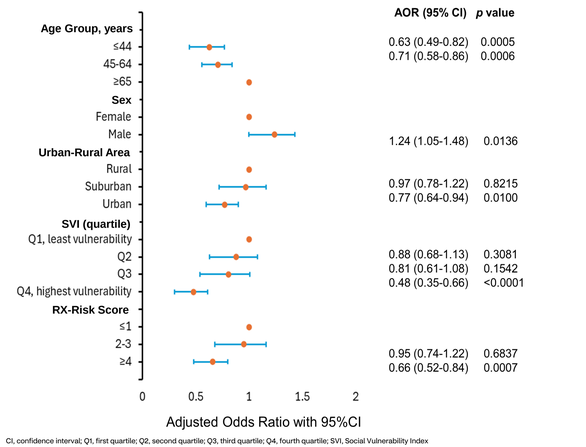
Characteristics	Total N =5,389	High PDC N =4,063	Low PDC N = 1,236	*p*-value
Age (years), mean (SD)	56.42(12.67)	57.08(12.41)	54.38(13.25)	<.0001
Age group N (%)				
≤44 years	930(17.26)	650(16.00)	280(21.12)	<.0001
45-64 years	2,912(54.04)	2,175(53.53)	737(55.58)	
≥65 years	1,547(28.71)	1,238(30.47)	309(23.30)	
Sex N (%)				
Female	3,060(56.78)	2,277(56.04)	783(59.05)	0.0549
Male	2,329(43.22)	1,786(43.96)	543(40.95)	
Geographic regions N (%)				
Northeast	1,098(20.37)	825(20.31)	273(20.59)	0.0499
Midwest	903(16.76)	703(17.30)	200(15.08)	
South	2,127(39.47)	1,615(39.75)	512(38.61)	
West	1,225(22.73)	890(21.90)	335(25.26)	
Urban-rural area N (%)				
Urban	1,801(33.42)	1,302(32.05)	499(37.63)	0.0006
Suburban	1,238(22.97)	963(23.70)	275(20.74)	
Rural	2,338(43.38)	1,789(44.03)	549(41.40)	
Median household income ($)				
Mean (SD)	60,918(22,191)	61,166(22,212)	60,156(22,119)	0.0678
Median (IQR)	57,226(28,619)	57,463(28,336)	56,044(29,551)	0.128
Social vulnerability index, mean (SD)	0.48 (0.23)	0.47 (0.23)	0.51 (0.24)	<.0001
Payer type N (%)				
Commercial insurance	4,086(75.82)	3,131(77.06)	955(72.02)	0.0002
Medicare	573(10.63)	424(10.44)	149(11.24)	

IQR, interquartile range; PDC, proportion of days covered; SD, standard deviation

Table 2. Multivariable Logistic Regression Results, Data represented as Adjusted Odds Ratios (95% Confidence Interval)

Characteristics	PDC ≥80%	Persistence	Discontinuation
Age ≤44 years (vs. ≥65)	0.63 (0.49-0.82)	0.63 (0.44-0.90)	1.56 (1.17-2.07)
Age 45-64 years (vs. ≥65)	0.71 (0.58-0.86)	0.74 (0.56-0.97)	1.43 (1.15-1.78)
Male (vs. Female)	1.24 (1.05-1.48)	1.57 (1.23-2.01)	0.75 (0.62-0.90)
Urban (vs. Rural)	0.77 (0.64-0.94)	0.80 (0.62-1.05)	1.37 (1.10-1.69)
Social Vulnerability index (Q4 vs Q1)	0.48 (0.35-0.66)	0.65 (0.42-0.99)	1.90 (1.35-2.66)
Rx-Risk Index Score >4 (vs. ≤1)	0.66 (0.52-0.84)	0.53 (0.38-0.74)	1.61 (1.24-2.09)

PDC, proportion of days covered; Q1, first quartile; Q4 fourth quartile



CI, confidence interval; Q1, first quartile; Q2, second quartile; Q3, third quartile; Q4, fourth quartile; SVI, Social Vulnerability Index

Figure 2. Forest plot of adjusted odds ratios (AOR) of sociodemographic and clinical characteristics for good resmetirom adherence (PDC ≥ 80%).

Conclusions

- Patients with MASH initiating resmetirom were geographically diverse, whereas early prescribers were predominantly located in urban areas and frequently affiliated with academic medical centers.
- Patients on resmetirom demonstrated high early adherence and persistence, with a slight decline at 12 months, indicating strong initial adoption among MASH patients and provider groups.
- Higher adherence and persistence were observed among patients who were older, male, residing in rural areas, and those with lower SVI or Rx-Risk Index scores.
- Significant differences in adherence to and persistence with resmetirom were seen between sexes.
- Sociodemographic factors and concomitant therapy patterns may guide strategies to sustain treatment engagement.
- Future research aimed at understanding long-term resmetirom utilization and patient clinical characteristics may support individualized and effective approaches to MASH management.

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