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Real-World Use of Once-Weekly Semaglutide in Type 2 Diabetes: Results from SemaglUtide Real-world Evidence (SURE) Germany

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ABSTRACT

Context Efficacy and safety of once-weekly semaglutide in type 2 diabetes were established in the phase 3 SUSTAIN trials, which included patients across the continuum of type 2 diabetes care. It is useful to complement these findings with real-world evidence.

Objective SURE Germany evaluated once-weekly semaglutide in a real-world type 2 diabetes patient population.

Design/setting The prospective observational study was conducted at 93 clinical practices in adults with ≥ 1 documented glycated haemoglobin value ≤ 12 weeks before initiation of semaglutide.

Intervention Once-weekly semaglutide was prescribed at the physicians' discretion.

Main outcomes The primary endpoint was change in glycated haemoglobin from baseline to end-of-study (~30 weeks). Secondary endpoints included changes in body weight and patient-reported outcomes. All adverse events were systematically collected and reported, including patient-reported documented and/or severe hypoglycaemia.

Results Of 779 patients in the full analysis set, 669 (85.9 %) completed the study on treatment with semaglutide, comprising the effectiveness analysis set. In this data set, estimated mean changes in glycated haemoglobin and body weight from baseline to end-of-study were −1.0 %point (−10.9 mmol/mol; $P < 0.0001$) and −4.5 kg (−4.2 %; $P < 0.0001$). Sensitivity analyses supported the primary analysis. Improvements were observed in other secondary endpoints, including patient-reported outcomes. No new safety concerns were identified.

Conclusions In a real-world population in Germany, patients with type 2 diabetes treated with once-weekly semaglutide experienced clinically significant improvements in glycaemic control and body weight. These results support the use of once-weekly semaglutide in routine clinical practice in adult patients with type 2 diabetes in Germany.

Introduction

More than 8 million people in Germany have type 2 diabetes (T2D), accounting for about 95 % of all diabetes cases [1]. The goals of T2D treatment are to prevent or delay complications and to maintain quality of life via glycaemic control and cardiovascular (CV) risk factor management [2]. The American Diabetes Association (ADA) Standards of Medical Care in Diabetes – 2022 guideline, [3] joint consensus reports from the ADA and the European Association for the Study of Diabetes (EASD) [4, 5] recommend individualized HbA_{1c} treatment targets, with an initial focus on cardiorenal risk reduction for patients with established or at high risk of developing cardiorenal disease. The national care guideline for T2D includes similar recommendations [6]. These guidelines recommend that an individualized HbA_{1c} target range is agreed upon based on considerations such as age and lifestyle [6]. The international and German guidelines also make recommendations about treatment options based on patient characteristics, including the presence of comorbidities, risk of hypoglycaemia, the need for weight loss and patient preference. For example, they suggest that patients at high risk of CV disease are treated with a glucagon-like peptide-1 receptor agonist (GLP-1RA) or sodium-glucose cotransporter-2 inhibitor (SGLT-2i) with proven CV benefits to reduce the risk of CV events [1–3].

GLP-1RAs reduce HbA_{1c} in a glucose-dependent manner and, thus, are associated with a low risk of hypoglycaemia [7]. GLP-1RAs also reduce body weight [8]. Semaglutide (Novo Nordisk A/S, Denmark) is a long-acting GLP-1RA, suitable for once-weekly (OW) subcutaneous (s.c.) dosing, with 0.5 and 1.0 mg doses approved by many regulatory authorities, including the US Food and Drug Administration and European Medicines Agency, to improve glycaemic control in adults with T2D [9–11]. The efficacy and safety of OW semaglutide 0.5 and 1.0 mg across the continuum of care in patients with T2D were established in the phase 3 SUSTAIN clinical trial programme [12–20]. In these trials, semaglutide consistently demonstrated superiority for reductions in HbA_{1c} and body weight, compared with placebo and a wide range of active comparators, including basal insulin glargine and other GLP-1RAs; its safety profile was similar to that of other GLP-1RAs [10–18]. In SUSTAIN 6, in patients with T2D and high CV risk, treatment with semaglutide 0.5 and 1.0 mg resulted in a significant reduction in the risk for major adverse CV events (MACE; hazard ratio 0.74, 95 % confidence interval [CI] 0.58 to 0.95, $P < 0.001$ for noninferiority and $P = 0.02$ for superiority) [21].

In randomized controlled trials (RCTs), such as the SUSTAIN trials, strict inclusion and exclusion criteria often result in trial populations that are not fully representative of patient populations encountered in daily clinical practice. While RCTs provide information on the efficacy of a drug when taken as intended, real-world evidence (RWE) studies provide evidence of the effectiveness of a drug when taken in routine clinical practice in a patient population representative of a wide range of clinical scenarios [22]. RWE studies can, therefore, complement the findings of RCTs and help to provide a complete picture of the advantages and disadvantages of medications during real-world use.

The SemaglUtide Real-world Evidence (SURE) Germany study was a multicentre, prospective, open-label, observational study investigating OW semaglutide in patients with T2D in routine clinical practice in Germany. SURE Germany is part of the SURE programme, which consists of nine separate observational RWE studies investigating OW semaglutide in routine clinical practice across 10 countries (Canada, Denmark/Sweden, France, Germany, Italy, the Netherlands, Spain, Switzerland, and the United Kingdom) [23–26].

Methods

Study design

SURE Germany was a prospective, open-label, observational study of approximately 30 weeks duration. The study assessed OW semaglutide in adult patients with T2D in routine clinical practice in Germany. The decision to initiate treatment with OW semaglutide or switch to semaglutide from another GLP-1RA was at the discretion of the treating physician and was made independently of the decision to include the patient in the study.

OW semaglutide was to be administered subcutaneously via a standard prefilled pen injector, according to routine clinical practice. The treating physician decided the maintenance dose of semaglutide and any subsequent changes to it. Treatment discontinuation was allowed at any time during the study at the physician's discretion, as was the prescription of diet and exercise and other antihyperglycaemic drugs.

