Semaglutide 2.4 mg Weight Outcomes Among Patients With Metabolic Dysfunction-Associated Steatotic Liver Disease in a Real-World Setting

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INTRODUCTION

- Metabolic dysfunction-associated steatotic liver disease (MASLD) is estimated to affect over 83 million people in the United States.[1-2]
- MASLD is often precipitated by obesity and type 2 diabetes (T2D), making many patients eligible for semaglutide treatment.
- In the STEP 1 clinical trial, semaglutide 2.4 mg treatment in combination with lifestyle changes was associated with an average reduction in body weight of 14.9% among participants without type 2 diabetes and with BMI ≥27 kg/m² and a weight-related comorbidity or obesity (BMI ≥30 kg/m²).[3]
- While trial results are promising, evidence on real-world medication use and effectiveness in the MASLD patient population is limited.

OBJECTIVES

- To evaluate real-world weight-loss outcomes among patients with MASLD starting semaglutide 2.4 mg for an approved indication.

METHODS

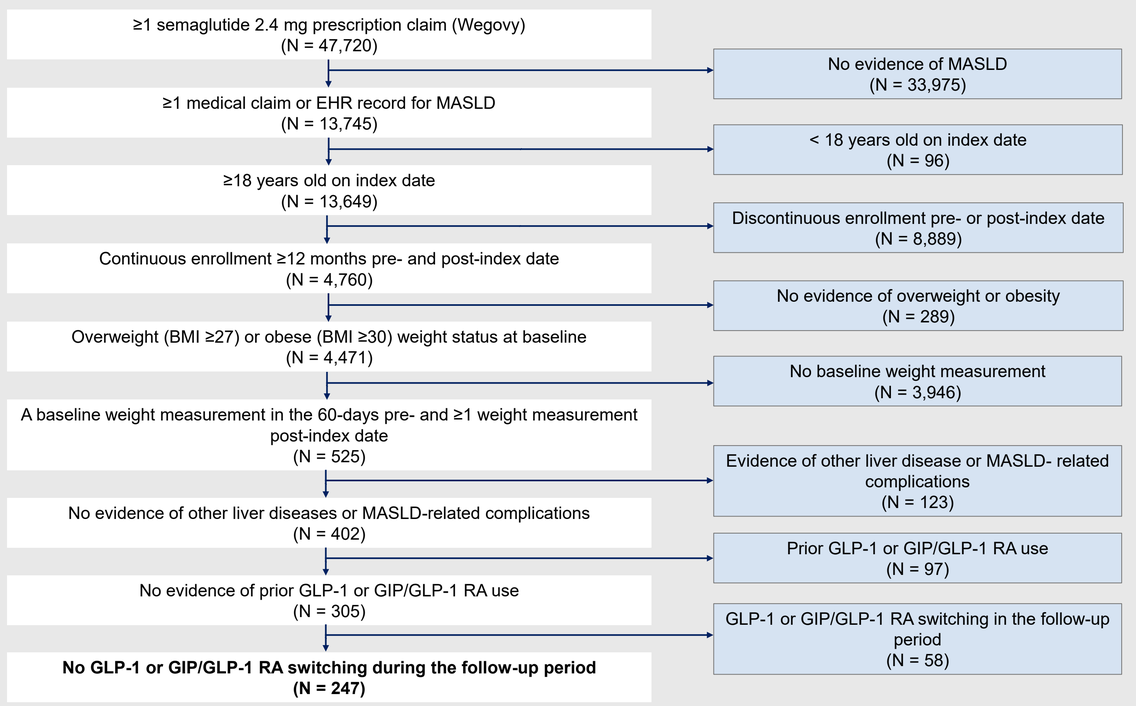
Study Design and Setting

- A descriptive analysis was conducted using Optum Market Clarity data from June 4, 2020, through September 30, 2024, with cohort entry starting on June 4, 2021.
- Overweight (defined here as BMI ≥27 kg/m²) and obese (BMI ≥30 kg/m²) patients with MASLD initiating semaglutide 2.4 mg were included. Weight change was assessed in the 12 months following the first observed semaglutide 2.4 mg dispensation (index date).
- The 12-month period preceding the index date was used for sample selection (Figure 1), covariate assessment, and baseline weight measurement (closest value ≤60 days pre-index).
- Medication use (titration and discontinuation) was defined prior to the latest observed weight measurement.
- Switching between branded versions of subcutaneous semaglutide was allowed.

