Treatment Patterns of Subcutaneous Semaglutide Use Among Patients with MASH

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Background

- Based on recent early reports from the ongoing phase 3 ESSENCE clinical trial,[1] metabolic dysfunction-associated steatohepatitis (MASH) study endpoints were met among patients who received sustained high doses (2.4 mg) of subcutaneous (SC) semaglutide
- In that trial, patients were expected to reach a target dose of 2.4 mg within 16 weeks and maintain that dosage for another 56 weeks for a total of 72 weeks; however, existing real-world research has shown high rates of discontinuation among individuals with obesity and/or type 2 diabetes taking SC semaglutide or other glucagon-like peptide-1 receptor agonists [2]
- As some patients with MASH have been prescribed SC semaglutide for the treatment of comorbid obesity and/or type 2 diabetes, [3,4] it is possible to assess real-world treatment patterns among patients with MASH

Objective

- This retrospective study aimed to assess real-world 72-week treatment patterns of SC semaglutide among patients with MASH with a focus on those who reached a dose of 2.4 mg

Methods

Data Source

- A deidentified linked dataset of electronic health records (Veradigm Network EHR) and healthcare billing claims (Komodo Healthcare Map)

Figure 1. Inclusion and Exclusion Criteria

≥1 pharmacy claim for subcutaneous (SC) semaglutide between 7/1/2018 and 6/30/2023. Index date was the date of the first claim for SC semaglutide
N = 3,074,629

↓

≥1 diagnosis code for MASH (ICD-10-CM: K75.81) any time before or up to 1 year after the index date
N=85,810

↓

No evidence of SC semaglutide use prior to the index date
N=85,433

↓

≥ 18 years old on the index date
N=85,330

↓

Excluded patients with viral hepatitis, alcoholism or alcoholic liver disease, opioid disorders, type 1 diabetes, gestational diabetes, or bariatric surgery at any time
N=52,891

↓

Excluded patients with cirrhosis, decompensated cirrhosis, ascites, encephalopathy, varices, liver transplant, or hepatic cell carcinoma at any time before the index date
N=34,436

↓

≥52 weeks of continuous enrollment in claims before the index date and ≥72 weeks of continuous enrollment after the index date
SC Semaglutide Cohort: N=6,537

↓

Patients who indexed on and received only Wegovy during the follow-up period
Wegovy Cohort: N=358

Methods

Study populations

- **SC Semaglutide cohort:** Adults (≥18 years) in the US with a diagnosis of MASH who newly started SC semaglutide
- **Wegovy cohort**: Adults (≥18 years) in the US with a diagnosis of MASH who indexed on Wegovy and only received Wegovy
  - A subgroup analyses were conducted among those who reached a target dose of 2.4 mg anytime during follow-up or within 16 weeks of the index date

Time Periods

- Baseline: 52 weeks preceding the index date
- Follow-up: 72 weeks following and including the index date

Patient Characteristics

- Age, sex, and year of index were captured on the index date
- Clinical comorbidities were captured in the baseline period
- Body mass index (BMI) was for people who had at least one BMI documented in both the baseline and follow-up periods
  - The baseline BMI was the BMI closest to the index date. The follow-up BMI was the BMI closest to the end of follow-up

Treatment Patterns

- Measured in the 72-week follow-up period
- Nonpersistence was defined as having a gap in treatment of interest of ≥45 days
- Restart was defined as a new prescription for the treatment of interest after nonpersistence

