Achievement of near-normal HbA_{1c} with early initiation of oral semaglutide: An exploratory subgroup analysis of PIONEER 1

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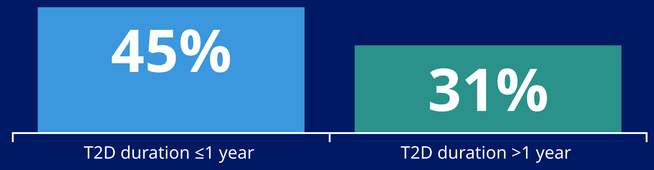
Early initiation of oral semaglutide within 1 year of T2D diagnosis results in a high proportion of patients achieving near-normal HbA_{1c}

HbA_{1c} <6.0%

% of patients receiving oral semaglutide 14 mg at week 26



Background and aims

- Early achievement of near-normal HbA_{1c} is associated with a reduced risk of future complications in type 2 diabetes (T2D),[1] and may help motivate patients to maintain treatment.
- The objective of this post-hoc analysis was to evaluate the impact of early initiation of oral semaglutide on glycemic efficacy, body weight, and achievement of targets in the PIONEER 1 trial.[2]

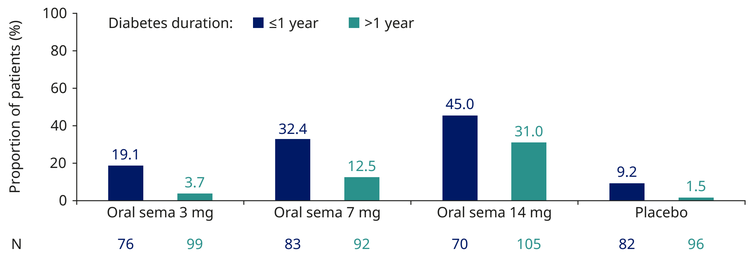
Methods

- In PIONEER 1, patients on diet and exercise were randomized to oral semaglutide 3, 7, or 14 mg once daily, or placebo.[2]
- Primary endpoints were change in baseline in HbA_{1c} and body weight at 26 weeks.
- In the current analysis, endpoints assessed at 26 weeks using the trial product estimand in patients with T2D duration ≤1 year and >1 year for comparison were:
  - HbA_{1c} (%) and body weight (kg) changes from baseline
  - Achievement of HbA_{1c} targets: <7.0%, ≤6.5%, and <6.0%
  - Achievement of composite targets:
    - HbA_{1c} <6.0% plus weight reduction ≥5%
    - HbA_{1c} ≤6.5% plus weight reduction ≥5%.

Key results

Key result

Figure 1: Achievement of near-normal HbA_{1c} (<6.0%)



Data are for the trial product estimand. Subgroup interaction between treatment (oral semaglutide vs placebo) and diabetes duration (≤1 vs >1 year) was not significant. Sema, semaglutide.

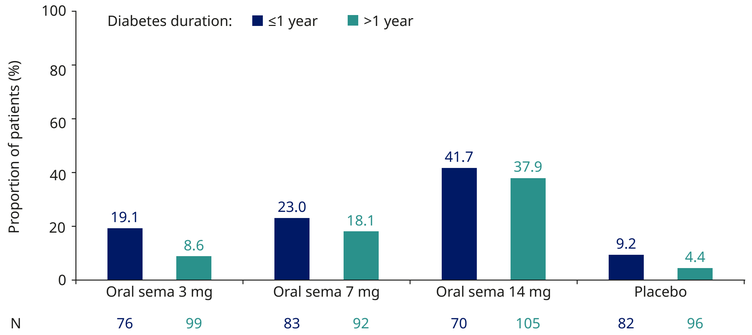
Baseline demographics (see **Poster+** slides for data):

- Patients with T2D duration ≤1 year were on average younger and had higher baseline body weight than those with duration >1 year; baseline HbA_{1c} was similar between the two subgroups. Mean T2D duration was ~4 months for the ≤1 year group and ~6 years for the >1 year group.

Glycemic and body weight outcomes:

- HbA_{1c} and body weight changes were greater with oral semaglutide 7 mg and 14 mg than placebo for both subgroups, and were greater in patients with T2D duration ≤1 year than >1 year (except for body weight with oral semaglutide 7 mg) (**Poster+** slides).
- A greater proportion of patients achieved HbA_{1c} ≤6.5% and <7.0% with oral semaglutide 3 mg and 7 mg (and placebo) in the ≤1 year than >1 year subgroups, but proportions were similar for oral semaglutide 14 mg (**Poster+** slides).
- A greater proportion of patients initiating oral semaglutide 3 mg, 7 mg, and particularly 14 mg ≤1 year after diagnosis reached near-normal HbA_{1c} (<6.0%) versus the >1-year group (**Figure 1**).

Figure 2: Achievement of composite target of HbA_{1c} ≤6.5% plus body weight loss ≥5%



Data are for the trial product estimand. Subgroup interaction between treatment (oral semaglutide vs placebo) and diabetes duration (≤1 vs >1 year) was not significant. Sema, semaglutide.

Composite targets:

- A high proportion of patients initiating oral semaglutide 14 mg with T2D duration ≤1 year reached a composite target of HbA_{1c} ≤6.5% plus body weight loss ≥5% (**Figure 2**).
- There was also greater achievement of the more stringent composite target of HbA_{1c} <6.0% plus body weight loss ≥5% with oral semaglutide 7 mg and 14 mg than placebo, and more so for patients with T2D duration ≤1 year than >1 year (see **Poster+** slides).
- Most subgroup interactions between treatment and T2D duration were not significant.

On-treatment adverse events:

- As expected, oral semaglutide was associated with more GI events than placebo (see **Poster+** slides). There was no clear or particular pattern in the incidence of adverse events, including gastrointestinal (GI) events and events leading to treatment discontinuation, by T2D duration subgroup.

Summary

- Greater and dose-dependent HbA_{1c} and weight reductions were seen for oral semaglutide 7 mg and 14 mg vs placebo, regardless of T2D duration.
- A high proportion of patients (45%) initiating oral semaglutide 14 mg within ≤1 year of T2D diagnosis reached near-normal HbA_{1c} (<6.0%)
  - Early achievement of near-normal glycemic and treatment targets may impact the course of T2D and the risk of complications.[1]
- A high proportion of patients (42%) in the oral semaglutide 14 mg ≤1 year subgroup reached the established clinical targets of HbA_{1c} ≤6.5% plus body weight reduction ≥5%.

Conclusions

- Initiation of oral semaglutide in patients within ≤1 year of T2D diagnosis resulted in robust HbA_{1c} and body weight reductions, and attainment of glycemic targets, including near-normal HbA_{1c}.
- These observations support the concept of early initiation of therapy and further study.

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References:
(**1**) American Diabetes Association. Diabetes Care 2021;44 (Suppl 1):S73–S84;
(**2**) Aroda VR, et al. Diabetes Care 2019;42:1724–1732.