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

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INTRODUCTION

- Metabolic dysfunction-associated steatohepatitis (MASH), a progressive and often underdiagnosed subtype of MASLD, is estimated to affect over 115 million people globally.[1-4]
- 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, 88% of participants followed the 16-week dose-escalation schedule and maintained a 2.4 mg dose.[4]
- Real-world evidence suggests that many patients initiating semaglutide 2.4 mg may not titrate to a target dose of 2.4 mg or remain persistent to treatment.

AIM

- To assess alignment between real-world titration patterns and those observed in the ESSENCE trial among MASLD patients starting semaglutide 2.4 mg for a currently approved indication.

METHODS

Study Design

- A descriptive analysis was conducted using Optum Market Clarity data from June 4, 2020, through September 30, 2024.
- Patients with MASLD initiating semaglutide 2.4 mg were included, with study outcomes assessed from the first observed dispensation (index date) until, death, dropout, or the end of data availability.
- The 12-month period preceding the index date was used for sample selection (Figure 1) and covariate measurement.
- Outcome probability and timing were assessed via Kaplan-Meier (KM) survival analysis and cumulative incidence curves plotted.
- Subgroup analysis was conducted among patients with 72 weeks of follow-up.

Study Outcomes

- ***Titration***: Presence of ≥1 prescription fill for a 2.4 mg dose of semaglutide during the follow-up period.
- ***Discontinuation***: Presence of a gap in SC semaglutide coverage of ≥45 days from the last day of medication availability using fill dates and days supply to account for excess medication.
- ***Time-to-event***: Time in days between index semaglutide 2.4 mg prescription and the first observed fill for a 2.4 mg dose (titration) or last day of medication coverage (discontinuation).

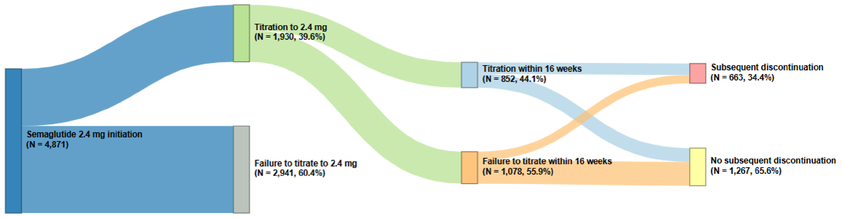
RESULTS

Table 1. *Demographic and Clinical Characteristics*

	Total N = 4,871	Titration to 2.4 mg N=1,930	No titration N=2,941
Age	-	-	-
Mean (SD)	47.2 (11.0)	47.7 (10.4)	46.9 (11.4)
Median (IQR)	48.0 (40.0, 55.0)	48.0 (41.0, 55.0)	48.0 (39.0, 56.0)
Sex, n (%)[1]	-	-	-
Female	3,313 (68.0%)	1,254 (65.0%)	2,059 (70.0%)
Male	1,550 (31.8%)	676 (35.0%)	874 (29.7%)
Race, n (%)	-	-	-
African American	350 (7.2%)	127 (6.6%)	223 (7.6%)
Asian	95 (2.0%)	42 (2.2%)	53 (1.8%)
Caucasian	3,595 (73.8%)	1,453 (75.3%)	2,142 (72.8%)
Other/unknown	831 (17.1%)	308 (16.0%)	523 (17.8%)
Ethnicity, n (%)	-	-	-
Hispanic	487 (10.0%)	158 (8.2%)	329 (11.2%)
Not Hispanic	3,577 (73.4%)	1,448 (75.0%)	2,129 (72.4%)
Unknown	807 (16.6%)	324 (16.8%)	483 (16.4%)
Region, n (%)	-	-	-
Midwest	1,520 (31.2%)	632 (32.7%)	888 (30.2%)
Northeast	1,675 (34.4%)	651 (33.7%)	1,024 (34.8%)
South	1,045 (21.5%)	405 (21.0%)	640 (21.8%)
West	409 (8.4%)	147 (7.6%)	262 (8.9%)
Other/Unknown	222 (4.6%)	95 (4.9%)	127 (4.3%)
Payer type, n (%)[1]	-	-	-
Commercial	4,053 (83.2%)	1,684 (87.3%)	2,369 (80.6%)
Medicaid	590 (12.1%)	166 (8.6%)	424 (14.4%)
Medicare	226 (4.6%)	79 (4.1%)	147 (5.0%)
Patient OOP copay ($)	-	-	-
Mean (SD)	157.7 (1,406.3)	113.9 (347.0)	188.8 (1,814.3)
Median (IQR)	25.0 (20.0, 50.0)	25.0 (25.0, 50.0)	25.0 (16.0, 50.0)
Type 2 diabetes, n (%)	511 (10.5%)	186 (9.6%)	325 (11.1%)