Results

- The study included 6,537 patients with MASH who initiated SC semaglutide, with 358 (5.5%) receiving only Wegovy (Figure 1)
- Patients were ~50 years old and majority female (Table 1)
- During the baseline period, obesity and type 2 diabetes were documented in 75.4% and 77.8% of the SC semaglutide cohort and 90.8% and 16.5% of the Wegovy cohort.
- During follow-up, 68.4% of the SC semaglutide cohort and 78.5% of the Wegovy cohort were nonpersistent on treatment and the mean time to nonpersistance was 24.8 (19.3) and 20.1 (16.9) weeks, respectively (Figure 2)
- Among the 79 (22.1%) patients in the Wegovy cohort with ≥1 BMI value in both baseline (11.3 [12.7] weeks before index) and follow-up (53.2 [17.5] weeks after index), mean BMI values were 35.8 (4.3) and 34.1 (4.9), respectively (Table 2)
- 182 (50.8%) patients in the Wegovy cohort reached a dose of 2.4 mg at some point during the 72 week follow-up, and 94 (26.3%) did so within the first 16 weeks
- Of those who reached 2.4 mg within 16 weeks, 28 (29.8%) sustained on that dosage for ≥56 weeks
  - Among the 69 (73.4%) who were nonpersistent, the mean duration of therapy was 21.3 (16.9) weeks, and 20 (29.0%) restarted the 2.4 mg dose after 13.1 (7.3) weeks.
- The most common dosage among those who reduced from 2.4mg was 1.7 mg (Figure 3)

Figure 2. Sankey Diagrams of Subcutaneous Semaglutide and Wegovy Treatment Patterns

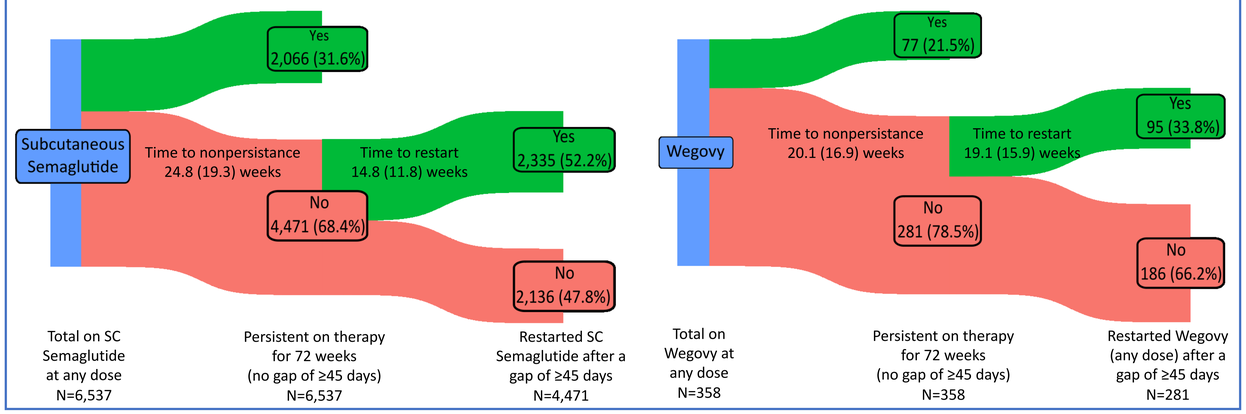


Table 1. Patient Characteristics

	SC Semaglutide N = 6,537	Wegovy N = 358
Age, Index, mean (SD)	53.0 (10.8)	48.9 (10.1)
Female, N (%)	4,268 (65.3)	256 (71.5)
Year of Index, N (%)		
2018	168 (2.6)	0 (0.0)
2019	785 (12.0)	0 (0.0)
2020	929 (14.2)	0 (0.0)
2021	1,857 (28.4)	121 (33.8)
2022	2,474 (37.9)	148 (41.3)
2023	324 (5.0)	89 (24.9)
≥1 BMI[a] in baseline and follow-up, N (%)	1,584 (24.2)	79 (22.1)
Baseline BMI, mean (SD)	35.6 (4.5)	35.8 (4.3)
Weeks from baseline BMI to index, mean (SD)	12.9 (13.2)	11.3 (12.7)
Follow-up BMI, mean (SD)	34.6 (5.0)	34.1 (4.9)
Weeks from index to follow-up BMI, mean (SD)	50.0 (19.9)	53.2 (17.5)
Clinical Conditions, N (%)		
Type 2 diabetes	5,085 (77.8)	59 (16.5)
Obesity	4,931 (75.4)	325 (90.8)
Hyperlipidemia	4,647 (71.1)	193 (53.9)

