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ORIGINAL RESEARCH

Study Design and Baseline Characteristics of Patients with T2DM in the Post-marketing Safety Study of Dulaglutide in China (TRUST-CHN)

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ABSTRACT

Background: TRUST-CHN is a prospective, post-marketing safety study in patients with type 2 diabetes mellitus (T2DM) in China to evaluate the safety and effectiveness of dulaglutide in real-world clinical practice. We report here the study design and baseline characteristics of enrolled patients.

Methods: The study design was described, and baseline data were analyzed, including demographic characteristics, T2DM duration, comorbidities, dulaglutide treatment patterns, and concomitant medications.

Results: For the present analysis of this ongoing study, data were collected from January 2020 to November 2021. A total of 3313 patients were enrolled, of whom 3294 patients were included in the safety analysis. In total, 1047 patients had a prior history of dulaglutide use before being enrolled in the study. The mean (standard deviation [SD]) age of study subjects was 50.1 (13.2) years, 85.1% were aged < 65 years; 67.9% were male, and 35.9% had an education of university level or higher. Mean (SD) duration of T2DM was 6.4 (6.7) years. Baseline mean (SD) glycated hemoglobin was 8.8% (2.2%), and mean (SD) body mass index was 28.1 (4.1) kg/m^2. A total of 2867 (87%) patients had at least one comorbidity, the most frequently reported of which were overweight/obesity (87.1%), hyperlipidemia (50.5%), hypertension (47.9%), diabetic neuropathy (18.9%), and coronary artery disease (15.7%). Almost all (99.7%) patients were treated with 1.5 mg dulaglutide; at baseline, 24.8% were treated with this medication as monotherapy and 75.2% in combination

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therapy with other medications, including metformin (42.3%), sodium glucose co-transporter2 inhibitor (26.7%), insulin (18.3%), α-glucosidase inhibitor (13.1%), sulfonylurea (5.3%), dipeptidyl peptidase 4 inhibitor (4.4%), glucagon-like peptide 1 receptor agonist (2.7%), and thiazolidinedione (2.4%).

Conclusion: The present analysis revealed real-world baseline characteristics of patients with T2DM in China who use dulaglutide enrolled in TRUST-CHN. These data will enable further exploration of the characteristics of patients with T2DM in China and provide an insight on the current use of dulaglutide in clinical practice.

Keywords: Baseline characteristics; Dulaglutide; Post-marketing safety study; T2DM in China

Key Summary Points

Why carry out this study?

The TRUST-CHN is a post-marketing, safety study which, following a request by the National Medical Product Administration of China, is investigating the safety and exploratory effectiveness of dulaglutide in patients with type 2 diabetes mellitus (T2DM) in real-world clinical practice in China.

This is the first and currently largest observational study of dulaglutide as well as the largest observational study of glucagon-like peptide-1 GLP-1 receptor agonists in patients with T2DM in China.

What was learned from the study?

The study design and baseline characteristics of patients with T2DM treated with dulaglutide in the TRUST-CHN study are reported.

Mean age was approximately 50 years; most patients were male, and mean disease duration was approximately 6 years. Common comorbidities were overweight/obesity, hyperlipidemia, hypertension, diabetic neuropathy, and coronary artery disease.

Data from the present analysis provides an insight into the T2DM patient profile and current treatment patterns of dulaglutide in clinical practice in China.

INTRODUCTION

The prevalence of diabetes in China has rapidly increased over the last 40 years [1], increasing to 10.6% in 2021 [2]. Type 2 diabetes mellitus (T2DM) seems to develop at a lower body mass index (BMI) in the Chinese population compared to the European population [3]. The Chinese Diabetes Society guidelines for T2DM recommend metformin as a first-line pharmacological treatment for T2DM [4]. When metformin monotherapy does not lead to glycemic control, it should be combined with one or two drugs with different mechanisms of action, followed by escalation to metformin plus multiple daily injections of premixed insulin [1].