During the initiation visit (visit 1 or 'baseline' at week 0), signed informed consent was obtained and treatment was initiated. This was followed by a number of intermediate visits according to local clinical practice (visits 2 to 5 from weeks 1 to 27), and an end-of-study (EOS) visit (visit 6) between weeks 28 and 38.

The study was conducted in compliance with the Declaration of Helsinki [27] and the Guidelines for Good Pharmacoepidemiology Practices [28]. The study received ethical approval from the Ärztekammer Nordrhein Ethik-Kommission (number 2019393). Patients provided signed informed consent before the commencement of any study-related activities. SURE Germany is registered with ClinicalTrials.gov, NCT04261933.

Study population

Patients from 93 sites in Germany were included, with the first visit of the first patient on 13 February 2020 and the last visit of the last patient on 25 May 2021. Male and female adult patients (age ≥ 18 years) who had been diagnosed with T2D at least 12 weeks prior to inclusion were eligible and were required to have an available and documented HbA_{1c} value ≤ 12 weeks prior to initiation of semaglutide. Exclusion criteria were: mental incapacity, unwillingness, or language barriers precluding adequate understanding or cooperation; treatment with any investigational drug within 90 days prior to enrolment into the study; hypersensitivity to semaglutide or to any of the excipients; and previous provision of signed informed consent in a SURE study.

Endpoints

The primary endpoint was the change from baseline to EOS in HbA_{1c} (%-point and mmol/mol). Secondary supportive endpoints included: the change from baseline to EOS in body weight (kg and %) and waist circumference (cm); the proportion of patients at EOS achiev-

ing HbA_{1c} targets < 8.0 % (64 mmol/mol), < 7.5 % (59 mmol/mol), and < 7.0 % (53 mmol/mol); the proportion of patients at EOS achieving an HbA_{1c} reduction ≥ 1 %-point from baseline; the proportion of patients at EOS achieving weight loss ≥ 3 % or ≥ 5 % from baseline; the proportion of patients at EOS achieving a composite endpoint of HbA_{1c} reduction ≥ 1 %-point and weight loss ≥ 3 %; and the proportion of patients who completed the study under treatment with semaglutide.

The study also included an assessment of patient-reported outcomes of treatment satisfaction and health-related quality of life (HRQoL). Change from baseline to EOS in the Diabetes Treatment Satisfaction Questionnaire status (DTSQs) score, which provides a measure of how satisfied patients are with their current diabetes treatment, was assessed, as was the DTSQ change (DTSQc) score at EOS, which compares the experience of the current treatment with previous treatment. HRQoL was assessed by the change from baseline to EOS in the Short-Form 36 Health Survey version 2 (SF-36v2) physical (PCS) and mental (MCS) summary component scores.

Prespecified exploratory assessments included: the weekly semaglutide dose at EOS; the proportion of patients who did not add a new antihyperglycaemic agent(s) to treatment with semaglutide at any time during the study; the proportion of patients deemed by the physician at EOS to have achieved clinical success in relation to the reason for initiating semaglutide treatment (yes/no); and the number of severe or documented hypoglycaemic episodes.

Change from baseline to EOS in systolic blood pressure (SBP) and diastolic blood pressure (DBP) by baseline blood pressure (BP) tertiles and the change from baseline to EOS in lipid parameters (high-density lipoprotein [HDL] cholesterol, low-density lipoprotein [LDL] cholesterol, total cholesterol, and triglycerides) were assessed as *post hoc* endpoints.

Safety

Adverse events (AEs) were to be reported by the treating physicians; all AEs occurring between the obtainment of consent and the EOS visit were systematically collected and reported. All episodes of patient-reported documented and/or severe hypoglycaemia were also recorded. Severe hypoglycaemia was defined as an episode of hypoglycaemia requiring the assistance of another person to actively administer carbohydrate or glucagon or take other corrective actions. Patient-reported documented hypoglycaemia was to be reported. Discontinuations and AEs in BP tertiles during the study observation period were analyzed *post hoc*.

Statistical analysis

Descriptive statistics (mean ± standard deviation [SD], median, range for continuous variables, and proportion for categorical variables) were used to describe patient characteristics at the time of semaglutide initiation. The full analysis set (FAS) included all patients who provided signed informed consent and initiated treatment with semaglutide. The effectiveness analysis set (EAS) included all patients who completed the study and received treatment with semaglutide at EOS, as assessed by the treating physician. In addition, two observation periods (in-study and on-treatment) were defined for the FAS: in-study was the time period during which patients were considered to be in the study, regardless of semaglutide treatment status, and on-treatment was the time period during which patients were considered as being treated with semaglutide.

The primary analysis of the primary and secondary endpoints was based on the EAS and used an analysis of covariance (ANCOVA) adjusted model with change from baseline as the dependent variable, excluding patients with missing information at EOS. These results are summarized as the number of patients with available values, least-squares means estimates for change from baseline, and associated two-sided 95 % CIs and *P*-values, as appropriate.

Sensitivity analyses of the primary and secondary endpoints were based on the FAS and used a mixed model for repeated measurements (MMRM) for the in-study and on-treatment observation periods. These analyses were performed to assess the impact of missing data in the primary analysis, from which patients were excluded if they had not completed the study, had discontinued treatment, or had missing information at EOS.

