Clinical And Patient-Reported Outcomes Associated With Oral Semaglutide Use In Adults With Type 2 Diabetes: A Pooled Analysis Of Six PIONEER REAL Prospective Real-World Studies

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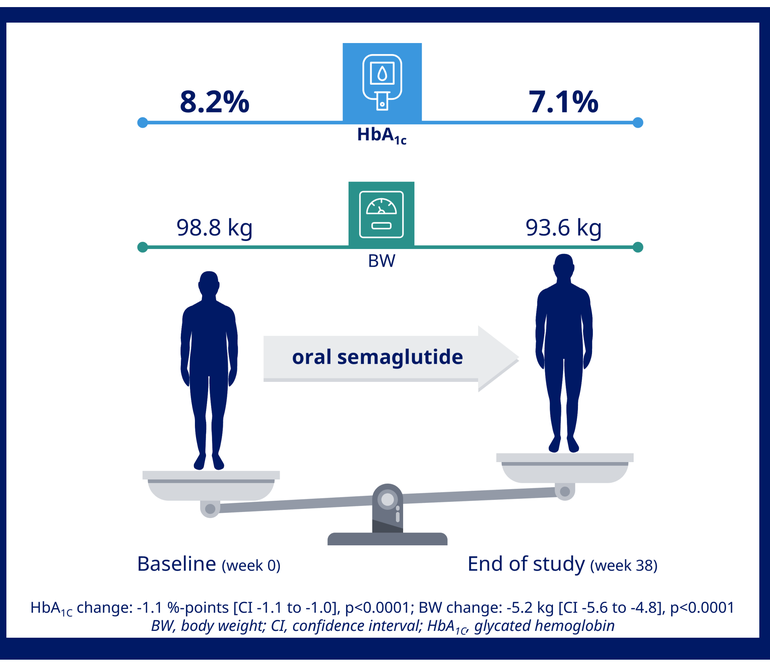
Semaglutide treatment of T2D in a real-world setting – *a pooled analysis of 6 countries*



HbA_{1c} change: -1.1 %-points [CI -1.1 to -1.0], p<0.0001; BW change: -5.2 kg [CI -5.6 to -4.8], p<0.0001
BW, body weight; CI, confidence interval; HbA_{1C}, glycated hemoglobin

Aim

Individual PIONEER REAL studies: assess clinical and participant-reported outcomes of oral semaglutide use in adults with type 2 diabetes (T2D) in routine clinical practice

Pooled analysis:

- Analyses of glycated hemoglobin (HbA_{1C}) and body weight changes as well as subgroup analyses of HbA_{1C} by baseline age (<60 years and ≥60 years) and physician setting (specialist vs. primary care)
- Treatment satisfaction assessed via Diabetes Treatment Satisfaction Questionnaires (DTSQ status and change)

Background

- Globally, more than 500 million adults were estimated to be living with diabetes in 2021 (**1**).
- Early and effective glycemic control after diagnosis prevent long-term complications for people living with T2D. Pharmacological interventions, weight loss and healthy lifestyle changes are part of the recommended treatment (**2**).
- Oral semaglutide is a glucagon-like peptide-1 receptor agonist (GLP-1RA) approved as an adjunct to diet and exercise to improve glycemic control in adults with T2D, and it may represent an attractive alternative to subcutaneous treatment.
- Safety and efficacy of oral semaglutide have been demonstrated across different T2D population groups in the PIONEER clinical development program (**3**).
- PIONEER REAL is a collection of 13 non-interventional studies aimed to complement findings from the PIONEER clinical development program by investigating the use of oral semaglutide initiated within routine clinical practice in a real-world setting of adults with T2D.
- A pooled analysis of six PIONEER REAL studies from Canada (**4**), Denmark, the Netherlands (**5**), Sweden (**6**), Switzerland (**7**), and the UK (**8**) is presented here.

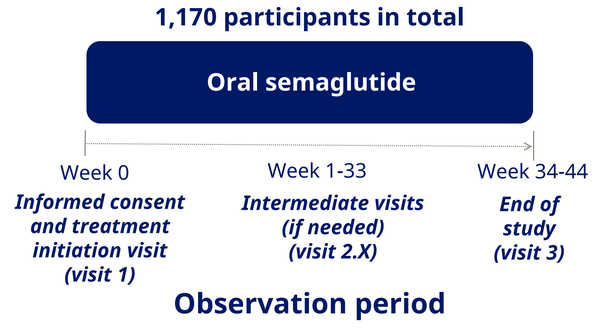
Methods

Study information

- 34-44-week, non-interventional, multi-center, single-armed, phase 4, prospective study with primary data collection
- Study participants received oral semaglutide in accordance with local clinical practice