Glucagon-like peptide-1 (GLP-1) is a gut-derived incretin hormone; GLP-1 receptor agonists (RAs) are injectable incretin mimetics that stimulate insulin, lower glucagon secretion, inhibit gastric emptying, and reduce appetite [5]. Dulaglutide is a long-acting human GLP-1 RA, with approximately 90% homology to endogenous GLP-1 [6, 7]. Long-term phase 3 trials in patients, the majority of whom were White, have shown that both dulaglutide monotherapy and dulaglutide as adjunct to metformin therapy provide superior glycemic control compared with metformin monotherapy and sitagliptin (dipeptidylpeptidase 4 [DPP4] inhibitor) monotherapy. Dulaglutide added to pioglitazone and metformin also showed superior glycemic control versus exenatide (GLP1 RA), with a tolerability profile consistent with that seen with other medications in the GLP-1 RA class [8–10]. In East Asian patients with T2DM, once-weekly dulaglutide monotherapy showed superior glycemic control compared with daily glimepiride [11]. In a population consisting mainly of Asian patients with T2DM who had previously failed to achieve optimal glycemic control on metformin

and/or a sulfonylurea treatment, once-weekly dulaglutide resulted in a greater improvement in glycated hemoglobin (HbA1c) levels, combined with weight loss and less-pronounced hypoglycemia, compared with once-daily insulin glargine [12].

GLP-1 RAs have shown a benefit in cardiovascular outcomes in phase 3 cardiovascular outcome trials (CVOTs), including LEADER® (liraglutide; ClinicalTrials.gov Identifier: NCT01179048) [13], SUSTAIN™-6 (semaglutide; NCT01720446) [14], EXSCEL (exenatide; NCT01144338) [15], and REWIND (dulaglutide; NCT01394952) [16]. However, the proportions of Chinese or even Asian patients in the study populations of these CVOTs were limited; consequently, the generalizability of these results to Chinese patients was further investigated in the REWIND trial, using once-weekly dulaglutide; the results were shown to be the most generalizable to Chinese patients among the four former CVOTs [17].

Dulaglutide was approved in the USA, EU, and China as an adjunct to diet and exercise to improve glycemic control in adults with T2DM [18–20] and, specifically in the USA, to reduce the risk of major adverse cardiovascular events in adults with T2DM who have cardiovascular disease or cardiovascular risk factors [19]. In China, dulaglutide is approved either as monotherapy for patients with T2DM with poor glycemic control (as an adjunct to diet and exercise) or as combination therapy for patients with poor glycemic control after metformin, or sulfonylureas, or metformin combined with sulfonylureas [20].

At the time of dulaglutide approval in China, and as per the National Medical Product Administration request, a post-marketing safety study (TRUST-CHN) was initiated to further investigate the safety of dulaglutide use in Chinese patients with T2DM. The TRUST-CHN study is a prospective, observational study designed to collect safety data from the real-world prescribing practice in a large cohort of patients with T2DM in China. The exploratory objectives are to evaluate the effectiveness and treatment satisfaction of dulaglutide in real-world clinical practice. Here, we describe the study design together with the baseline characteristics of Chinese patients with T2DM who are enrolled in the TRUST-CHN study.

METHODS

The primary outcomes of the TRUST-CHN study are treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs) in patients with T2DM treated with dulaglutide over a 24-week period. Exploratory objectives include evaluation of the effectiveness of dulaglutide and treatment satisfaction after 24 weeks of treatment. The study was ongoing at the time of the present analyses, in which we describe patients' baseline characteristics. The data were collected from January 2020 to November 2021 (cutoff September 2021 and programmed November 2021).

Study Design and Study Population

This is a single-country, prospective, non-interventional, safety study to collect and estimate the incidence of TEAEs, SAEs, and adverse drug reactions) in patients in China with T2DM receiving treatment with dulaglutide over a 24-week period. The present analysis is the first readout of the entire baseline data. Patients had three scheduled visits, at baseline (Visit 1), after 4 weeks (Visit 2), and after 24 weeks (Visit 3) of treatment (see Fig. 1).

As exploratory objectives (data not presented here), the effectiveness of dulaglutide will also be evaluated by collecting data on HbA1c and body weight, as well as on treatment satisfaction using the Diabetes Treatment Satisfaction Questionnaire (DTSQ) [21, 22], after 24 weeks of treatment.