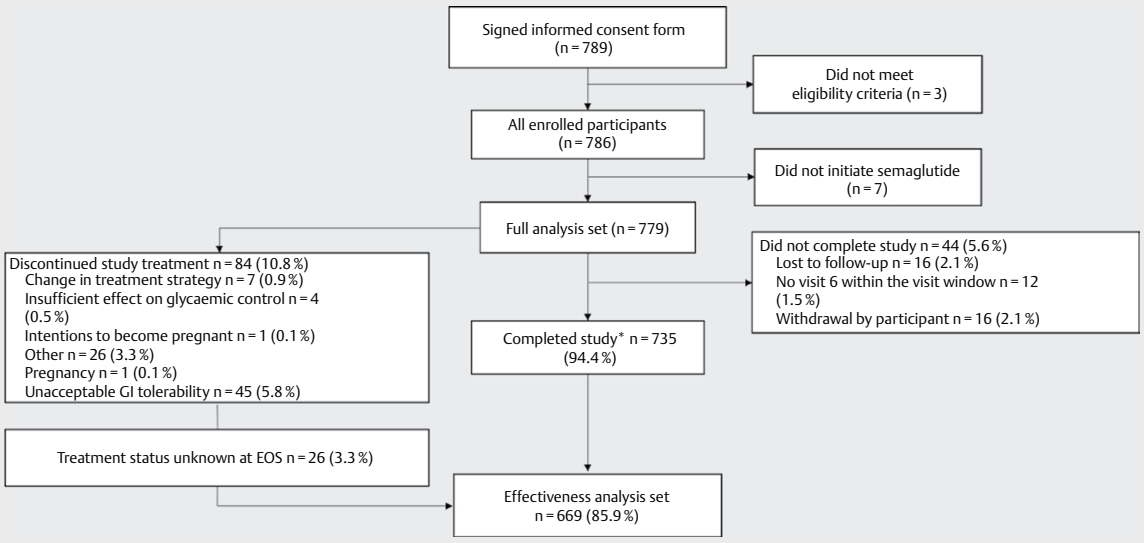
Data were analyzed for the total population and for the following predefined subgroups: pre-initiation use of an oral antihyperglycaemic drug (OAD) or OADs as the only antihyperglycaemic medication (OAD only); pre-initiation use of a GLP-1RA, irrespective of other medication; and pre-initiation use of insulin ± OAD(s) without GLP-1RA. *Post hoc* analyses of BP and lipids were performed using analyses similar to those for the primary analyses of the primary endpoint. *Post hoc* analyses were performed to investigate the impact of baseline HbA_{1c} (≤ 7.0 %, > 7.0– < 8.5 %, ≥ 8.5 % and > 9.0 %) or baseline body mass index (BMI: ≤ 30, > 30 and > 35 kg/m^2) on the primary endpoint, change in HbA_{1c}, and the secondary supportive endpoint, change in body weight, using the same methodology as for the primary endpoint (adjusted ANCOVA in the EAS). Safety was analyzed for the in-study period between informed consent and the final follow-up visit/EOS visit.

Results

Patient disposition and baseline characteristics

Patient disposition is shown in ▶ **Fig. 1**. Of 789 patients who were enrolled and provided signed informed consent, three did not meet the eligibility criteria and seven did not initiate treatment with semaglutide; the FAS therefore comprised 779 patients. A total of 735 (94.4 %) patients completed the study. Of the 779 patients in the FAS, 669 patients (85.9 %) completed the study on treatment with semaglutide, 84 patients (10.8 %) discontinued study treatment, and 26 patients (3.3 %) had an unknown treatment status at EOS; the EAS therefore comprised 669 patients.

Baseline characteristics in the FAS were generally similar across the previous medication subgroups (OAD only, GLP-1RA, and insulin ± OAD without GLP-1RA; ▶ **Table 1**). Forty-two percent of patients were in the insulin ± OAD without GLP-1-RA subgroup and 19 % of patients were in the GLP-1RA subgroup (**Supplementary Fig. 1**). The overall mean HbA_{1c} level was 8.0 %, with 164 (21.1 %) patients having an HbA_{1c} < 7.0 %; mean diabetes duration for the overall population was 11.4 years. A total of 643 (82.5 %) patients had hypertension and 488 (62.6 %) had dyslipidaemia. The most



▶ **Fig. 1** Patient disposition. Abbreviations: EOS: end of study; GI: gastrointestinal. * Patients who initiated the semaglutide treatment and attended the EOS visit.

▶ **Table 1** Demographics and baseline characteristics of patients by baseline medication subgroups from the FAS.

Characteristics	OAD only (n = 282)	GLP-1RA (n = 148)	Insulin ± OAD without GLP-1RA (n = 329)	No anti-diabetes medication (n = 20)	Total (N = 779)
Age, years	57.6 (9.89)	60.5 (10.35)	62.5 (9.77)	56.0 (10.06)	60.2 (10.16)
Female, n (%)	121 (42.9)	74 (50.0)	134 (40.7)	13 (65.0)	342 (43.9)
Baseline HbA_{1c}, %	8.0 (1.54)	7.6 (1.09)	8.2 (1.35)	7.3 (1.27)	8.0 (1.40)
Baseline HbA_{1c}, mmol/mol	63.8 (16.84)	59.2 (11.94)	66.6 (14.81)	56.3 (13.86)	63.9 (15.34)
Fasting plasma glucose, mg/dL	174.3 (59.29)	149.7 (42.53)	174.1 (61.97)	160.5 (57.71)	169.3 (58.33)
Body weight, kg	106.4 (22.71)	105.5 (21.87)	108.9 (22.92)	113.2 (19.18)	107.5 (22.58)
Body mass index, kg/m^2	35.7 (6.66)	36.3 (7.05)	36.9 (6.71)	39.2 (7.04)	36.4 (6.79)
Waist circumference, cm	118.9 (14.45)	120.0 (15.56)	123.1 (15.23)	121.9 (11.29)	121.0 (15.02)
Diabetes duration, years	8.2 (6.32)	13.2 (7.16)	13.6 (7.66)	5.1 (5.63)	11.4 (7.55)
eGFR, mL/min/1.73 m^2	83.2 (21.44)	82.6 (19.63)	76.5 (21.08)	83.1 (26.02)	80.3 (21.22)
Starting dose of semaglutide, n (%)					
0.25 mg	258 (91.5)	81 (54.7)	298 (90.6)	20 (100.0)	657 (84.3)
0.5 mg	23 (8.2)	53 (35.8)	28 (8.5)	0	104 (13.4)
1.0 mg	1 (0.4)	14 (9.5)	3 (0.9)	0	18 (2.3)
Reasons to initiate semaglutide, n (%)*					
Improve glycaemic control	228 (80.9)	115 (77.7)	284 (86.3)	13 (65.0)	640 (82.2)
Weight reduction	231 (81.9)	134 (90.5)	277 (84.2)	17 (85.0)	659 (84.6)
Issues with hypoglycaemia	2 (0.7)	3 (2.0)	12 (3.6)	0	17 (2.2)
Address cardiovascular risk factors	72 (25.5)	61 (41.2)	112 (34.0)	4 (20.0)	249 (32.0)
Simplify the current treatment regimen	16 (5.7)	43 (29.1)	42 (12.8)	3 (15.0)	104 (13.4)
Convenience	8 (2.8)	17 (11.5)	17 (5.2)	1 (5.0)	43 (5.5)
Other	2 (0.7)	2 (1.4)	7 (2.1)	1 (5.0)	12 (1.5)

