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Real-world use of oral semaglutide in adults with type 2 diabetes

Contents

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Statistical analysis

To ensure 90% and 99% probability of detecting changes from baseline in glycated haemoglobin (HbA_{1c}) of ≥ 0.46 percentage points and ≥ 1 percentage points, respectively, 145 participants with HbA_{1c} measurements were required.

Primary, continuous secondary and exploratory endpoints were analysed using a mixed model for repeated measures or analysis of covariance (for Diabetes Treatment Satisfaction Questionnaire status [DTSQs] endpoints) on the full analysis set (FAS) (in-study observation period). Categorical secondary and exploratory endpoints were measured as proportions of participants at end of study (EOS), based on the FAS.

Analyses were performed using a crude and an adjusted model. Estimated response and change in response analyses from baseline (BL) to EOS used the BL measure being assessed (HbA_{1c}, body weight or DTSQs), age and BL body mass index as covariates and sex, number of oral glucose-lowering medications at BL, diabetes duration and study site as fixed factors with random intercept and time (slope). Time and time-squared were included as covariates in the models for change from BL in HbA_{1c} and body weight. DTSQ analyses included BL HbA_{1c} as a covariate.

A sensitivity analysis was performed for the primary endpoint using a pattern-mixture model fitted to all participants in the FAS in-study observation period.

Statistical tests were performed as two-sided tests, where $p < 0.05$ indicated statistical significance. Statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA). Statistical methodology aligns with previous PIONEER REAL studies [1, 2].

TABLE S1 Inclusion and exclusion criteria.

Inclusion criteria

For a participant to be considered eligible for inclusion in the study, all inclusion criteria must be answered 'yes'.

1. Diagnosed with type 2 diabetes.
2. Signed consent obtained before any study-related activities (study-related activities are any procedure related to recording of data according to the protocol).
3. The decision to initiate treatment with commercially available oral semaglutide was made by the patient/Legally Acceptable Representative (LAR) and the treating physician based on local label before and independently from the decision to include the patient in this study.
4. Male or female, aged ≥ 18 years at the time of signing informed consent.
5. Available HbA_{1c} value ≤ 90 days prior to the 'Informed Consent and Treatment Initiation visit' or HbA_{1c} measurement taken in relation to the 'Informed Consent and Treatment Initiation visit' if in line with local clinical practice.
6. Treatment naïve to injectable glucose-lowering drug(s). An exception is short-term insulin treatment for acute illness for a total of ≤ 14 days.

Exclusion criteria

For a participant to be considered eligible for inclusion in the study, all exclusion criteria must be answered 'no'.

1. Previous participation in this study. Participation is defined as having given informed consent in this study.
2. Treatment with any investigational drug within 30 days prior to enrolment into the study.
3. Mental incapacity, unwillingness or language barriers precluding adequate understanding or cooperation.

HbA_{1c} = glycated haemoglobin.

TABLE S2 Treatment satisfaction.

Treatment satisfaction was assessed using DTSQ scores [3, 4].

- DTSQs and DTSQc were used to measure absolute and relative treatment satisfaction, respectively, from baseline to EOS.
- DTSQs and DTSQc each contained the same eight items to measure participant satisfaction with treatment.
- In DTSQs, participants scored each item on a Likert scale from 0 (very dissatisfied) to 6 (very satisfied), except for items 2 and 3 which were rated as 0 (never) to 6 (most of the time). All item scores, except items 2 and 3, were added to give a total treatment satisfaction score (range 0–36).
- In DTSQc, participants rated their change in treatment satisfaction before and after treatment on a scale of −3 (less satisfied now) to +3 (more satisfied now), with 0 representing no change.

DTSQs/DTSQc = Diabetes Treatment Satisfaction Questionnaire status/change; EOS = end of study.

TABLE S3 Summary of medical histories.

Medical history	N (%)
Number of participants	**96**
Participants with a medical history	43 (44.8)
Participants with a CV-related medical history[a], including CKD, microalbuminuria, haemoglobinopathy and dyslipidaemia	41 (42.7)
Participants with a CV-related medical history[a]	39 (40.6)
Atrial fibrillation	3 (3.1)
Hypertension	33 (34.4)
Dyslipidaemia	16 (16.7)
Coronary heart disease	4 (4.2)
Myocardial infarction	0
Stable coronary heart disease	3 (3.1)
Unstable angina	0
Other	1 (1.0)
Revascularisation	1 (1.0)
Coronary	1 (1.0)
Carotid	0
Peripheral	0
Other	0
Chronic heart failure	0
Stroke or transient ischaemic attack	5 (5.2)
Peripheral artery disease	0
Lower limb arterial disease	0
Carotid	0
Other	0

FAS.

CKD = chronic kidney disease; CV = cardiovascular; FAS = full analysis set.

a) CV-related medical history includes atrial fibrillation, chronic heart failure, coronary heart disease, hypertension, peripheral artery disease, revascularisation, stroke or transient ischaemic attack.

TABLE S4 Concomitant medications.