Patients who were aged ≥ 18 years, diagnosed with T2DM, prescribed dulaglutide according to the Chinese label, and who provided written consent for the release of their data were included in the study. Patients contraindicated for dulaglutide use or simultaneously participating in a different study with a treatment intervention, and patients who were pregnant, breastfeeding, or intending to become pregnant during the study were excluded.

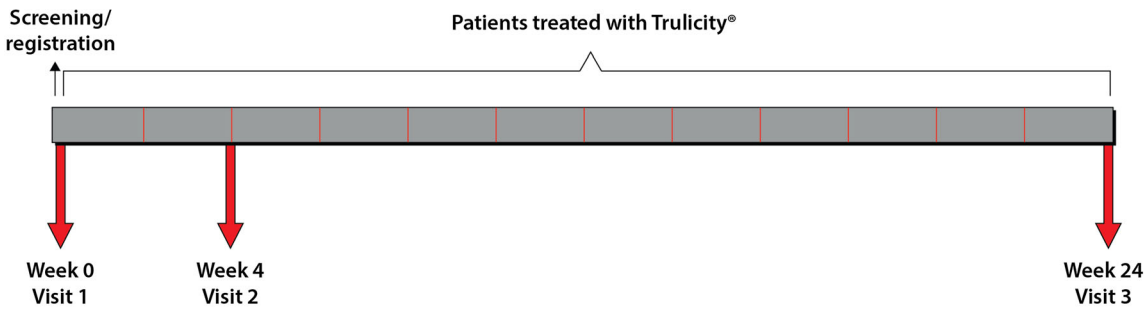

Fig. 1 Flow diagram of study design

The safety analysis population included all patients who took at least one dose of dulaglutide. This population was used for the primary endpoints and baseline analyses. The effectiveness analysis population included all patients who took at least one dose of dulaglutide and participated in at least one post-baseline follow-up visit within the defined visit window, i.e., those for whom baseline and any post-baseline observation data were available. The effectiveness analysis population was used for the exploratory endpoints.

Dulaglutide-naïve patients were defined as those who had never treated been with dulaglutide prior to study entry. Dulaglutide-experienced patients were those who had already been treated with dulaglutide prior to study entry, whether or not they were still receiving dulaglutide as treatment.

Treatment Setting

Treatment was prescribed in accordance with the dulaglutide (Trulicity®; Eli Lilly and Company, Indianapolis, IN, USA) prescribing information in China and the investigator's/physician's judgement. During dulaglutide treatment, blood glucose self-monitoring was not required; however, blood glucose self-monitoring may be required to adjust the sulfonylurea dose [20].

Outcomes

Patients will be observed for approximately 24 weeks following enrollment, with a total of three visits during the study, to enable data collection on patient demographics, patient-reported HbA1c, body weight, medical history, dulaglutide treatment patterns, concomitant medications, adverse events, and reasons for discontinuation (see Electronic Supplementary Material [ESM] Appendix 1: Table S1).

Only baseline data are presented in the current study, including demographic characteristics, T2DM disease history, comorbidities present at baseline, dulaglutide treatment history, other T2DM treatment history, concomitant T2DM medications, dulaglutide prescription patterns, HbA1c levels, body weight measurements, vital signs, and laboratory measurements, with a cutoff date of 8 November 2021.

Statistical Analyses

Demographic characteristics, duration of T2DM, comorbidities, dulaglutide treatment patterns, and concomitant medications were summarized using descriptive statistics.

The results of the analyses of categorical variables are presented as the frequency and percentage (with the percentage excluding the number missing in the denominator), and those of continuous variables are presented as the mean and standard deviation (SD). The disposition of all patients who entered the study was summarized. Statistical analysis was performed using SAS version 9.4 software (SAS Institute, Cary, NC, USA).

Compliance with Ethics

This non-interventional, post-marketing safety study was submitted to ethical review boards for approval whenever required by local law. Regardless of local law, all primary data collection observational studies were submitted to at least one independent body for review and to confirm that the study is non-interventional. Additional information on the Ethics Review Board is provided in ESM Appendix 2.

Regulatory authorities were notified, and approval was sought as required by local laws and regulations. Progress reports were submitted to Ethics Review Boards and regulatory authorities as required by local laws and regulations. This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practices and applicable laws and regulations of China.

