SEMAGLUTIDE DISCONTINUATION AMONG PATIENTS WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE (MASLD)

S. CLARK[1], D. NUNAG[1], M. DAVIS[1], A. CHADHA[1], N. ATREJA[2], B.THOMAS[2], F. LOBO[2]

1. Medicus Economics, Milton, MA
2. Madrigal Pharmaceuticals, West Conshohocken, PA

AASLD The Liver Meeting®

Madrigal

INTRODUCTION

- Metabolic dysfunction-associated steatohepatitis (MASH), a progressive and often underdiagnosed subtype of MASLD, is estimated to affect over 115 million people globally.[1-3]
- Semaglutide 2.4 mg was recently granted accelerated approval for the treatment of noncirrhotic MASH, with full approval pending completion of the ongoing phase 3 ESSENCE trial.
- At 72-weeks of follow-up, over 89% of trial participants remained persistent to treatment.[4]
- While trial results are promising, current evidence suggests that rates of semaglutide persistence may be lower in clinical practice, and data on real-world medication use in the MASLD population remain limited.

AIM

- To evaluate alignment between real-world subcutaneous (SC) semaglutide persistence and that observed in the ESSENCE trial among MASLD patients initiating treatment for an approved indication.

METHODS

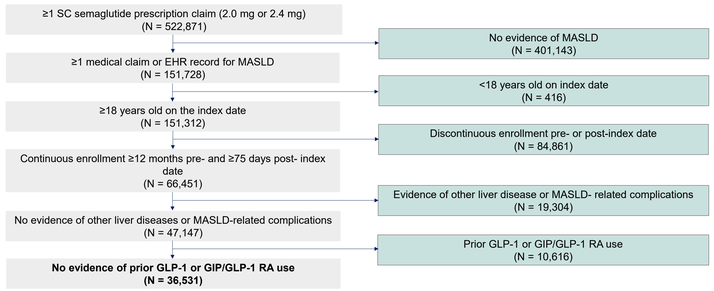
Study Design and Setting

- A descriptive analysis was conducted using Optum Market Clarity Data from December 5, 2016, through September 30, 2024, with cohort entry starting on December 5, 2017.
- Patients with MASLD initiating SC semaglutide were identified and discontinuation was assessed from the first-observed prescription claim (index date) until death, dropout, or the end of data availability.
- The 12-month baseline period preceding the index date was used for sample selection (Figure 1) and covariate measurement.
- Kaplan-Meier (KM) curves illustrating probability of and time to discontinuation were constructed and key metrics extracted.

Study Measures

- Discontinuation: Presence of a gap in SC semaglutide coverage of ≥45 days from the last day of medication availability using fill dates and days of medication supplied to account for excess (carryover) medication from previous fills. Switching between branded versions of SC semaglutide was allowed.
- Persistence: Absence of a gap in medication coverage ≥45 days.

***Figure 1**. Sample Selection Diagram*



Abbreviations: **EHR**, electronic health record; GLP-1, glucagon-like peptide-1 receptor agonist; GIP, glucose-dependent insulinotropic polypeptide.

RESULTS

- Of the 36,531 adults included in the final sample, the majority had evidence of either type 2 diabetes (T2D; 69.5%) or obesity (80.4%) at baseline (**Table 1**).
- Patients were predominantly Caucasian (>72%), covered by commercial insurance (>68%), and had a mean (standard deviation [SD]) age of 52.6 years.
- Baseline characteristics by discontinuation status were similar, with a slightly higher mean out-of-pocket payment for patients who discontinued than for those who did not ($79.8 vs $66.5).
- Mean (SD) time to discontinuation was 24.7 (28.6) weeks and mean (SD) follow-up time was 77.9 (57.6) weeks from index date.
- Overall, 64.3% of patients discontinued SC semaglutide, with 22.2% (n=8,098) of users doing so after their first prescription fill.

***Table 1**. Demographic and Clinical Characteristics*

	Overall (N = 36,531)	Discontinued (N = 23,473)	Persistent (N = 13,058)
Age			
Mean (SD)	52.6 (12.0)	52.2 (12.1)	53.3 (11.7)
Median (IQR)	53.0 (45.0, 61.0)	53.0 (44.0, 61.0)	54.0 (46.0, 62.0)
Gender, n (%)[1]			
Female	23,021 (63.0%)	14,961 (63.7%)	8,060 (61.7%)
Male	13,371 (36.6%)	8,430 (35.9%)	4,941 (37.8%)
Race, n (%)			
African American	2,952 (8.1%)	1,974 (8.4%)	978 (7.5%)
Asian	919 (2.5%)	545 (2.3%)	374 (2.9%)
Caucasian	26,416 (72.3%)	16,956 (72.2%)	9,460 (72.4%)
Other/Unknown	6,244 (17.1%)	3,998 (17.0%)	2,246 (17.2%)
Ethnicity, n (%)			
Hispanic	4,198 (11.5%)	2,734 (11.6%)	1,464 (11.2%)
Not Hispanic	26,965 (73.8%)	17,336 (73.9%)	9,629 (73.7%)
Unknown	5,368 (14.7%)	3,403 (14.5%)	1,965 (15.0%)