Medication	At baseline n (%)	At EOS n (%)
Number of participants	96	96
Concomitant anti-diabetic medications		
Metformin	59 (61.5)	63 (65.6)
Sodium-glucose cotransporter-2 inhibitors	13 (13.5)	13 (13.5)
Dipeptidyl peptidase-4 inhibitors	1 (1.0)	0
Sulfonylureas	0	0
Alpha glucosidase inhibitors	0	0
Thiazolidinediones	0	0
Glucagon-like peptide-1 receptor agonists	0	0
Meglitinides	0	0
Other[a]	1 (1.0)	1 (1.0)
No medication	34 (35.4)	31 (32.3)
Concomitant fixed-dose combinations		
Empagliflozin and metformin	2 (2.1)	3 (3.1)
Concomitant CV medications	81 (84.4)	
Cardiac therapy	2 (2.5)	
Diuretics	25 (30.9)	
Beta-blocking agents	18 (22.2)	
Calcium channel blockers	27 (33.3)	
Agents acting on the renin–angiotensin system	50 (61.7)	
Lipid-modifying agents	62 (76.5)	
Vitamin K antagonists	2 (2.5)	
Platelet aggregation inhibitors excluding heparin	14 (17.3)	

Direct thrombin inhibitors	1 (1.2)
Direct factor Xa inhibitors	4 (4.9)
Other[a]	1 (1.2)
Concomitant hypothyroidism medication	5 (5.2)
Levothyroxine	5 (100)

CV = cardiovascular; EOS = end of study.

a) Includes medications other than listed anatomical therapeutic chemical classification system for respective indications (diabetes, CV disease, obesity, hypothyroidism).

TABLE S5 Primary and secondary endpoints at BL and EOS (in-study observation period[a]).

Endpoint	Total (N=96)
HbA_{1c}, %	
n	93
Observed mean (SD) at BL	7.9 (1.6)
Estimated mean at EOS	6.9
Estimated mean (SE) change from BL	−0.9 (0.2)
95% CI	−1.2, −0.6
p value	< 0.0001
HbA_{1c}, mmol/mol	
n	93
Observed mean (SD) at BL	62.6 (17.2)
Estimated mean at EOS	52.5
Estimated mean (SE) change from BL	−9.9 (1.6)
95% CI	−13.1, −6.6
p value	< 0.0001
Body weight, kg	
n	86
Observed mean (SD) at BL	100.9 (21.4)
Estimated mean at EOS	96.6
Estimated mean (SE) change from BL, kg	−4.4 (0.5)
95% CI	−5.4, −3.4
p value	< 0.0001
Estimated mean (SE) change from BL, %	−4.5 (0.5)
95% CI	−5.5, −3.5
p value	< 0.0001
DTSQs score, points	
n	68
Observed mean (SD) at BL	27.5 (7.6)
Estimated mean at EOS	29.4
Estimated mean (SE) change from BL	1.9 (0.8)
95% CI	0.2–3.5
p value	0.0273
DTSQc score, points	
n	68
Observed mean (SD) at BL	27.3 (6.9)
Estimated mean (SD) at EOS	10.5 (6.7)
Estimated mean (SE) change at EOS	10.5 (0.8)
95% CI	8.9–12.2