Abbreviations: eGFR: estimated glomerular filtration rate; GLP-1RA: glucagon-like peptide-1 receptor agonist; FAS: full analysis set; n/N: number of patients; OAD: oral antihyperglycaemic drug; SD: standard deviation. *More than one reason could be chosen. Values are mean (SD) unless otherwise specified.

▶ **Table 2** Change from baseline to EOS in HbA_{1c}, body weight, and waist circumference in the EAS.

Endpoint	OAD only	GLP-1RA	Insulin ± OAD without GLP-1RA	No anti-diabetes medication*	Total
HbA_{1c}					
Patients analyzed, n	232	130	271	16	649
Observed mean at baseline (SD)					
%-point	8.0 (1.47)	7.6 (1.09)	8.2 (1.38)	7.4 (1.38)	8.0 (1.38)
mmol/mol	64.2 (16.09)	59.1 (11.93)	66.5 (15.04)	57.0 (15.05)	63.9 (15.12)
Observed mean at EOS (SD)					
%-point	6.8 (0.94)	7.1 (1.06)	7.2 (0.99)	6.4 (0.67)	7.0 (1.00)
mmol/mol	50.7 (10.26)	53.9 (11.63)	55.1 (10.78)	46.2 (7.32)	53.1 (10.92)
Change from baseline to EOS (SD)					
%-point	−1.2 (0.05)	−0.5 (0.06)	−1.0 (0.05)		−1.0 (0.03)
mmol/mol	−13.5 (0.58)	−5.2 (0.64)	−11.4 (0.60)		−10.9 (0.36)
[95 % CI]					
%-point	[−1.34 to −1.13]	[−0.59 to −0.36]	[−1.15 to −0.93]		[−1.06 to−0.93]
mmol/mol	[−14.64 to −12.37]	[−6.45 to −3.91]	[−12.54 to −10.19]		[−11.59 to−10.17]
P-value	< 0.0001	< 0.0001	< 0.0001		< 0.0001
Body weight					
Patients analyzed, n	233	132	275	17	657
Observed mean at baseline (SD)					
kg	106.4 (22.71)	105.9 (22.34)	109.8 (22.20)	110.4 (19.28)	107.8 (22.36)
Observed mean at EOS (SD)					
kg	101.3 (22.87)	103.2 (22.68)	105.1 (22.33)	105.5 (17.78)	103.4 (22.51)
Change from baseline to EOS (SD)					
kg	−5.1 (0.35)	−2.7 (0.38)	−4.7 (0.36)		−4.5 (0.21)
%	−4.9 (0.33)	−2.6 (0.35)	−4.3 (0.33)		−4.2 (0.20)
[95 % CI]					
kg	[−5.81 to−4.45]	[−3.47 to −1.98]	[−5.42 to−4.00]		[−4.88 to−4.04]
%	[−5.59 to−4.30]	[−3.34 to −1.94]	[−4.99 to−3.67]		[−4.60 to−3.81]
P-value	< 0.0001	< 0.0001	< 0.0001		< 0.0001
Waist circumference, cm					
Patients analyzed, n	164	91	202	13	470
Observed mean at baseline (SD)	118.5 (14.20)	120.6 (16.28)	123.0 (14.49)	119.3 (10.91)	120.9 (14.76)
Observed mean at EOS (SD)	113.5 (14.93)	117.2 (16.50)	117.6 (15.06)	117.3 (10.58)	116.1 (15.28)
Change from baseline to EOS (SD)	−5.0 (0.49)	−3.4 (0.65)	−5.4 (0.46)		−4.8 (0.30)
[95 % CI]	[−6.00 to −4.05]	[−4.65 to −2.08]	[−6.31 to −4.48]		[−5.37 to −4.18]
P-value	< 0.0001	< 0.0001	< 0.0001		< 0.0001

Abbreviations: BMI: body mass index; BW: body weight; CI: confidence interval; DPP-4i: dipeptidyl peptidase-4 inhibitor; EAS: effectiveness analysis set; EOS: end of study; GLP-1RA: glucagon-like peptide-1 receptor agonist; n: number of patients; OAD: oral antihyperglycaemic drug; SD: standard deviation; T2D: type 2 diabetes; WC: waist circumference. * Observed mean. Data were analyzed using an adjusted analysis of covariance model, with a change from baseline in HbA_{1c}, BW, WC, analyzed among the patients on semaglutide at the EOS visit. The primary analysis of the primary endpoint included baseline value, T2D duration, age, BMI, pre-initiation use of GLP-1RA, pre-initiation use of DPP-4i, pre-initiation use of insulin, number of OADs used pre-initiation (0–1/2 +), and sex as covariates.