RESULTS

Baseline Analyses

Patient Disposition and Demographic Characteristics

Data from January 2020 to November 2021 were analyzed. A total of 3313 patients were enrolled in the study; of these, four were inadvertently enrolled who were subsequently deemed not eligible, due to inclusion/exclusion criteria, and excluded. Of the eligible patients, 3294 were included in the safety analysis population. Of these, 1047 were dulaglutide-experienced and 2247 were dulaglutide-naïve. In the effectiveness analysis population, 3201 patients were included; of these, 1028 were dulaglutide-experienced and 2173 were dulaglutide-naïve.

Demographic characteristics, including age, sex, and education level, are presented in Table 1. The mean age of the population was approximately 50 years, with 2803 (85.1%) patients aged < 65 years. The majority of patients were male (2236; 67.9%) and 1182 (35.9%) of patients had an educational level of university level or higher.

Baseline HbA1c Levels, Body Weight, and BMI

Mean HbA1c levels at baseline were 8.8%, and mean baseline body weight was 80.2 kg. Body weight and HbA1c levels in the effectiveness analysis population are summarized in Table 2.

In the safety analysis population, based on the global BMI classification, 52.0% of patients were overweight and 27.1% were obese at baseline. However, based on the Chinese BMI classification [23], 41.4% of patients were overweight and 45.7% were obese. Data on baseline BMI, waistline, hipline, and waist-to-hip ratio by dulaglutide treatment experience were analyzed further using the safety analysis population and is summarized in Table 2.

Medical History and Comorbidities

Data on T2DM disease history, including age at diagnosis and disease duration, are presented in Table 3. The mean age at T2DM diagnosis was approximately 43 years, with a mean disease duration of 6.4 years.

Of the 3294 patients in the safety analysis population, 2867 (87.0%) had at least one existing medical condition at baseline. Comorbidities reported in ≥ 5% of the total safety analysis population are presented in Table 3. The most frequently reported (≥ 15% patients) comorbidities were overweight/obesity, hyperlipidemia, hypertension, diabetic neuropathy, and coronary artery disease.

Concomitant T2DM Medications at Baseline

In the safety analysis population, 2178 (66.1%) patients were being treated with at least one concomitant medication for T2DM at baseline; the most commonly reported medications were metformin (42.3%) and sodium glucose co-transporter-2 (SGLT2) inhibitor (26.7%). The types of concomitant medications are summarized in Table 4. The history of other T2DM treatments is summarized in ESM Appendix 1: Table S2.

Dulaglutide Prescription Patterns

In the safety analysis population, 816 (24.8%) patients received dulaglutide monotherapy; 2478 (75.2%) received combination therapy at

Table 1 Demographic characteristics of safety analysis population

Demographic characteristics	Dulaglutide-experienced (N = 1047)	Dulaglutide-naïve (N = 2247)	Total (N = 3294)
Age (years)			
n	1047	2247	3294
Mean (SD)	50.4 (12.9)	49.9 (13.4)	50.1 (13.2)
Age categories, *n* (%)			
n	1047	2247	3294
18 to < 65 years	890 (85.0)	1913 (85.1)	2803 (85.1)
≥ 65 years	157 (15.0)	334 (14.9)	491 (14.9)
Sex, *n* (%)			
n	1047	2247	3294
Male	746 (71.3)	1490 (66.3)	2236 (67.9)
Female	301 (28.7)	757 (33.7)	1058 (32.1)
Education, *n* (%)			
n	1047	2247	3294
Non-educated	10 (1.0)	37 (1.6)	47 (1.4)
Middle school and below	205 (19.6)	571 (25.4)	776 (23.6)
High school	146 (13.9)	391 (17.4)	537 (16.3)
College or university and above	428 (40.9)	754 (33.6)	1182 (35.9)
Unknown	258 (24.6)	494 (22.0)	752 (22.8)

N Number of patients studied, *n* number of patients with available data, *SD* standard deviation

baseline. Data on the dosage and frequency of dulaglutide administration are summarized in Table 5. Dulaglutide treatment history is summarized in ESM Appendix 1: Table S3.

