Weight loss induced by semaglutide once weekly contributes to improved health-related quality of life and treatment satisfaction

John P. H. Wilding[1]; Helena W. Rodbard[2]; Kari T. Uusinarkaus[3]; Luc Van Gaal[4]; Thomas Hansen[5]; Anna M. L. Sandberg[5]; Sayeh Tadayon[5]; Melanie J. Davies[6]

[1]Institute of Ageing and Chronic Disease, University of Liverpool, Liverpool, UK; [2]Endocrine and Metabolic Consultants, Rockville, MD, USA; [3]DaVita Medical Group, Colorado Springs, CO, USA; [4]Antwerp University Hospital, Antwerp, Belgium; [5]Novo Nordisk A/S, Søborg, Denmark; [6]University of Leicester, Leicester, UK.

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Aim

- Semaglutide (Novo Nordisk, Denmark) is a glucagon-like peptide-1 (GLP-1) analogue approved for the once-weekly subcutaneous treatment of type 2 diabetes (T2D),[1] and has shown reductions in HbA_{1c} and body weight across the SUSTAIN clinical trial programme.[2–7]
- Health-related quality of life (HRQoL) and treatment satisfaction were evaluated in the SUSTAIN 2–5 and 7 trials using the Short Form-36 Health Survey version 2® (SF-36v2®) and Diabetes Treatment Satisfaction Questionnaire status version (DTSQs), respectively.[3–7]
- Studies have suggested that weight loss in patients with T2D may be associated with an increase in HRQoL.[8,9]
- The aim of this *post hoc* analysis was to assess if weight loss was associated with improvements in patient-reported HRQoL and treatment satisfaction in SUSTAIN 2–5 and 7.

Methods

- Changes in HRQoL (SF-36v2®) and treatment satisfaction scores (DTSQs) were evaluated in subjects who achieved ≥5% and ≥10% weight loss ('responders') vs those who did not ('non-responders') at end of treatment (30, 40, or 56 weeks) in SUSTAIN 2–5 and 7.
- The weight-loss responders were chosen to represent meaningful changes at the individual level, as weight losses of ≥5% and ≥10% are known to be clinically meaningful.[10] Estimated responder differences are evaluated in this analysis.
- Data were pooled across the trials (N=2,808; comparator data not evaluated), and presented by dose (semaglutide 0.5 mg or 1.0 mg) and overall.

Patient-reported outcome (PRO) scales

- Norm-based scoring was used for the SF-36v2®, setting the general population mean to 50 for each domain; higher and increasing scores indicate better health.
  - » Scores from the Physical Component Summary (PCS), Mental Component Summary (MCS), and all subdomains were analysed.
- The standard DTSQs scales range from 0 to 6 on a 7-point Likert scale, where 6 indicates the highest treatment satisfaction and 0 the lowest, with the exception of questions on the perception of hyperglycaemia and hypoglycaemia, where 6 indicates the lowest treatment satisfaction and 0 the highest.
  - » The overall treatment satisfaction is the sum of all scores, excluding the perception of hyperglycaemia and hypoglycaemia.

Statistical analysis

- Body weight and PROs were analysed using 'on-treatment without rescue medication' data.
  - » Missing body weight (kg) data were imputed from a mixed model for repeated measurements with treatment, region and stratum as fixed factors, and baseline value as covariate, all nested within visit.
  - » PRO data were analysed using an analysis of covariance controlled for treatment strata, and baseline values of body weight, and PROs.
- Safety was assessed using 'on-treatment' data.

Results

Baseline characteristics and demographics

- Subject disposition and baseline characteristics for SUSTAIN 2–5 and 7 are shown in Table 1.

Table 1: Subject disposition and baseline characteristics and demographics in SUSTAIN 2–5 and 7

	Semaglutide 0.5 mg	Semaglutide 1.0 mg	Semaglutide pooled (0.5 mg and 1.0 mg)
Subject disposition, n (%)			
Randomised	1,205	1,610	2,815
Exposed*	1,204 (99.9)	1,604 (99.6)	2,808 (99.8)
Trial completers*	1,128 (93.6)	1,510 (93.8)	2,638 (93.7)
Treatment completers†	1,041 (86.5)	1,339 (83.5)	2,380 (84.8)
Subjects who discontinued treatment prematurely‡	163 (13.5)	265 (16.5)	428 (15.2)
Baseline characteristics§			
Male, n (%)	647 (53.7)	845 (52.7)	1,492 (53.1)
Diabetes duration, years	7.9 (5.8)	8.6 (6.5)	8.3 (6.2)
HbA_{1c}, %	8.2 (0.9)	8.2 (0.9)	8.2 (0.9)
Body weight, kg	93.0 (21.8)	93.5 (21.9)	93.3 (21.8)
BMI, kg/m²	33.0 (6.5)	33.1 (6.7)	33.1 (6.6)

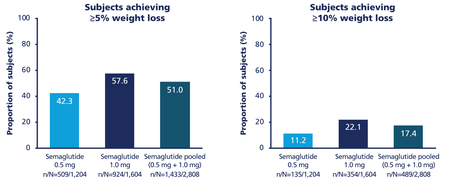
*Denominator for the percentage is the number of subjects randomised. †Denominator for the percentage is the full analysis set. §Baseline characteristics are calculated using full analysis set data; values are mean (SD) unless otherwise indicated. BMI, body mass index; n, number of subjects; SD, standard deviation.

- Overall, 82.7% of subjects receiving semaglutide completed all questions in the SF-36v2® questionnaire.
- Overall, 81.5% of subjects receiving semaglutide reported a treatment satisfaction score, and completed the perception of hyperglycaemia and perception of hypoglycaemia questions of the DTSQs.