RESULTS

***Table 1**. Demographic and Clinical Characteristics (continued)*

	Overall (N = 36,531)	Discontinued (N = 23,473)	Persistent (N = 13,058)
Payer type, n (%)[1]			
Commercial	25,062 (68.6%)	16,126 (68.7%)	8,936 (68.4%)
Medicaid	4,172 (11.4%)	2,642 (11.3%)	1,530 (11.7%)
Medicare	7,236 (19.8%)	4,666 (19.9%)	2,570 (19.7%)
Out-Of-Pocket Payment			
Mean (SD)	75.1 (549.1)	79.8 (648.1)	66.5 (289.8)
Median (IQR)	25.0 (4.6, 50.0)	25.0 (5.0, 50.0)	25.0 (4.3, 50.0)
Charlson Comorbidity Index			
Mean (SD)	2.8 (1.8)	2.8 (1.8)	2.8 (1.8)
Median (IQR)	2.0 (2.0 - 4.0)	2.0 (2.0 - 4.0)	2.0 (2.0 - 4.0)
Obesity, n (%)			
Yes	29,377 (80.4%)	18,995 (80.9%)	10,382 (79.5%)
No	7,154 (19.6%)	4,478 (19.1%)	2,676 (20.5%)
Type 2 diabetes, n (%)			
Yes	25,371 (69.5%)	15,940 (67.9%)	9,431 (72.2%)
No	11,160 (30.5%)	7,533 (32.1%)	3,627 (27.8%)

[1]Patients whose sex or payer type was categorized as unknown were excluded from the table but included in the overall study population (<1%).
Abbreviation: IQR, interquartile range; SD, standard deviation

- In KM survival analysis accounting for censoring, 64% of patients (95% confidence interval (CI): 63%-64%) discontinued SC semaglutide by one year and 72% (95% CI: 71%-72%) discontinued within 72 weeks following treatment initiation (**Figure 2**).
- Patients with T2D exhibited lower discontinuation rates in stratified KM analysis, with 69% (95% CI: 68%-70%) discontinuing by week 72 compared to 78% (95% CI: 77%-79%) of patients without T2D (**Figure 3**).

***Figure 2**. Discontinuation over the follow-up period, Overall*

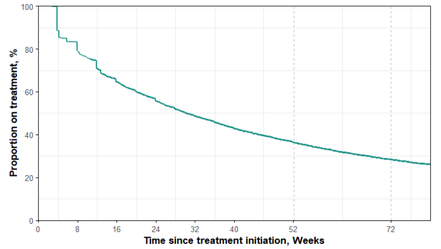
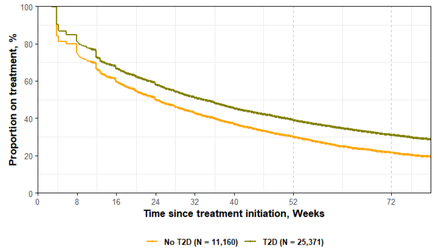


***Figure 3**. Discontinuation over the follow-up period, T2D*



CONCLUSIONS

- Most MASLD patients discontinued SC semaglutide, with 72% doing so within 72 weeks of initiation and higher discontinuation rates observed among patients without type 2 diabetes.
- Results are consistent with findings from similar observational studies and highlight the importance of monitoring SC semaglutide use in real-world settings, especially with respect to resultant liver and metabolic outcomes.
- Key limitations include a reliance on pharmacy claims to measure medication use, an inability to capture compounded semaglutide or fills outside insurance coverage, lack of data on semaglutide use specifically for MASH, and an inability to differentiate between patient-driven non-adherence versus that due to supply shortages.

QR CODE

ACKNOWLEDGEMENTS

- SC, DN, MD, and AC are all employees of Medicus Economics, LLC.
- NA, BT, and FL are all employees of Madrigal Pharmaceuticals.
- The authors thank Avery Mohan of Medicus Economics, LLC for assistance drafting this poster.

REFERENCES

1. Loomba R, Friedman SL, Shulman GI. Mechanisms and disease consequences of nonalcoholic fatty liver disease. Cell. 2021 May 13;184(10):2537–64; **2.** British Liver Trust. International NASH Day. Available at: https://britishlivertrust.org.uk/nashday/. Last accessed: August 2025; **3.** Fishman J, Kim Y, Nunag D, Davis M. Estimating the underdiagnosis of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis in Medicare claims data. Presented at: AMCP Nexus 2024; October 14-17, 2024; Las Vegas, NV. Poster K5; **4.** Sanyal AJ, Newsome PN, Kliers I, et al. Phase 3 Trial of Semaglutide in Metabolic Dysfunction-Associated Steatohepatitis. N Engl J Med. 2025;392(21):2089-2099