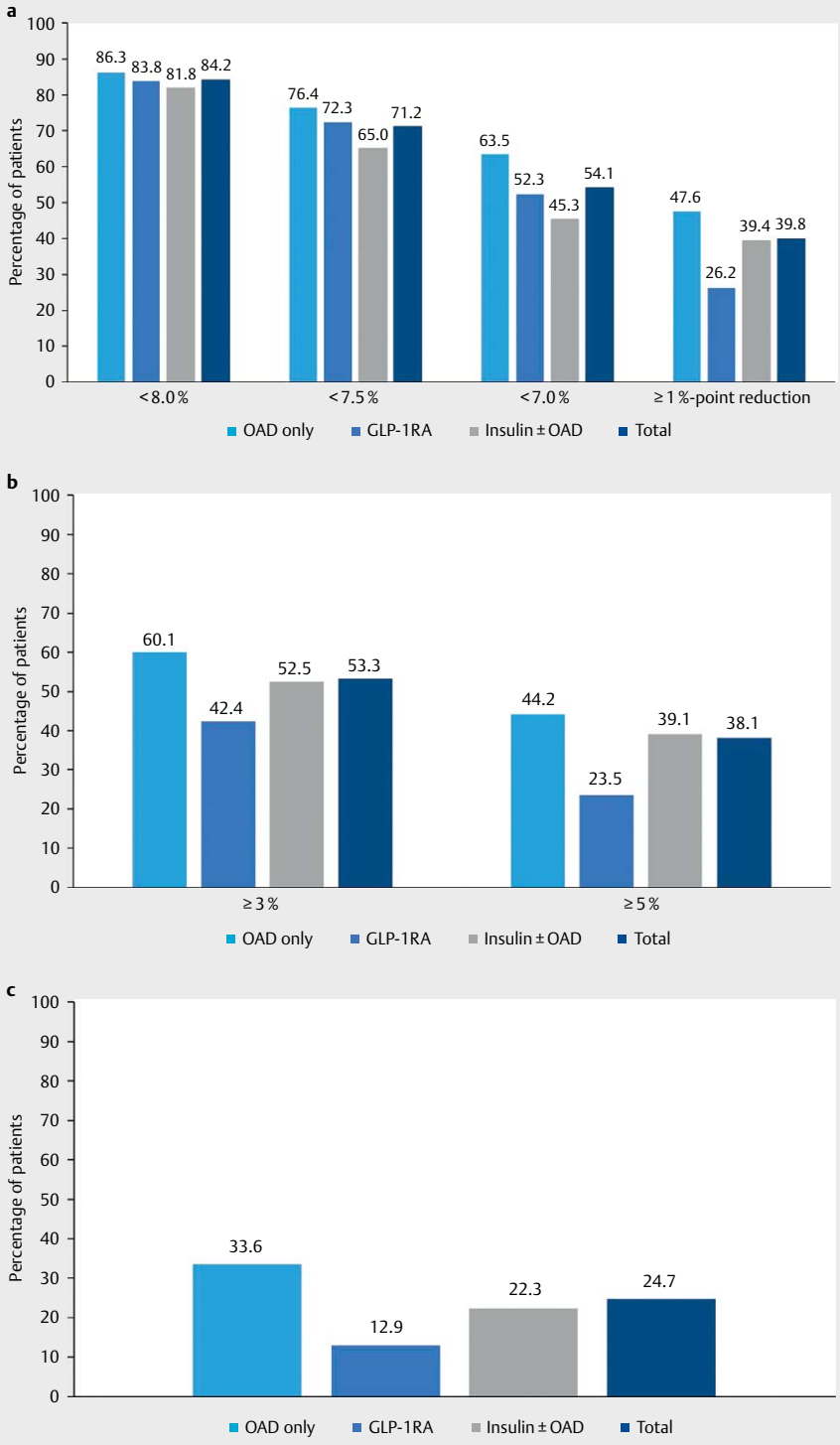
common reason for initiating OW semaglutide, other than to improve glycaemic control (n = 640, 82.2 %), was weight reduction (n = 659, 84.6 %; ▶ **Table 1**). The majority of patients in the FAS were taking metformin (n = 599; 76.9 %); 14 (1.8 %) were taking sulphonylurea and 385 (49.4 %) had basal insulin.

HbA_{1c}

Overall, patients experienced reductions in HbA_{1c}. In the EAS, the estimated mean change in HbA_{1c} from baseline (8.0 % [63.9 mmol/mol]) to EOS (7.0 % [53.1 mmol/mol]) was −1.0 %-point (−10.9 mmol/mol; [95 % CI −1.06 to −0.93]; $P < 0.0001$; ▶ **Table 2**). The primary analysis in the EAS was supported by the MMRM in-study sensitivity analysis of the FAS, which showed an HbA_{1c} change of −1.0 %-point [95 % CI −1.11 to −0.99], corresponding to −11.5 mmol/mol [95 % CI −12.12 to−10.79] ($P < 0.0001$). Results were similar to the sensitivity analyses evaluating the influence of patients who did not complete the study, had missing HbA_{1c} data at EOS or had discontinued treatment. Overall, at EOS, 84.2 % (n = 550), 71.2 % (n = 465) and

54.1 % (n = 353) of patients achieved HbA_{1c} < 8.0 % (64 mmol/mol), < 7.5 % (59 mmol/mol), and < 7.0 % (53 mmol/mol), respectively (▶ **Fig. 2a**). Furthermore, 39.8 % (n = 260) of patients achieved an HbA_{1c} reduction of ≥ 1 %-point.