Efficacy

- Overall, 51.0% and 17.4% of subjects achieved ≥5% and ≥10% weight loss with semaglutide, respectively (Figure 1).
- Significantly greater improvements in the overall PCS score and most of its components were reported in responders vs non-responders in the semaglutide 1.0 mg and pooled groups (Figure 2A).
- Overall treatment satisfaction was improved in responders vs non-responders in the semaglutide 1.0 mg and pooled groups (Figure 2B).
- Perception of hyperglycaemia, but not hypoglycaemia, improved in responders vs non-responders with both doses of semaglutide and in the pooled groups (Figure 2C).

Figure 1: Proportions of subjects achieving weight-loss responses in SUSTAIN 2–5 and 7



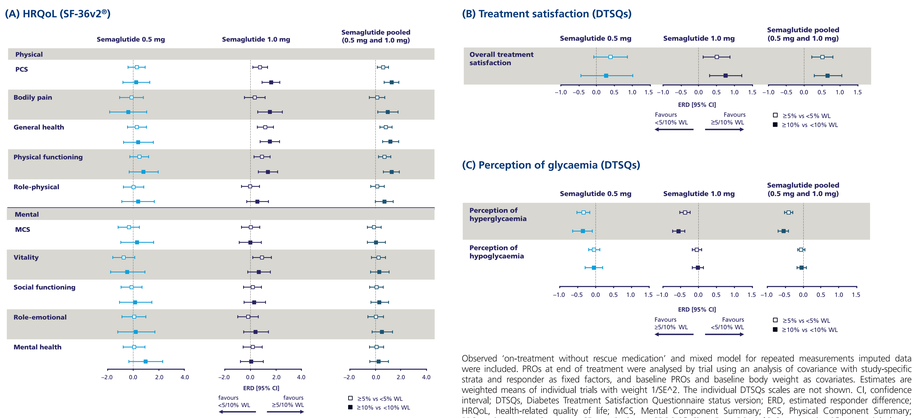
Observed 'on-treatment without rescue medication' data with missing body weight (kg) values imputed from a mixed model for repeated measurements with treatment, region, and stratum as fixed factors and baseline value as covariate, all nested within visit. All imputed continuous data were dichotomised. N, number of subjects contributing to the analysis; n, number of subjects responding.

Safety

- Overall, across SUSTAIN 2–5 and 7, similar proportions of subjects experienced adverse events (AEs) in both the semaglutide 0.5 mg and 1.0 mg dose groups.
- AEs were experienced by 70.9% and 71.7% of semaglutide 0.5 mg and 1.0 mg dose groups, respectively; 71.4% in the pooled dose group.
- The most frequent AEs were gastrointestinal, and occurred in 44.5% of subjects in the pooled treatment groups. Nausea was the most frequently reported gastrointestinal AE, followed by vomiting and constipation (occurring in 19.9%, 8.9% and 13.5% of subjects in the pooled treatment groups, respectively).
- The incidence of severe or blood glucose-confirmed hypoglycaemia was low, and occurred in 3.9% of subjects in the pooled treatment groups.
- The incidence of serious AEs was low, with similar proportions of subjects reporting them in both dose groups (7.0% in the pooled dose group).

Figure 2: Estimated responder differences for HRQoL and treatment satisfaction in SUSTAIN 2–5 and 7

Key results



Observed 'on-treatment without rescue medication' and mixed model for repeated measurements imputed data were included. PROs at end of treatment were analysed by trial using an analysis of covariance with study-specific strata and responder as fixed factors, and baseline PROs and baseline body weight as covariates. Estimates are weighted means of individual trials with weight 1/SE^2. The individual DTSQs scales are not shown. CI, confidence interval; DTSQs, Diabetes Treatment Satisfaction Questionnaire status version; ERD, estimated responder difference; HRQoL, health-related quality of life; MCS, Mental Component Summary; PCS, Physical Component Summary; PRO, patient-reported outcome; SE, standard error; SF-36v2®, Short Form-36 Health Survey version 2®; WL, weight loss.

Discussion

- This analysis found that weight loss was associated with improvements in the PCS score of SF-36v2®, overall treatment satisfaction and perception of hyperglycaemia in subjects achieving weight-loss responses vs those not achieving these responses.
  - » This association appeared to be dose-dependent for the PCS score and overall treatment satisfaction. The changes observed in the pooled semaglutide group were driven by the semaglutide 1.0 mg data.
- In all semaglutide groups, there was a significant association between weight loss and the perception of hyperglycaemia. There was no difference in the perception of hypoglycaemia, potentially due to the low rate of hypoglycaemia observed in the SUSTAIN trials.
- The safety profile of semaglutide in the SUSTAIN 2–5 and 7 trials was consistent with that of other GLP-1 receptor agonists (GLP-1RAs).[11,12]
- GLP-1RAs may offer HRQoL and treatment satisfaction benefits, which are often associated with the drugs' effects on weight.[13]
- PROs are assessed by patients, and subjective interpretations may confound results; therefore, it can be difficult to infer how changes in HRQoL are influenced by AEs.
- The results of this analysis may be also confounded in part by the greater numbers of responders in the semaglutide 1.0 mg groups than in the semaglutide 0.5 mg groups.
- The focus of this analysis was the effect of weight loss on treatment satisfaction; it did not compare the 10% vs 5% responder groups.
- The results in the present analysis are clinically relevant as they suggest that weight loss can be a driver for treatment satisfaction and improved HRQoL.

Conclusion

- Weight loss was associated with improvements in the PCS score of the SF-36v2®, overall treatment satisfaction, and the perception of hyperglycaemia across the SUSTAIN 2–5 and 7 trials.
- These data suggest that weight loss may be an important factor affecting HRQoL and treatment satisfaction improvements during T2D treatment with semaglutide.

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