Key inclusion criteria

- Adults diagnosed with T2D
- Decision to initiate oral semaglutide treatment made by treating physician in agreement with participant
- Available HbA_{1C} value ≤90 days prior to visit 1 or taken at visit 1 in line with local clinical practice
- Treatment naïve to injectable glucose-lowering drug(s)

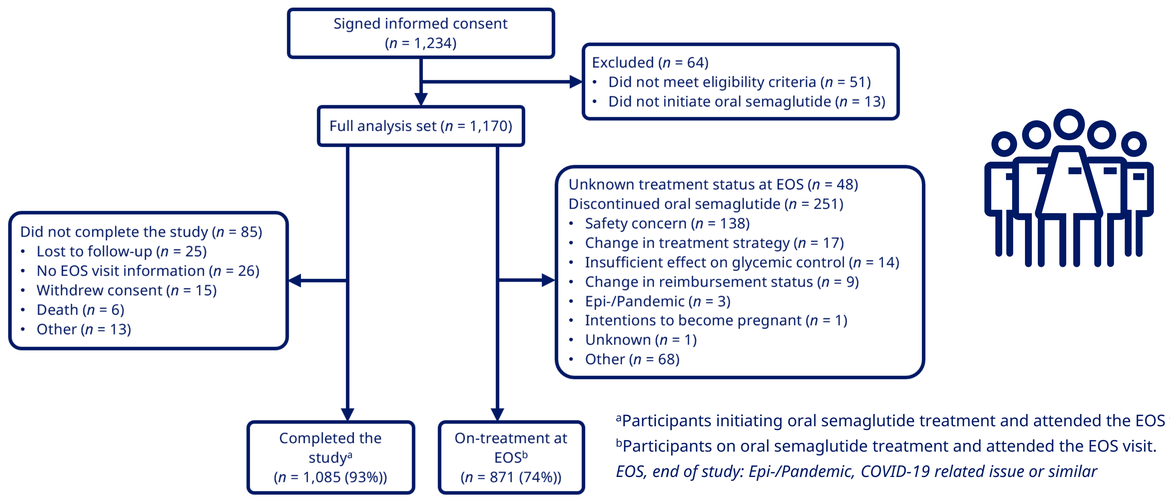


Procedures and analyses

- Data were collected from pre-existing records and during study visits. All information was documented in an electronic case report form (eCRF).
- Absolute and relative treatment satisfaction were assessed by DTSQ status (DTSQs) and DTSQ change (DTSQc), respectively (**9**). DTSQ assessments were not included in PIONEER REAL Switzerland.
- Changes in HbA_{1C} and body weight from baseline to end of study (EOS) were analyzed using a random coefficient mixed model for repeated measurements (MMRM).
- As the EOS visit could take place anytime between weeks 34 and 44, results at EOS are *estimated* for week 38 based on the MMRM.
- Tests for interaction between HbA_{1C} change and physician setting/baseline age were performed within the MMRM model.

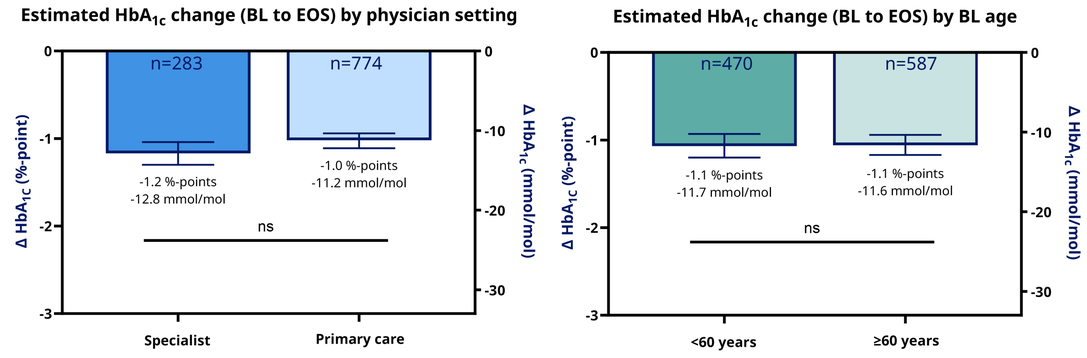
Results

- **Figure 1: Participant disposition**



[a]Participants initiating oral semaglutide treatment and attended the EOS visit.
[b]Participants on oral semaglutide treatment and attended the EOS visit.
EOS, end of study: Epi-/Pandemic, COVID-19 related issue or similar

Figure 2: Glycemic control improvement irrespective of physician setting and participant age



Left panel: Estimated HbA_{1C} change stratified by physician setting (mean with 95% confidence interval is plotted). Right panel: Estimated HbA_{1C} change stratified by baseline age (mean with 95% confidence interval is plotted).
BL, baseline; EOS, end of study; HbA_{1C}, glycated hemoglobin; n, total number of participants contributing to the statistical analysis; ns, non-significant.