When evaluated according to baseline HbA_{1c}, in the EAS, mean changes from baseline in HbA_{1c} were −0.2 %-points, −0.8 %-points, −2.0 %-points and −2.6 %-points in patients with baseline HbA_{1c} ≤ 7.0 %, > 7.0–< 8.5 %, ≥ 8.5 % and > 9.0 %, respectively (all P < 0.0001;



▶ **Fig. 2** Proportions of patients achieving prespecified targets at EOS (total and by medication subgroup from the EAS): (**a**) HbA_{1c} targets of < 8.0 %, < 7.5 %, < 7.0 %, and ≥ 1.0 %-point reduction, (**b**) weight-loss responses of ≥ 3 % and ≥ 5 %, (**c**) composite endpoint of HbA_{1c} reduction ≥ 1 %-point and weight loss ≥ 3 %. Abbreviations: EAS: effectiveness analysis study; EOS: end of study; GLP-1RA: glucagon-like peptide-1 receptor agonist; OAD: oral antihyperglycaemic drug; GI: gastrointestinal; N: number of patients; NA: not applicable; SADR: serious adverse drug reaction.

Supplementary Table 1). Mean changes in HbA_{1c} in subgroups according to treatment at baseline were −1.2 %-points, −0.5 %-point, and −1.0 %-point in, respectively, the OAD only, GLP-1RA, and insulin ± OAD without GLP-1RA subgroups (all $P < 0.0001$) (▶ **Table 2**). An HbA_{1c} reduction of ≥ 1 %-point was achieved by 47.6 % (n = 111), 26.2 % (n = 34), and 39.4 % (n = 108) of patients in, respectively, the OAD only, GLP-1RA, and insulin ± OAD without GLP-1RA subgroups (▶ **Fig. 2a**). When evaluated according to baseline BMI, in the EAS, mean changes from baseline in HbA_{1c} were −1.1 %-points, −1.0 %-point, and −1.0 %-point in patients with baseline BMI ≤ 30 kg/m², > 30 kg/m² and > 35 kg/m², respectively (all $P < 0.0001$; **Supplementary Table 1**).

Body weight and waist circumference

In the EAS, the estimated mean change in body weight from baseline (107.8 kg) to EOS (103.4 kg) was −4.5 kg [95 % CI −4.88 to −4.04], corresponding to a relative body weight reduction of −4.2 % [95 % CI −4.60 to −3.81] ($P < 0.0001$) (▶ **Table 2**). Sensitivity analyses supported these results. The proportion of patients achieving ≥ 3 % and ≥ 5 % weight loss was 53.3 % and 38.1 %, respectively (▶ **Fig. 2b**). The estimated mean change from baseline to EOS in waist circumference was −4.8 cm [95 % CI −5.37 to −4.18] from 120.9 cm at baseline to 116.1 cm at EOS ($P < 0.0001$) (▶ **Table 2**).

When evaluated according to baseline treatment subgroups, changes in body weight were observed in the OAD only, GLP-1RA, and insulin ± OAD without GLP-1RA subgroups (all $P < 0.0001$) (▶ **Table 2**). The proportions of patients achieving ≥ 3 % and ≥ 5 % weight loss ranged from 42.4 % to 60.1 % and 23.5 % to 44.2 %, respectively, in the subgroups according to treatment at baseline (▶ **Fig. 2b**). Changes in waist circumference were also observed in the OAD only, GLP-1RA, and insulin ± OAD without GLP-1RA subgroups (all $P < 0.0001$) (▶ **Table 2**).

When evaluated according to baseline BMI, in the EAS, mean changes from baseline in body weight were −2.7 kg, −4.8 kg, and −4.9 kg in patients with baseline BMI ≤ 30 kg/m², > 30 kg/m², and > 35 kg/m², respectively (all $P < 0.0001$; **Supplementary Table 1**).

Composite endpoint

The proportion of patients achieving the composite endpoint of both an HbA_{1c} reduction ≥ 1 %-point and weight loss ≥ 3 % at EOS was 24.7 % in the EAS overall and 33.6 %, 12.9 %, and 22.3 %, respectively, in the OAD only, GLP-1RA, and insulin ± OAD without GLP-1RA subgroups (▶ **Fig. 2c**).

Patient-reported outcomes

In the EAS, there was a significant improvement in the SF-36v2 PCS score, with an estimated change from baseline to EOS of 2.2 [95 % CI 1.64 to 2.70] (**Supplementary Table 2**). Similar improvements were observed in all subgroups. There was a significant improvement in the SF-36v2 MCS score, with an estimated change from baseline to EOS of 0.8 [95 % CI 0.18 to 1.43] (**Supplementary Table 2**). SF-36v2 MCS scores indicated a trend towards improvement in all subgroups.

There was a significant improvement in DTSQs, with an estimated change from baseline to EOS in DTSQs score of 2.9 [95 % CI 2.58 to 3.32] (**Supplementary Table 2**). Similar improvements were observed in all subgroups. Overall, at EOS, the estimated mean DTSQc score was 13.4 [95 % CI 12.96 to 13.79], with similar scores in all the subgroups (**Supplementary Table 2**).

Semaglutide dose at EOS

In the FAS, the proportion of patients who completed the study on treatment with semaglutide was 85.9 % in the overall population and 84.4 %, 90.5 %, and 85.1 % in, respectively, the OAD, GLP-1RA, and insulin ± OAD without GLP-1RA subgroups.

In the EAS, the mean exposure to OW semaglutide in the study was 34.1 weeks, and the overall mean dose of semaglutide at EOS was 0.76 ± 0.28 mg. The majority of patients (n = 379, 56.7 %) were receiving a 1.0 mg dose of OW semaglutide; 235 (35.1 %) were receiving a 0.5 mg dose and 51 (7.6 %) a 0.25 mg dose. Two patients (0.3 %) were receiving a semaglutide dose < 0.25 mg and two patients (0.3 %) received a dose > 0.5 mg and < 1.0 mg (**Supplementary Table 3**): neither are approved doses [10].