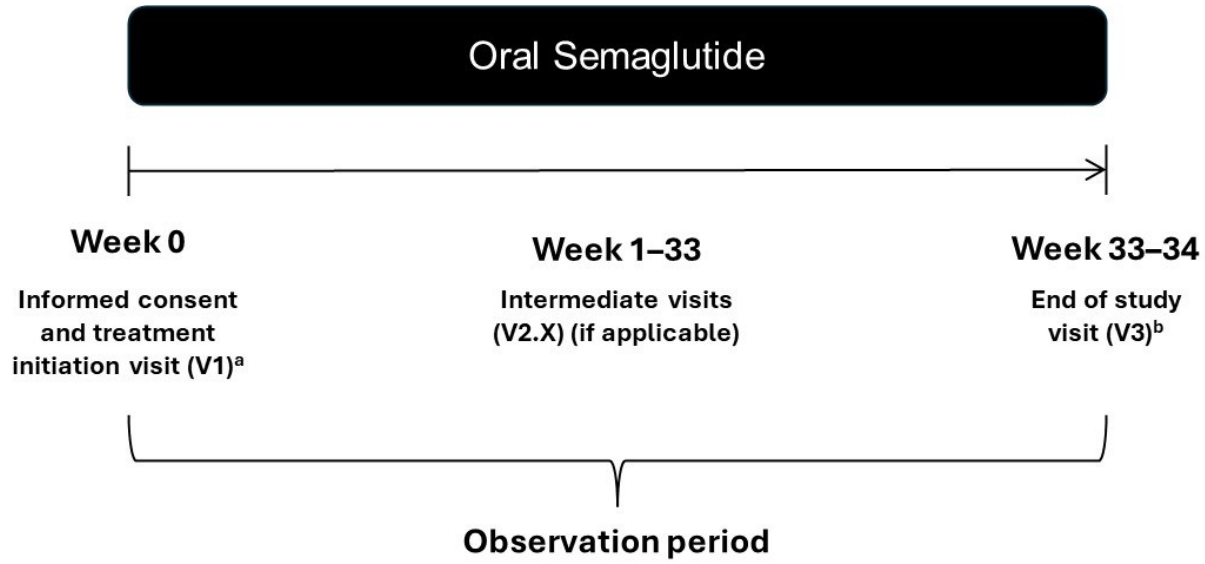
p value	< 0.0001

Patients with at least one post-baseline body weight measurement were included in the analysis. Estimated response and change in response were analysed from BL to week 38 as EOS visit spans 34–52 weeks using BL body weight, age, baseline BMI, time and time-squared as covariates and sex, oral antidiabetics at baseline, diabetes duration and site as fixed factors with random intercept and time (slope). p value reported for no mean change. For DTSQs, 0 = very dissatisfied and 36 = very satisfied. For DTSQc, −18 = much less satisfied and +18 = much more satisfied.

BL = baseline; BMI = body mass index; CI = confidence interval; DTSQc = Diabetes Treatment Satisfaction Questionnaire change; DTSQs = Diabetes Treatment Satisfaction Questionnaire status; EOS = end of study; FAS = full analysis set; HbA_{1c} = glycated haemoglobin; N = number of patients in FAS; n = number of patients in statistical analysis; SD = standard deviation; SE = standard error.

a) The in-study observation period refers to the time period when participants were considered in the study regardless of potential discontinuation of oral semaglutide.

FIGURE S1 Study design.

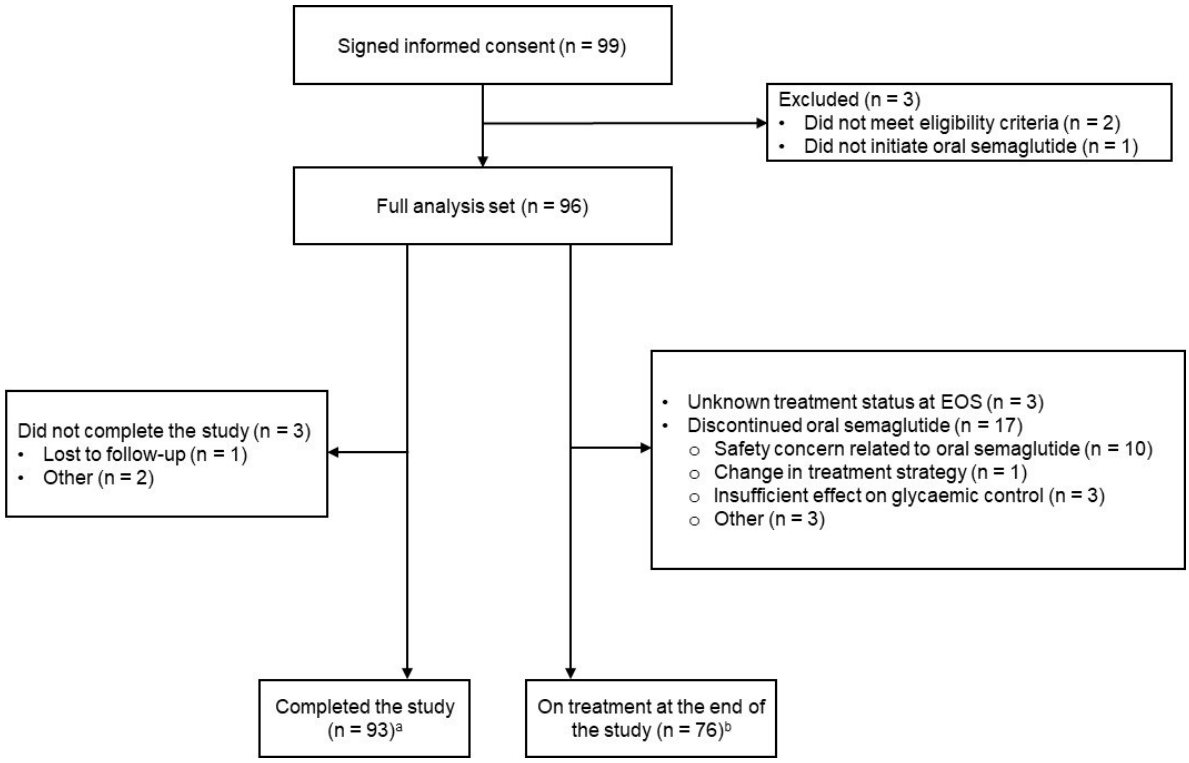


V = visit.

a) During the treatment initiation visit, participants or their legally acceptable representative provided informed consent, their medical history was collected and the reason(s) for initiating oral semaglutide were recorded by the treating physicians.

b) Owing to the COVID-19 pandemic and associated safety concerns, EOS visits outside the 34–44-week window were permitted. In instances where an HbA_{1c} measurement was unavailable in the 34–44-week window, the first HbA_{1c} measurement taken thereafter, up until the last patient last visit, was recorded.

FIGURE S2 Participant disposition.



EOS = end of study.

a) Participants who initiated oral semaglutide treatment and attended the EOS visit.

b) Participants who were receiving oral semaglutide treatment and attended the EOS visit.

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