Baseline Vital Signs

At baseline, 60.3% patients had a systolic blood pressure in the range of 120–140 mmHg, and 43.4% had a diastolic blood pressure in the range of 80–90 mmHg. Mean systolic and diastolic blood pressure was 130.7 and 81.6 mmHg, respectively. Systolic blood pressure, diastolic blood pressure, and heart rate at baseline according to dulaglutide treatment experience are summarized in ESM Appendix 1: Table S4.

Baseline Laboratory Measurements

At baseline, among patients whose laboratory measurements were taken, 71.9% (612/851) had fasting insulin levels within the normal limit, with a mean value of 20.0 mU/L. Fasting blood glucose was above the upper normal limit in 80.9% (954/1179) of patients, with a mean value of 9.1 mmol/L. Two hours post-prandial blood glucose was above the upper normal limit in 79.1% (566/716) of patients, with a mean value of 15.5 mmol/L. Laboratory measurements at baseline according to dulaglutide treatment experience are further summarized in ESM Appendix 1: Table S5.

Table 2 Baseline data on glycated hemoglobin levels, body weight, body mass index, waistline, hipline, and waist-to-hip ratio

Baseline data	Effectiveness analysis population		
	Dulaglutide-experienced (*N* = 1028)	Dulaglutide-naïve (*N* = 2173)	Total (*N* = 3201)
HbA1c (%)			
n	562	1206	1768
Mean (SD)	8.8 (2.2)	8.9 (2.2)	8.8 (2.2)
HbA1c categories, *n* (%)			
< 7%	133 (23.7)	261 (21.6)	394 (22.3)
≥ 7 to < 8%	96 (17.1)	236 (19.6)	332 (18.8)
≥ 8 to < 9%	97 (17.3)	185 (15.3)	282 (16.0)
≥ 9 to < 10%	87 (15.5)	166 (13.8)	253 (14.3)
≥ 10 to < 11%	54 (9.6)	139 (11.5)	193 (10.9)
≥ 11%	95 (16.9)	219 (18.2)	314 (17.8)
Weight (kg)			
n	1008	2101	3109
Mean (SD)	80.9 (14.4)	79.9 (14.4)	80.2 (14.4)

Baseline data	Safety analysis population		
	Dulaglutide-experienced (*N* = 1047)	Dulaglutide-naïve (*N* = 2247)	Total (*N* = 3294)
BMI (kg/m^2)			
n	1021	2169	3190
Mean (SD)	28.0 (4.1)	28.1 (4.1)	28.1 (4.1)
Chinese classification, *n* (%)			
Underweight (< 18.5 kg/m^2)	4 (0.4%)	3 (0.1%)	7 (0.2%)
Normal (≥ 18.5 to < 24.0 kg/m^2)	127 (12.4%)	277 (12.8%)	404 (12.7%)
Overweight (≥ 24.0 to < 28.0 kg/m^2)	434 (42.5%)	886 (40.8%)	1320 (41.4%)
Obese (≥ 28.0 kg/m^2)	456 (44.7%)	1003 (46.2%)	1459 (45.7%)
Global classification, *n* (%)			
Underweight (< 18.5 kg/m^2)	4 (0.4%)	3 (0.1%)	7 (0.2%)
Normal (≥ 18.5 to < 25.0 kg/m^2)	215 (21.1%)	446 (20.6%)	661 (20.7%)
Overweight (≥ 25.0 to < 30.0 kg/m^2)	533 (52.2%)	1125 (51.9%)	1658 (52.0%)
Obese (≥ 30.0 kg/m^2)	269 (26.3%)	595 (27.4%)	864 (27.1%)
Waistline (cm)			
n	680	1660	2340

Table 2 continued

Baseline data	Safety analysis population		
	Dulaglutide-experienced (N = 1047)	Dulaglutide-naïve (N = 2247)	Total (N = 3294)
Mean (SD)	98.1 (10.6)	97.9 (11.0)	97.9 (10.9)
Hipline (cm)			
n	636	1591	2227
Mean (SD)	102.1 (9.0)	102.3 (9.7)	102.2 (9.5)
Waist-to-hip ratio			
n	636	1590	2226
Mean (SD)	1.0 (0.1)	1.0 (0.1)	1.0 (0.1)

