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Reasons for Discontinuation of Glucagon-like Peptide-1 Receptor Agonists (GLP-1 RAs) Among Patients with MASH: An Analysis of Real-world Clinical Notes

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Background

- Currently, comorbidity management (i.e. obesity, type 2 diabetes) in patients with metabolic dysfunction-associated steatohepatitis (MASH) may include treatment with glucagon-like peptide-1 receptor agonists (GLP-1 RAs) or dual GLP-1/glucose-dependent insulinotropic polypeptide (GIP) agonists, and these drugs are currently under investigation for treatment of MASH.[1,2]
- Based on recent reports from phase 2b and phase 3 trials,[3,4] MASH study endpoints were met among patients receiving high doses of GLP-1 RAs; therefore, sustained treatment on high dose is important to assess in a real-world setting in patients with MASH.
- Although recent literature shows that, regardless of GLP-1 RA dose, discontinuation can occur within the first year of treatment, data are limited regarding the reasons for discontinuation.[5]
- A recent cross-sectional analysis extracted reasons for GLP-1 treatment modification or discontinuation from an EHR; the analysis found that reasons for discontinuation were mostly non-medical.[6]

Objective

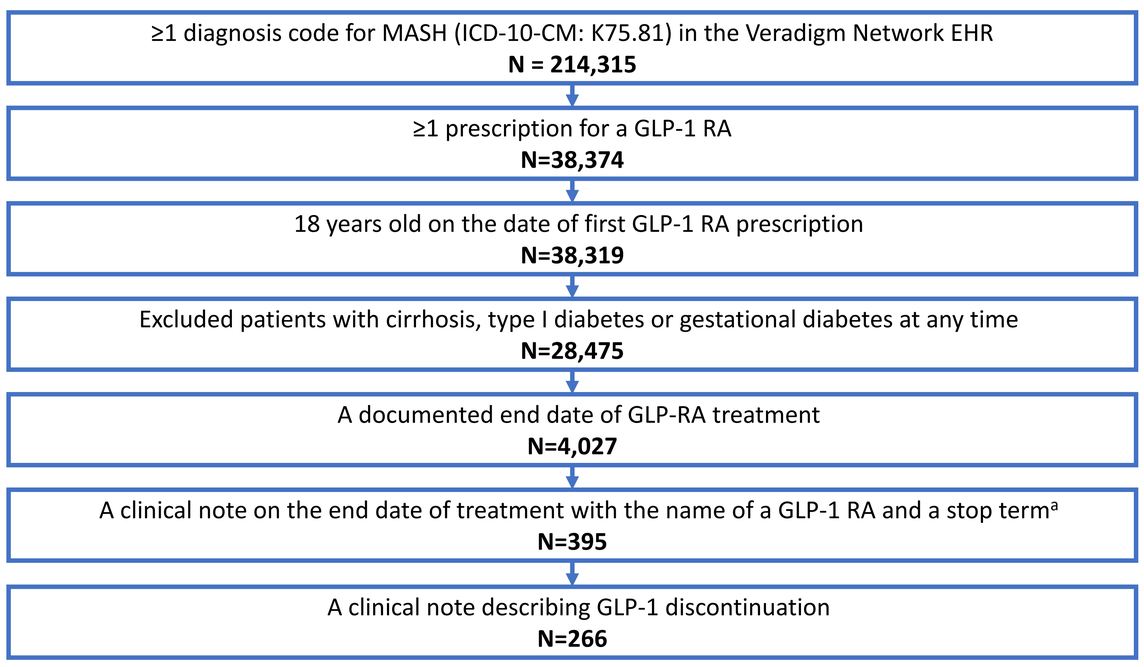
- The aim of this exploratory, descriptive analysis of provider notes was to characterize documented reasons for discontinuation of any FDA-approved GLP-1 RAs, regardless of dose, in patients with MASH.