Study Measures

- Body weight: Absolute and percentage weight change from baseline to the latest observed measurement within 12 months from the index date.
- Weight loss ≥10%: The proportion of patients achieving a reduction in body weight from baseline of at least 10%.
- Titration and Persistence: Patients were grouped into the following cohorts based on titration to a target dose of 2.4 mg and persistence (no gaps in medication coverage ≥45-days) over the follow-up period:
  - No titration or persistence
  - No titration with persistence
  - Titration with no persistence
  - Titration with persistence

FIGURE 1. Sample Selection Diagram



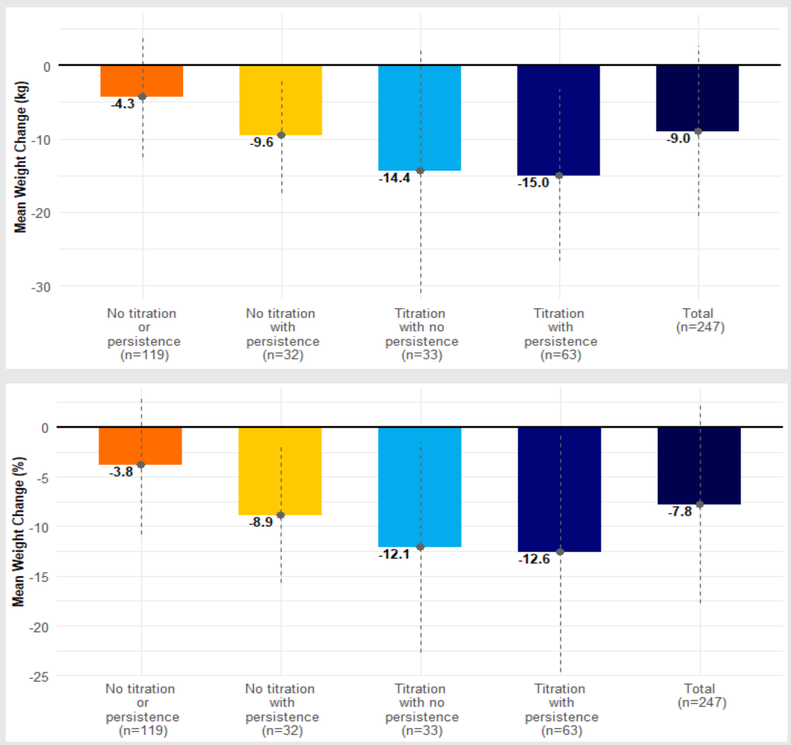
RESULTS

- Almost half (48.2%; n = 119) of the 247 patients in the final sample did not titrate or remain persistent to semaglutide 2.4 mg prior to their latest weight measurement. Patients who did not titrate but remained persistent, titrated without persistence, and titrated and remained persistent comprised 13.0% (n = 32), 13.4% (n = 33), and 25.5% (n = 63) of the sample, respectively.
- Patients across groups were predominantly female (>55%) and Caucasian (>71%), with the proportion of patients with T2D varying from 3.1% among patients who did not titrate and remained persistent to 30.3% in patients who titrated but did not remain persistent (Table 1).
- Mean (standard deviation [SD]) baseline weight and BMI were 114.1 (24.2) kg and 40.0 (8.1) kg/m2, respectively, and mean (SD) time to latest follow-up weight measurement was 38.0 (13.2) weeks.