N number of patients studied, *n* number of patients with available data
Body mass index (BMI), waistline, hipline, and waist-to-hip ratio were summarized in the safety analysis population. Weight and glycated hemoglobin (HbA1c) were measured in the effectiveness analysis population

DISCUSSION

The TRUST-CHN study is the first and largest observational study of dulaglutide conducted to date, as well as the largest observational study of GLP-1 RA in patients with T2DM in China. Baseline data from this study provide an insight into the current use of dulaglutide in real-world clinical practice, the demographic characteristics of patients with T2DM outside of the clinical trial setting, and the medical history of these patients. Among the 3294 patients included in the safety analysis set, the mean age was approximately 50 years, the majority of patients (67.9%) were male, and approximately one-third of patients had an educational background of university level or higher (35.9%).

The mean patient age at T2DM diagnosis was approximately 43 years, with a mean disease duration of 6.4 years at this time. Mean HbA1c levels were 8.8% and 8.9% in the dulaglutide-experienced and dulaglutide-naïve patients, respectively. The mean BMI was 28.1 kg/m^2; based on the Chinese BMI classification, 45.7% of patients were obese and 41.4% were overweight and, therefore, 87.1% of the patients were overweight or had obesity. In comparison, based on the global BMI classification, 27.1% of patients were in the obesity category and 52.0% were in the overweight category.

Most patients (87%) had at least one existing comorbid condition at baseline, with the most frequent comorbidities being overweight/obesity (87.1%), hyperlipidemia (50.5%), hypertension (47.9%), diabetic neuropathy (18.9%), and coronary artery disease (15.7%).

Among the 3294 patients included in the safety analysis set, 1047 had already received dulaglutide prior to this being enrolled in this study. In total, 66.1% of patients were on at least one concomitant medication for T2DM at baseline, most commonly metformin (42.3%) and SGLT-2 inhibitors (26.7%). These observations suggest that metformin remains one of the most common T2DM medications, followed by SGLT-2 inhibitors. In total, 33.1% and 21.3% patients were on one and two oral anti-diabetic medications, respectively, which suggests that concomitant use of oral anti-diabetic drugs is common in clinical practice.

The Chinese Diabetes Society guidelines recommend that when patients cannot achieve the blood glucose target on metformin monotherapy, they should be put on dual therapy with insulin secretagogues, α-glucosidase inhibitors, DPP4 inhibitors, thiazolidinedione, SGLT-2 inhibitors, or GLP-1 RAs [1], with

Table 3 Medical history of patients in safety analysis population

Parameters	Dulaglutide-experienced (*N* = 1047)	Dulaglutide-naïve (*N* = 2247)	Total (*N* = 3294)
Age at T2DM diagnosis (years)			
n	1042	2239	3281
Mean (SD)	43.3 (11.2)	43.6 (11.5)	43.5 (11.4)
T2DM duration (years)			
n	1042	2239	3281
Mean (SD)	7.0 (6.7)	6.1 (6.7)	6.4 (6.7)
Patients with at least one comorbidity ongoing at baseline, *n* (%)	923 (88.2)	1944 (86.5)	2867 (87.0)
Comorbidities reported in at least 5% of patients, n (%)			
Overweight/obesity[a]	890 (87.2)	1889 (87.0)	2779 (87.1)
Hyperlipidemia	537 (51.3)	1126 (50.1)	1663 (50.5)
Hypertension	524 (50.0)	1055 (47.0)	1579 (47.9)
Diabetic neuropathy	258 (24.6)	366 (16.3)	624 (18.9)
Coronary artery disease	176 (16.8)	342 (15.2)	518 (15.7)
Hepatic steatosis	210 (20.1)	258 (11.5)	468 (14.2)
Hepatic function abnormal	105 (10.0)	347 (15.4)	452 (13.7)
Hyperuricemia	138 (13.2)	318 (14.2)	456 (13.8)
Non-alcoholic fatty liver disease	138 (13.2)	258 (11.5)	396 (12.0)
Diabetic nephropathy	164 (15.7)	206 (9.2)	370 (11.2)
Diabetic vascular disorder	148 (14.1)	149 (6.6)	297 (9.0)
Thyroid mass	103 (9.8)	175 (7.8)	278 (8.4)
Diabetic retinopathy	103 (9.8)	134 (6.0)	237 (7.2)
Peripheral arterial occlusive disease	74 (7.1)	118 (5.3)	192 (5.8)