Insulin dose and anti-diabetes medication use

Glucose-lowering drugs used at baseline and EOS in the EAS overall and in the different subgroups are shown in **Supplementary Table 4**. In the EAS, 521 (77.9 %) patients were taking metformin, 13 (1.9 %) a sulphonylurea, and 330 (49.3 %) were on basal insulin (**Supplementary Table 4**). The mean total insulin dose (bolus, basal and premixed) for all patients receiving insulin at baseline (n = 356) in the EAS was 57.9 IU ± 45.78 IU, decreasing to 56.1 IU ± 44.31 IU at EOS. Eighteen patients had stopped bolus insulin use by EOS (**Supplementary Table 5**). In the EAS, the mean number of antihyperglycaemic drugs (including semaglutide) used by patients at baseline in comparison with EOS was 2.4 versus 3.0 overall; corresponding usage in the subgroups was 1.6 versus 2.4 (OAD only), 3.1 versus 3.1 (GLP-1RA), 2.8 versus 3.6 (insulin ± OAD without GLP-1RA) and 0.0 versus 1.4 (no antihyperglycaemic medication). The majority of patients in the EAS (n = 639, 95.5 %) and the baseline medication subgroups (range 95.4–100 %) did not add any new antihyperglycaemic drugs during the study period.

Blood pressure and lipids

In the EAS, baseline BP tertiles were determined as ≤ 130 mmHg, 131–145 mmHg, and > 145 mmHg for SBP, and < 80 mmHg, 80–86 mmHg, and > 86 mmHg for DBP. Overall, in the EAS, SBP decreased from baseline to EOS by 2.7 mmHg [95 % CI −3.81 to −1.62], from 139.7 mmHg to 137.0 mmHg ($P < 0.0001$) (**Supplementary Table 6**). Decreases in SBP were observed in the higher tertiles but not in the lower tertile (**Supplementary Table 6**). Overall, in the EAS, DBP decreased from baseline to EOS by −1.1 mmHg [95 % CI −1.78 to −0.37], from 83.3 mmHg to 82.2 mmHg ($P = 0.003$) (**Supplementary Table 6**). Decreases in DBP were observed in the higher tertiles but not in the lower tertile (**Supplementary Table 6**).

For blood lipids, in the EAS, the change from baseline to EOS for HDL cholesterol was 0.2 mg/dL [95 % CI −0.64 to 1.07], from 47.3 mg/dL to 47.5 mg/dL ($P = 0.6273$); for LDL cholesterol it was −8.3 mg/dL [95 % CI −11.31 to −5.32], from 101.9 mg/dL to 93.5 mg/dL ($P < 0.0001$); for total cholesterol, it was −14.1 mg/dL [95 % CI −17.54 to −10.66], from 180.1 mg/dL to 166.0 mg/dL ($P < 0.0001$); and for triglycerides it was −48.0 mg/dL [95 % CI −58.22 to−37.84], from 242.4 mg/dL to 194.4 mg/dL ($P < 0.0001$) (**Supplementary Table 6**).

Clinical success

At EOS in the EAS, 87.7 % of patients were considered by their treating physician to have achieved clinical success in relation to the reason to initiate semaglutide. The results were comparable across the baseline medication subgroups (data not shown).

Safety

In the FAS, 569 AEs were reported in 281 (36.1 %) patients during the study: 44 serious AEs (SAEs) in 34 (4.4 %) patients and 525 non-serious AEs in 261 (33.5 %) patients (▶ **Table 3**). No AEs leading to death were reported. A total of 345 AEs in 212 patients were considered probably or possibly related to OW semaglutide. Of the 525 non-serious AEs, the most frequent were gastrointestinal (GI) (295 events), mainly nausea (109 events) and diarrhoea (59 events).

Two SAEs were reported in two patients before the initiation of semaglutide treatment, and 39 SAEs reported for 32 patients were assessed by the physician as unlikely to be related to semaglutide. Five SAEs in three patients were classified as serious adverse drug reactions (SADRs), possibly or probably related to treatment with semaglutide (▶ **Table 3**): one event each of acute pancreatitis, nausea, vomiting, hyperglycaemia, and hip arthroplasty. Four of the five SADRs were recovered/resolved by the EOS, with one SADR reported as not recovered. This patient experienced hyperglycaemia on day 92 and nausea and vomiting on day 96, and semaglutide treatment was consequently interrupted.

A total of 66 AEs in 44 patients led to permanent discontinuation of semaglutide, of which 62 AEs (including 40 GI AEs) in 42 patients were non-serious (▶ **Table 3**). The most frequent non-serious AEs leading to permanent treatment discontinuation were GI disorders (40 events in 30 patients), of which the most common were nausea (16 events in 16 patients), diarrhoea (11 events in 11 patients) and vomiting (4 events in 4 patients).

When considered by baseline SBP and DBP tertiles, treatment discontinuation was highest in patients with the lowest BP at baseline; SBP ≤ 130 mmHg (11.6 %) and DBP < 80 mmHg (13.4 %) (**Supplementary Table 7**).

During the study, 18 (2.3 %) patients in the FAS reported documented hypoglycaemic episodes. No severe hypoglycaemic episodes were reported (▶ **Table 3**).

Discussion

The SURE Germany study demonstrated that in a diverse real-world population of adults with T2D in routine clinical practice, the use of OW semaglutide was associated with clinically relevant reductions in HbA_{1c}, body weight, and waist circumference over 30 weeks. In addition, patients treated with OW semaglutide generally experienced favourable changes in other markers of CV risk, such as SBP, DBP, LDL cholesterol, total cholesterol, and triglycerides. Patients also reported improvements in diabetes treatment satisfaction (both DTSQs and DTSQc) and the physical component of the SF-36v2 HRQoL questionnaire. These results were consistent between patients who were GLP-1RA-naïve and those who switched to semaglutide from another GLP-1RA.

While reductions in BP were observed in the two highest baseline SBP and DBP tertiles, reductions were not observed in the lower tertiles. The highest SBP and DBP tertiles also experienced the lowest rate of treatment discontinuation.