SC, subcutaneous; SD, standard deviation.
[a] BMI is capped at 40 in the data source as part of the deidentification process

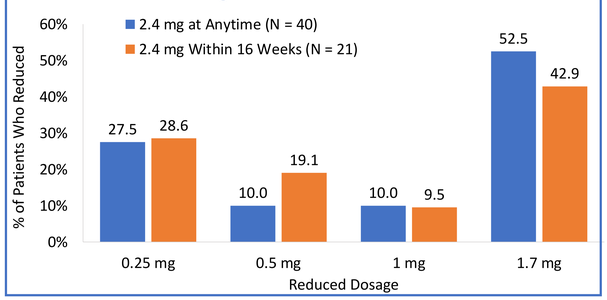
Limitations

- This analysis could not capture medication received from a compounding pharmacy as these drugs are not assigned National Drug Codes
- While this study assumed that patients taking Wegovy intended to reach a target dose of 2.4 mg within 16 weeks,[5] real-world target dosages and titrations likely varied based on individual patient and prescriber decision-making
  - This study cannot confirm if the medications were used as prescribed as patients may have dose reduced at home
- Patient behavior may differ by treatment indication and the results may not be representative of patients who are prescribed SC semaglutide for the treatment of MASH rather than the treatment of related comorbidities

Table 2. Treatment Patterns Among Wegovy Patients Who Reached a Dose of 2.4 mg

	2.4 mg at Anytime N = 182	2.4 mg Within 16 Weeks N = 94
Weeks to reach 2.4mg dose, mean (SD)	17.3 (13.2)	8.3 (5.6)
Weeks on 2.4 mg dose, mean (SD)	31.5 (21.4)	32.4 (23.6)
Sustained on 2.4 mg dose for ≥56 weeks, N (%)	28 (15.4)	28 (29.8)
Nonpersistent on 2.4 mg dose[a], N (%)	111 (61.0)	69 (73.4)
Weeks to nonpersistence on 2.4 mg, mean (SD)	20.0 (15.9)	21.3 (16.9)
Restarted 2.4 mg dose, N (%)	26 (23.4)	20 (29.0)
Weeks to restart of 2.4mg, mean (SD)	12.3 (6.7)	13.1 (7.3)
Reduced dosage from 2.4 mg	40 (22.0)	21 (22.3)

Figure 3. Subsequent Dosage Among Wegovy Patients Who Reduced From a 2.4 mg Dose



Conclusions

- Similar to prior studies among patients with obesity or type 2 diabetes, discontinuation was common among patients with MASH who initiated SC Semaglutide
- Among the 358 patients who initiated on Wegovy, only 7.8% reached a dose of 2.4mg within 16 weeks and then sustained that dose for 56 weeks
- This suggests that patients may struggle to achieve and maintain the required dosing regime that was associated with live-related benefits in the ESSENCE clinical trial

Disclosures
This study was funded by Madrigal Pharmaceuticals. T Ryan, N Zeng, JP Winer-Jones, and M Bonafede are employees of Veradigm, which received fees from Madrigal Pharmaceuticals related to this work. Y Kim, F Lobo, and J O'Donnell are employees of Madrigal Pharmaceuticals.

References
1. Newsome et al. The Liver Meeting Late Breaking Abstract Supplement. 2024: San Diego **2.** Do et al. JAMA Netw Open 7(5), e2413172 (2024) **3.** Rinella et al. Hepatology 77(5), 1797–1835 (2023) **4.** Cusi et al. Endocr Pract 28(5), 528–562 (2022). **5. Wegovy® [package insert]. Plainsboro, NJ: Novo Nordisk Inc.**