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

Figure 2. *Semaglutide 2.4 mg Titration Patterns*



Sample Characteristics

- Of the 4,871 adults included in the final sample (**Figure 1**), 10.5% (n=511) had a diagnosis for type 2 diabetes at baseline and the overall mean (SD) follow-up time was 59.3 (33.1) weeks (**Table 1**).
- Patients who did not titrate were more likely than those who did to be publicly insured through Medicare/Medicaid (19.4% vs 12.7%) and have a higher mean out-of-pocket copay ($188.8 vs. $113.9).

Titration

- Overall, 39.6% (n=1,930) of patients titrated to a 2.4 mg dose, with a mean (SD) time to titration of 20.1 (15.6) weeks (**Figure 2**).
- Among patients who titrated, 16.8% (n=325) reduced their dose and 34.4% (n = 663) discontinued treatment after reaching 2.4 mg.
- In KM survival analysis accounting for censoring, 17% (95% confidence interval (CI): 16%-19%) of patients titrated by 16 weeks and 45% (95% CI: 43%-46%) titrated within 72 weeks (**Figure 3**).

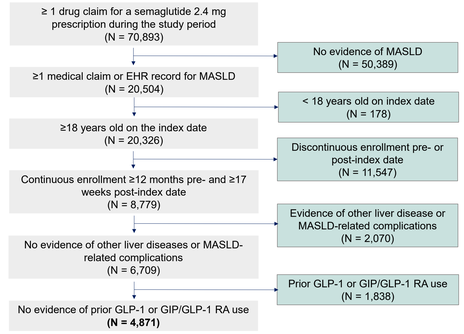
Discontinuation

- Approximately 70% of patients (n=3388) discontinued treatment, with a mean (SD) time-to-discontinuation of 15.5 (17.3) weeks.
- Accounting for censoring, 49% (95% CI: 47%-50%) of patients discontinued by 16 weeks and 78% (95% CI: 77%-80%) discontinued within 72 weeks.

Subgroup Analysis: 72 Weeks of Follow-up

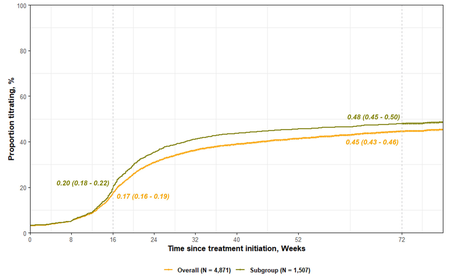
- The titration rate among the 1,507 patients with 72 weeks of follow-up was 49.8% overall, with 19.9% titrating by 16 weeks, and 48.0% within 72 weeks. Mean (SD) time to titration was 23.3 (19.7) weeks.
- Among patients who titrated, 14.3% subsequently reduced their dose and 42.9% discontinued treatment by week 72.
- Of the patients who titrated within 16 weeks, 39.3% remained on a 2.4 mg dose at week 72.
- Survival analysis results were consistent across samples.

Figure 1. *Sample Selection*



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

Figure 3. *Titration status over the follow-up period*



CONCLUSIONS

- Less than half of MASLD patients titrated to a 2.4 mg semaglutide dose over the follow-up period, with only 17% doing so within 16 weeks and 78% discontinuing by week 72.
- In subgroup analysis, most patients who titrated within 16 weeks did not remain on a 2.4 mg dose at week 72.
- Results are consistent with findings from similar observational studies and highlight the importance of monitoring SC semaglutide 2.4 mg use patterns in a real-world setting.
- 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 for MASH, and an inability to identify changes in medication use due to shortages.

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