The SURE Germany data complement those from the other studies in the SURE programme [23–26] and from the SUSTAIN clinical trial programme [12–20]. The reduction from baseline to EOS in HbA_{1c} of −1.0 %-point and in body weight of −4.5 kg observed in SURE Germany is consistent with that reported in a pooled analysis of the completed SURE studies (SURE Canada, Denmark/Sweden, Switzerland and the UK) [29]. In the pooled analysis, which included 1,212 patients (comprising 960 GLP-1RA-naïve patients and 252 patients switched to semaglutide from another GLP-1RA), HbA_{1c} was reduced from baseline to EOS by −1.1 %-point and body

▶ **Table 3** Adverse events and documented and/or severe hypoglycaemic episodes in the FAS.

	Serious			Non-serious			Total		
	N	(%)	E	N	(%)	E	N	(%)	E
AEs	34	(4.4)	44	261	(33.5)	525	281	(36.1)	569
Severity									
Mild	3	(0.4)	3	197	(25.3)	380	199	(25.5)	383
Moderate	19	(2.4)	22	95	(12.2)	142	108	(13.9)	164
Severe	15	(1.9)	19	3	(0.4)	3	18	(2.3)	22
GI disorders	6	(0.8)	7	173	(22.2)	295	177	(22.7)	302
Nausea	1	(0.1)	1	82	(10.5)	109	82	(10.5)	110
Diarrhoea	0	–	–	51	(6.5)	59	51	(6.5)	59
Constipation	0	–	–	21	(2.7)	22	21	(2.7)	22
SADRs	3	(0.4)	5	NA	NA	NA	3	(0.4)	5
AEs leading to treatment discontinuation	4	(0.5)	4	42	(5.4)	62	44	(5.6)	66
Patient-reported documented hypoglycaemic episodes*	–	–	–	–	–	–	18	(2.3)	39

Abbreviations: AE: adverse event; E: event; FAS: full analysis set; GI: gastrointestinal; N: number of patients; NA: not applicable; SADR: serious adverse drug reaction. * No severe hypoglycaemic episodes were reported during the study.

weight by –4.7 kg in the overall population. Safety observations collected during the SURE Germany study were consistent with the safety profile of semaglutide known from the SUSTAIN clinical development programme and other SURE studies, and no new safety concerns were identified.

The 1.0 %-point reduction in HbA_{1c} observed in SURE Germany was at the lower end of the ranges reported in the phase 3 SUSTAIN clinical trial programme, in which HbA_{1c} was reduced from baseline by up to 1.1 %-points and 1.8 %-points with semaglutide 0.5 mg and 1.0 mg, respectively [12–20]. Nevertheless, a 1.0 %-point reduction in HbA_{1c} in a real-world setting is an impressive and clinically meaningful result. The slightly lower reduction in HbA_{1c} in SURE Germany, compared with the RCTs, may have been due to several reasons, one being that comparatively more patients in the SURE study had prior treatment with another GLP-1RA and an HbA_{1c} < 7.0 % at baseline. As insulin therapy is frequently used for patients with T2D in Germany, [30] a substantial proportion of patients in SURE Germany were receiving insulin at baseline, and this may have impacted the extent of HbA_{1c} reduction in response to semaglutide use. Furthermore, the reduction in the mean insulin dose during the SURE Germany study may have confounded the findings in terms of HbA_{1c} reduction. Other factors may include the number of antihyperglycaemic medications other than semaglutide used and that the dose of semaglutide was not maximized during the SURE study. Finally, the COVID-19 pandemic was ongoing while the SURE Germany study was being conducted and may have had an influence on the study population and the results [31]. In contrast, the reduction in body weight (4.5 kg) in SURE Germany was comparable to that observed in the phase 3 SUSTAIN clinical trial programme (up to 3.5 kg and 6.5 kg with semaglutide 0.5 mg and 1.0 mg, respectively). It is also notable that the proportion of AEs in SURE Germany was similar to that reported in semaglutide RCTs [12–20], indicating that semaglutide OW appears to be well tolerated, despite the health implications of the COVID-19 pandemic.

There are several limitations to this study, owing to its observational nature. It had no comparator arm, so it was not possible to determine whether the changes in HbA_{1c} and other endpoints resulted from semaglutide treatment or from spontaneous variation or study effects. Confounding factors could not be ruled out. Data were collected as part of routine clinical practice, rather than through mandatory assessments at prespecified time points, which may have affected the robustness and completeness of the data. The primary analysis of the primary endpoint was based on patients who had completed the study on-treatment with semaglutide and had an HbA_{1c} value available at EOS. This may have resulted in larger reductions in HbA_{1c} and body weight than anticipated in clinical practice because patients who had experienced the beneficial effects of treatment with semaglutide may have been more likely to continue treatment than those who had not. However, the sensitivity analyses, which included all patients who initiated treatment, showed similar reductions to the primary analysis, making this unlikely.

The study has a number of strengths. Semaglutide treatment was administered according to local clinical practice, and the study population included adult patients with T2D for whom the treating physician had already decided to initiate treatment with semaglutide, independently of the decision to include the patient in this study. The inclusion and exclusion criteria were thus broader than those typically used in RCTs and were chosen to reflect the real-world population with T2D in Germany. Because of such considerations, the results reflect the use of semaglutide and patient outcomes in real-world clinical practice.

Conclusion

In a real-world population in Germany, patients with T2D treated with OW semaglutide experienced clinically significant improvements in glycaemic control and reductions in body weight. Furthermore, patients treated with OW semaglutide experienced favourable changes in additional CV risk factors, such as SBP, DBP, LDL cholesterol, total cholesterol, and triglycerides. Patients also reported improvements in diabetes treatment satisfaction and HRQoL. Patients who were switched to OW semaglutide from another GLP-1RA experienced reductions in HbA_{1c} and body weight, despite previous treatment with another agent of the same class. No new safety concerns were identified during this study and the benefit-risk balance of OW semaglutide remains positive.

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