Methods

Study population

- Using the Veradigm Network EHR, we identified adults (≥18 years) in the United States with a diagnosis of MASH anytime before 7/1/2024, a GLP-1 RA prescription (4/28/2005–7/1/2024), and a note on the end date of treatment (Figure 1)

Figure 1. Inclusion and Exclusion Criteria



[a]stop, stopped, discontinued, discontinue, discontinuation, d/c, gap, quit

Notes Analysis

- For every stop term in a clinical note, we extracted a note snippet of 150 characters (50 characters before and 100 characters after the stop term)
- The snippets were examined for reasons for discontinuation and snippets not related to GLP-1 discontinuation were excluded

Subgroup Analysis

- Patients were stratified by time to discontinuation: ≤6 months or >6 months

Patient Characteristics

- Demographic characteristics were captured on the date of the first GLP-1 RA prescription
- Baseline body mass index (BMI) was captured in the 6 months preceding the first GLP-1 RA prescription
- Presence of GLP-1 RA indications, type 2 diabetes and obesity (BMI ≥ 30), was captured anytime prior to first GLP-1 RA prescription

Results

- 496 qualifying notes were identified in the records of 395 patients with MASH
- 363 snippets, from 266 patients, described GLP-1 discontinuation
- Patients were, on average, 55.0 (SD: 12.9) years old and 66.8% were female

Table 1. Demographic Characteristics

	All Patients N = 265[a]
Age, Index, mean (SD)	55.0 (12.9)
Female, N (%)	177 (66.8)
Race, N (%)	
Asian	11 (4.2)
African American/Black	8 (3.0)
White	162 (61.1)
Other/Unknown/Not Reported	84 (31.7)
Geographic Region, N (%)	
Northeast	43 (16.2)
Midwest	43 (16.2)
South	114 (43.0)
West	60 (22.6)
Other/Unknown	5 (1.9)

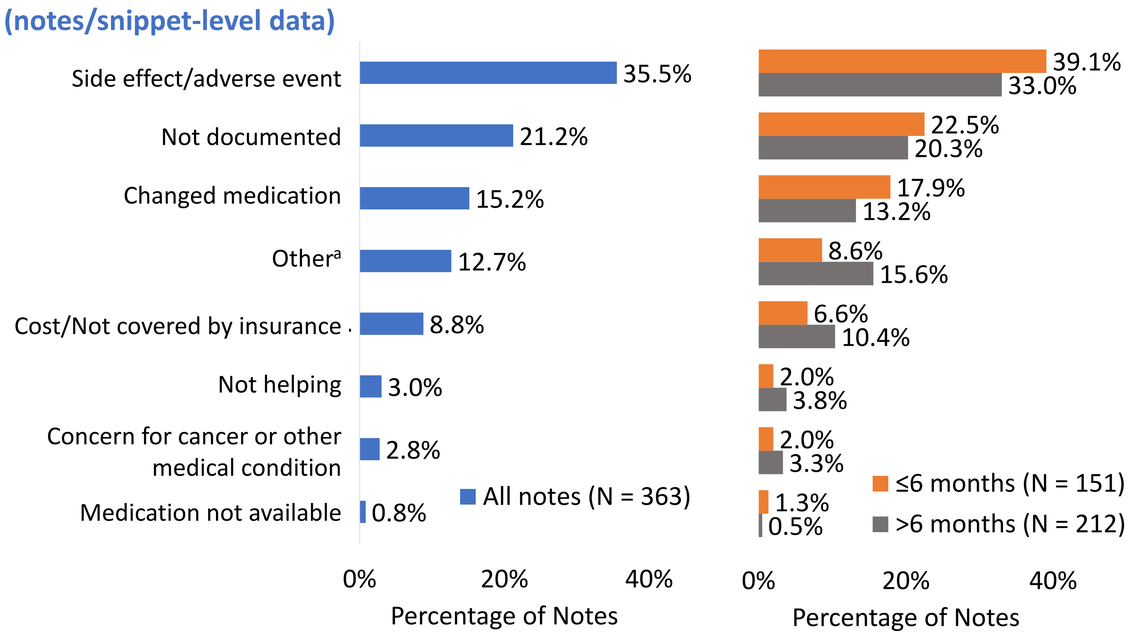
[a] One patient could not be linked back to the EHR after notes extraction
SD, standard deviation