N number of patients studied, *n* number of patients with available data

[a]Overweight/obesity were reported based on the Chinese classification for baseline BMI and obesity/overweight. Other comorbidities were reported based on the Medical Dictionary for Regulatory Activities (MedDRA) Preferred Term (PT). MedDRA version 22.1

the last typically initiated when patients no longer achieve glycemic control with one or more oral anti-hyperglycemic drugs [1, 24]. Another challenge in the treatment of patients with T2DM is the control of risk factors for cardiovascular disease [3]. Both the ADA and EASD recommend the combination of metformin with either a SGLT-2 inhibitor or a GLP-1 RA for T2DM patients with atherosclerotic cardiovascular disease, with proven cardiovascular benefit [24].

Dulaglutide has shown reduced cardiovascular outcomes in T2DM patients with or without previous cardiovascular disease, with an effect size similar to that observed with other GLP-1 RAs CVOTs [16]. The REWIND trial

Table 4 Concomitant medications for type 2 diabetes mellitus—safety analysis population

Concomitant medication history	Dulaglutide-experienced (*N* = 1047)	Dulaglutide-naïve (*N* = 2247)	Total (*N* = 3294)
Patients on at least one concomitant medication for T2DM at baseline	785 (75.0)	1393 (62.0)	2178 (66.1)
Concomitant medications for T2DM at baseline included:			
Metformin	518 (49.5)	875 (38.9)	1393 (42.3)
SGLT-2 inhibitor	367 (35.1)	513 (22.8)	880 (26.7)
Insulin	201 (19.2)	401 (17.8)	602 (18.3)
α-Glucosidase inhibitor	136 (13.0)	296 (13.2)	432 (13.1)
Sulfonylurea	51 (4.9)	125 (5.6)	176 (5.3)
DPP-4 inhibitor	43 (4.1)	103 (4.6)	146 (4.4)
GLP-1 RA	11 (1.1)	78 (3.5)	89 (2.7)
Thiazolidinedione	22 (2.1)	56 (2.5)	78 (2.4)
Number of oral anti-diabetic treatments used for T2DM at baseline (i.e., not including insulin and GLP-1 RAs)			
Any	736	1254	1990
1	404 (38.6)	685 (30.5)	1089 (33.1)
2	266 (25.4)	435 (19.4)	701 (21.3)
≥ 3	66 (6.3)	134 (6.0)	200 (6.1)

Data in table are presented as the number (*n*) of patients with the percentage in parentheses
DPP-4 Dipeptidyl-peptidase-4, *GLP-1* glucagon like peptide-1, *SGLT* sodium-glucose co-transporter-2, *T2DM* type 2 diabetes mellitus, *RA* receptor agonist

enrolled 9901 patients with T2DM who had either a previous cardiovascular event or a cardiovascular risk factor. Of these, 4949 were treated with dulaglutide; 53.4% of patients were male, 75.9% were White, mean age was 66.2 years, and mean T2DM disease duration was 10.5 years [16].

In a subgroup analysis of the AWARD-CHN2 trial, once-weekly dulaglutide was compared with once-daily insulin glargine in a Chinese T2DM population, of whom 60.9% were male, the mean age was 54.5 years, the mean diabetes duration was 7.9 years, and the mean BMI was 26.0 kg/m^2 [25]. Once weekly-dulaglutide was shown to be superior to once-daily glargine, with more pronounced reductions in body weight and hypoglycemia rates in Chinese patients with T2DM who had inadequate glycemic control with one to two oral anti-hyperglycemic medications [25]. The baseline characteristics of the TRUST-CHN study presented here are similar to those of this subgroup analysis, with a numerically higher percentage of male patients (67.9%), slightly younger mean age (50 years), and a higher mean BMI (28.1 kg/m^2).