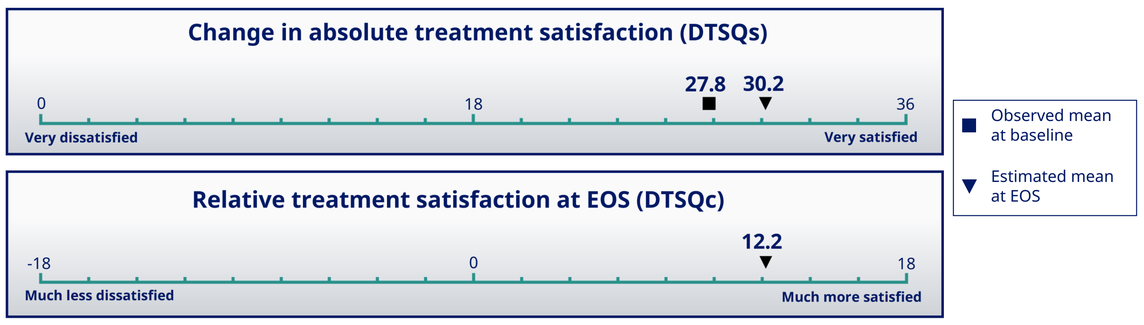
Table 1: Adverse events

	Serious			Non-serious			Total		
	N (%)	E	R	N (%)	E	R	N (%)	E	R
Adverse events	45 (3.8)	60	6.7	475 (40.6)	1053	117.1	491 (42.0)	1113	123.8
Mild	5 (0.4)	5	0.6	364 (31.1)	720	80.1	366 (31.3)	725	80.6
Moderate	20 (1.7)	25	2.8	172 (14.7)	312	34.7	188 (16.1)	337	37.5
Severe	24 (2.1)	30	3.3	14 (1.2)	20	2.2	37 (3.2)	50	5.6
Deaths	7 (0.6)	7	0.8	0	-	-	7 (0.6)	7	0.8
Self-reported severe hypoglycemia[a]	N/A	N/A	N/A	N/A	N/A	N/A	14 (1.2)	28	-

Data are for the in-study observation period, which represents the period during which participants were part of the study, regardless of oral semaglutide treatment status.
[a]Severe hypoglycemia can be defined as a severe event characterized by altered mental and/or physical functioning that requires assistance from another person for recovery.
%, percentage of participants; E, number of events; N, number of participants; N/A, not applicable; R, event rate per 100 years of observation time.

No new safety concerns observed

Figure 3: Treatment satisfaction enhancement



Top panel: Change in absolute treatment satisfaction (DTSQs) at EOS (n=663, p<0.0001). Bottom panel: Relative treatment satisfaction (DTSQc) at EOS (n=674, p<0.0001). DTSQc and DTSQs assessments were not completed in PIONEER REAL Switzerland.
DTSQc, diabetes treatment satisfaction questionnaire-change; DTSQs, diabetes treatment satisfaction questionnaire-status; EOS, end of study.

Discussion

- Results from this PIONEER REAL pooled analysis are similar to results from the PIONEER program, where oral semaglutide treatment was studied in randomized clinical studies in participants with T2D (**3**).
- Moreover, results from this pooled analysis are similar to results from the SURE multinational program, where subcutaneous semaglutide treatment was evaluated in real-world studies in participants with T2D (**10**).
- Due to the real-world setting of the individual PIONEER REAL studies, typical limitations applied, including lack of a comparator arm, the purely observational nature of the studies, as well as challenges in obtaining robust and complete datasets.

Conclusion

- Results from the PIONEER REAL pooled analysis provide broadly applicable insights to oral semaglutide treatment in routine clinical practice.
- Participants across the six PIONEER REAL studies experienced substantial enhancements in glycemic control and body weight reduction after 34-44 weeks of treatment.
- Notably, these outcomes were irrespective of physician setting or participant age and were seen alongside improvements in treatment satisfaction.

The PIONEER REAL studies are sponsored by Novo Nordisk and are registered with ClinicalTrials.gov: Canada NCT04559815, Denmark NCT04537637, The Netherlands NCT04601740, Sweden NCT04601753, Switzerland NCT04537624, and the UK NCT04862923.

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