Table 2. Clinical Characteristics

	All Patients N = 265[a]
Baseline BMI, N (%)	202 (76.2)
Median (IQR)[b]	35 (31–40)
GLP-1 RA Indications[c]	
Type 2 Diabetes	210 (79.3)
Obesity	223 (84.2)
Index GLP-1 RA	
Semaglutide	127 (47.9)
Dulaglutide	66 (24.9)
Liraglutide	52 (19.6)
Tirzepatide	11 (4.2)
Exenatide	7 (2.6)
Albiglutide	2 (0.8)

[a] One patient could not be linked back to the EHR after notes extraction
[b] BMI is capped at 40 to ensure deidentification
[c] Documented anytime prior to index
BMI, body mass index; IQR, interquartile range

Figure 2. Reasons for Discontinuation: All Notes or Stratified by Time to Discontinuation (notes/snippet-level data)



[a] Includes reasons that could not be easily categorized and only occurred in a few patients. Examples include intolerance, excessive weight loss, pregnant or trying to become pregnant

Results, Cont.

- Among the 76.2% of patients with a BMI value, the median BMI was 35.0, and 98% of those with a BMI value had a BMI ≥25 when the initiated therapy (Table 2).
- The most common GLP-1 RAs at baseline were semaglutide (47.9%), dulaglutide (24.9%), and liraglutide (19.6%)
- In the 363 clinical notes examined for this study, side effects/adverse events were the most commonly documented reason for stopping therapy (n=129 [35.5%]) (Figure 2)
- Other common reasons included switched medications (n=55 [15.2%]) and cost/insurance barriers (n=32 [8.8%])
- Overall, trends in reason for discontinuation were similar among the 41.6% of documented discontinuation within the first 6 months and the 58.4% with documented discontinuations after 6 months; however, there were some notable differences (Figure 2)
  - Side effects or adverse events were reported as the reason for discontinuation among 39.1% of documented discontinuations within the first 6 months and among 33.0% of documented discontinuations after 6 months (Δ = -6.1%)
  - 8.6% of reasons documented discontinuations within the first 6 months and 15.6% of reasons documented discontinuations after 6 months were categorized as other (Δ = 7.0%)

Limitations

- As some patients had more than one note snippet, some reasons might be double-counted or miscategorized as not documented
- This analysis did not capture medication restarts, switches between GLP-1 RAs, or GLP-1 RA dosage, all of which may impact the reason for discontinuation.
- Prospective data or a more comprehensive analysis may be needed to confirm these results
- Small sample size of available notes and snippets limits generalizability

Conclusions

- In this exploratory descriptive analysis, among provider notes, side effects or adverse events were the most commonly documented reason for discontinuation
- Further research is needed to assess the reasons for discontinuing treatment among notes that did not document reasons and the inherent limitations of this study limits generalizability

Disclosures

This study was funded by Madrigal Pharmaceuticals. T Ryan, N Zeng, R Carter, JP Winer-Jones, M Bonafede, and A Manfredo are employees of Veradigm, which received fees from Madrigal Pharmaceuticals related to this work. Y Kim is an employee of Madrigal Pharmaceuticals. EB Tapper is an employee at the University of Michigan, which received unrestricted financial support to the institution related to this work.

References

1. Newsom et al. *N Engl J Med* 2021;384(12):1113–1124 **2.** Mantovani et al. *Metabolites* 2021;11(2):73. **3.** Newsome et al. The Liver Meeting Late Breaking Abstract Supplement. 2024: San Diego, CA; **4.** Loomba R et al. *N Engl J Med.* 2024 Jul 25;391(4):299-310. **5.** Kumar et al. ISPOR EU 2024: Barcelona, Spain. **6.** Barritt et al. EASL 2024: Milan, Italy.