TABLE 1. Baseline Characteristics

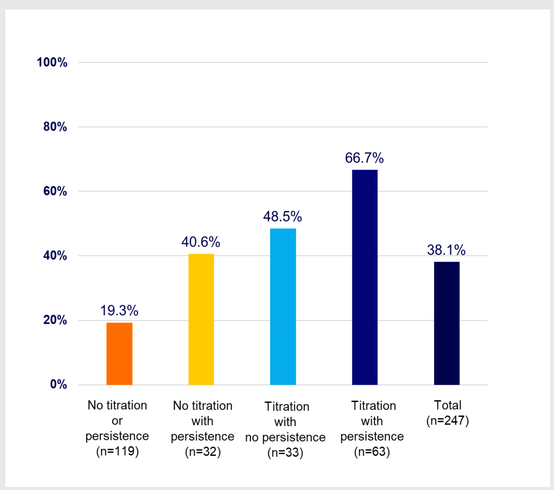
	Overall (N = 247)	No titration or persistence (N = 119)	No titration with persistence (N = 32)	Titration with no persistence (N = 33)	Titration with persistence (N = 63)
Age					
Mean (SD)	47.9 (10.9)	48.1 (11.5)	47.2 (9.2)	49.8 (11.9)	46.8 (10.0)
Median (IQR)	49.0 (41.0, 57.0)	50.0 (42.0, 57.0)	48.0 (38.0, 54.0)	53.0 (45.0, 58.0)	48.0 (41.0, 54.0)
Gender, n (%)					
Female	155 (62.8)	73 (61.3)	21 (65.6)	26 (78.8)	35 (55.6)
Male	91 (36.8)	45 (37.8)	11 (34.4)	7 (21.2)	28 (44.4)
Unknown	1 (0.4)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
Race, n (%)					
African American	24 (9.7)	15 (12.6)	2 (6.3)	4 (12.1)	3 (4.8)
Asian	6 (2.4)	3 (2.5)	3 (9.4)	0 (0.0)	0 (0.0)
Caucasian	191 (77.3)	89 (74.8)	23 (71.9)	28 (84.8)	51 (81.0)
Other/Unknown	26 (10.5)	12 (10.1)	4 (12.5)	1 (3.0)	9 (14.3)
Ethnicity, n (%)					
Hispanic	32 (13.0)	14 (11.8)	7 (21.9)	2 (6.1)	9 (14.3)
Not Hispanic	196 (79.4)	97 (81.5)	24 (75.0)	29 (87.9)	46 (73.0)
Unknown	19 (7.7)	8 (6.7)	1 (3.1)	2 (6.1)	8 (12.7)
Payer Type, n (%)					
Commercial	193 (78.1)	95 (79.8)	22 (68.8)	25 (75.8)	51 (81.0)
Medicaid	37 (15.0)	18 (15.1)	7 (21.9)	6 (18.2)	6 (9.5)
Medicare	17 (6.9)	6 (5.0)	3 (9.4)	2 (6.1)	6 (9.5)
Weight [kg]					
Mean (SD)	114.1 (24.2)	114.8 (22.9)	106.7 (17.9)	112.1 (28.7)	117.5 (26.5)
Median (IQR)	111.6 (97.1, 132.0)	113.2 (97.2, 133.1)	104.3 (95.1, 117.5)	104.0 (96.2, 123.4)	114.8 (98.7, 136.9)
BMI					
Mean (SD)	40.0 (8.1)	40.4 (8.1)	38.0 (5.2)	39.9 (7.4)	40.4 (9.4)
Median (IQR)	39.1 (34.9, 43.3)	39.5 (35.3, 43.3)	37.6 (34.0, 40.8)	38.8 (35.1, 44.6)	38.3 (34.6, 44.6)
T2D, n (%)					
Yes	37 (15.0)	18 (15.1)	1 (3.1)	10 (30.3)	8 (12.7)
No	210 (85.0)	101 (84.9)	31 (96.9)	23 (69.7)	55 (87.3)

FIGURE 2. Absolute and Percentage Mean Weight Change



- Average weight loss from baseline was 7.8% overall, ranging from 3.8% in patients who neither titrated nor remained persistent to 12.6% in patients who titrated and remained persistent (Figure 2).
- Only 38.1% of patients achieved a reduction in body weight of at least 10% from baseline, ranging from 19.3% among patients who did not titrate or remain persistent to 66.7% in patients who titrated and remained persistent (Figure 3).
- The average semaglutide 2.4 mg dose per week over the follow-up period was 0.74 mg, with a modal dose of 2.4 mg.

FIGURE 3. Patients Achieving Weight loss ≥10%



CONCLUSION

- **In this real-world study, nearly half of patients did not titrate or remain persistent, both of which were associated with limited weight reduction benefits.**
- **Findings suggest a lack of alignment between semaglutide trial results and weight-related outcomes for MASLD patients in clinical practice.**
- **Key limitations include a reliance on pharmacy claims to measure medication use, inability to measure weight and assess weight change at standard follow-up times, limited generalizability to the Optum population with electronic health record data, random variability due to small sample size, and an inability to capture compounded semaglutide or fills outside insurance coverage.**

ABBREVIATIONS

BMI: Body mass index; GIP: Glucose-dependent insulinotropic polypeptide; GLP-1 RA: Glucagon-like peptide-1 receptor agonist; IQR: Interquartile range; MASH: Metabolic dysfunction-associated steatohepatitis; MASLD: Metabolic dysfunction-associated steatotic liver disease; SD: Standard deviation; T2D: Type 2 diabetes

DISCLOSURES AND ACKNOWLEDGEMENTS

- AM, AC, DN, SC and MD are all employees of Medicus Economics, LLC
- NA, BT and FL are all employees of Madrigal Pharmaceuticals

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