In a post-hoc analysis of two Chinese patient populations with T2DM, the efficacy of dulaglutide was further evaluated according to baseline HbA1c < 8.5% or ≥ 8.5% after 26 weeks of treatment [26]. Dulaglutide achieved a greater HbA1c reduction, combined with weight loss and lower risk of hypoglycemia, compared with active comparators (glimepiride and insulin glargine) regardless of baseline HbA1c; patients with a higher baseline HbA1c did achieve greater HbA1c reductions [26]. In the same Chinese populations, another

Table 5 Dulaglutide prescription patterns at baseline—safety analysis population

Dulaglutide prescription patterns	Dulaglutide-experienced (*N* = 1047)	Dulaglutide-naïve (*N* = 2247)	Total (*N* = 3294)
Type of therapy, *n* (%)			
n	1047	2247	3294
Monotherapy	241 (23.0)	575 (25.6)	816 (24.8)
Combination therapy	806 (77.0)	1672 (74.4)	2478 (75.2)
Dosage, *n* (%)			
n	1047	2247	3294
0.75 mg	1 (0.1)	10 (0.4)	11 (0.3)
1.5 mg	1046 (99.9)	2237 (99.6)	3283 (99.7)
Dosage and type of therapy, *n* (%)			
n	1047	2247	3294
Patients with 0.75 mg monotherapy, *n* (%)	0	3 (0.1)	3 (0.1)
Patients with 0.75 mg combination therapy, *n* (%)	1 (0.1)	7 (0.3)	8 (0.2)
Patients with 1.5 mg monotherapy, *n* (%)	241 (23.0)	572 (25.5)	813 (24.7)
Patients with 1.5 mg combination therapy, *n* (%)	805 (76.9)	1665 (74.1)	2470 (75.0)

N number of patients studied, *n* number of patients with available data

post-hoc analysis showed that dulaglutide improved glycemic control combined with a slight body weight reduction and low hypoglycemia risk in patients with a BMI < 25 kg/m^2; this result suggests that BMI is not a necessary consideration for dulaglutide treatment in Chinese patients with T2DM [27]. In the present study, baseline HbA1c levels were patient-reported, with a mean value of 8.8% and a mean BMI of 28.1 kg/m^2; these values indicate that Chinese diabetologists tend to prescribe dulaglutide for relatively obese patients or for patients with higher HbA1c in real-world clinical practice.

In a cross-sectional, observational study of 25,817 patients with T2DM in China, comorbid hypertension and/or dyslipidemia were seen in 72% of patients [28]. This is a trend that was also seen in the baseline characteristics of the present study, with hypertension and hyperlipidemia being the two most frequently reported comorbidities, occurring in 47.9% and 50.5% of patients, respectively. A recent review of real-world data from 29 studies across Canada, Europe, India, Japan, Malaysia, the Republic of Korea, and the USA showed dulaglutide to be beneficial in these populations [29]. However, more real-world data, specifically in Chinese patients, are needed to further elucidate the use and benefit of dulaglutide in patients with T2DM in China.

While the current study is designed to provide real-world data, it does have several limitations. The study duration was relatively short and HbA1c level was patient-reported. As this was a real-world sample, patients were included regardless of disease severity, and any factors that might have led to the decision of using

dulaglutide versus alternative medications are not known.

CONCLUSIONS

To our knowledge, this is the first and largest observational study to date in patients with T2DM in China, who received dulaglutide either as monotherapy or in combination with other T2DM treatments.

Real-world data and evidence will help further advance knowledge on the benefit of dulaglutide in clinical practice and will enable further studies on the characteristics of patients with T2DM in China that may shape future, more individualized treatment algorithms.

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Compliance with Ethics Guidelines This non-interventional, post-marketing safety study was submitted to ethical review boards for approval whenever required by local law. Regardless of local law, all primary data collection observational studies were submitted to at least one independent body for review and to confirm that the study is considered non-interventional. Additional information on the Ethics Review Board is provided in ESM Appendix 2. Regulatory authorities were notified, and approval was sought as required by local laws and regulations. This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki (1964 and its later amendments) and that are consistent with good clinical practices and applicable laws and regulations of China.

Data Availability The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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