



Clinical trial results:

A 12-week Randomized, Controlled Trial to Compare TOUJEO® and TRESIBA® in Terms of Glucose Values in Target Range and Variability During Continuous Glucose Monitoring in Patients With Type 1 Diabetes Mellitus

Summary

EudraCT number	2017-002756-91
Trial protocol	HU GB NL
Global end of trial date	16 September 2021

Results information

Result version number	v1 (current)
This version publication date	29 September 2022
First version publication date	29 September 2022

Trial information

Trial identification

Sponsor protocol code	LPS14947
-----------------------	----------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04075513
WHO universal trial number (UTN)	U1111-1197-8171

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91385
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 October 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	16 September 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of insulin glargine 300 units per millilitre (U/ml) in comparison to insulin degludec 100 U/ml on glycemic control and variability in subjects with diabetes mellitus.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy:

Protocol-mandated background therapy was mealtime insulin analog (i.e., rapid insulin analogs [e.g., insulin glulisine, insulin lispro or insulin aspart]). Subjects in both treatment groups continued their short-acting mealtime insulin analogs at least 30 days before the screening visit and continued throughout the study. Dose adjustment was based on a pattern of post-meal self-monitoring of plasma glucose data from the prior 3 days (simple titration) or the carbohydrate content of the meal. Different injection sites were used for the background therapy.

Evidence for comparator: -

Actual start date of recruitment	09 October 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	Germany: 29
Country: Number of subjects enrolled	Hungary: 45
Country: Number of subjects enrolled	Brazil: 96
Country: Number of subjects enrolled	Turkey: 3
Country: Number of subjects enrolled	United States: 160
Worldwide total number of subjects	343
EEA total number of subjects	76

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	323
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study was conducted at 40 active sites in 7 countries. 550 subjects were screened between 09 October 2019 and 06 May 2021, of which 343 subjects were enrolled and randomised by interactive response technology (IRT) (1:1 ratio) to receive Toujeo or Tresiba. A total of 207 subjects were screen failure mainly due to not meeting eligibility criteria.

Pre-assignment

Screening details:

Randomisation was stratified by hemoglobin A1c (HbA1c) at screening (less than [$<$] 8.0 percent [%]; greater than or equal to [\geq] 8.0%). Subjects continued their short-acting mealtime insulin analogue (i.e., rapid insulin analogs) which they had used for at least 30 days before the screening visit and continued the same throughout the study.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Toujeo

Arm description:

Toujeo (Insulin Glargine, 300 U/ml) subcutaneous (SC) injection, once daily in the morning before breakfast for 12 weeks on top of rapid acting insulin analog.

Arm type	Experimental
Investigational medicinal product name	Toujeo
Investigational medicinal product code	HOE901-U300
Other name	Insulin glargine
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Insulin Glargine 300 U/ml self-administered SC injection, once daily in the morning using a pre-filled pen for 12 weeks.

Arm title	Tresiba
------------------	---------

Arm description:

Tresiba (Insulin Degludec, 100 U/ml) SC injection, once daily in the morning before breakfast for 12 weeks on top of rapid acting insulin analog.

Arm type	Active comparator
Investigational medicinal product name	Tresiba
Investigational medicinal product code	
Other name	Insulin degludec
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Insulin Degludec 100 U/ml self-administered SC injection, once daily in the morning using a pre-filled pen for 12 weeks.

Number of subjects in period 1	Toujeo	Tresiba
Started	172	171
Completed	164	167
Not completed	8	4
Lost to follow-up	4	2
Switch to insulin pump	1	-
Withdrawal by subject	2	2
Lack of efficacy	1	-

Baseline characteristics

Reporting groups

Reporting group title	Toujeo
-----------------------	--------

Reporting group description:

Toujeo (Insulin Glargine, 300 U/ml) subcutaneous (SC) injection, once daily in the morning before breakfast for 12 weeks on top of rapid acting insulin analog.

Reporting group title	Tresiba
-----------------------	---------

Reporting group description:

Tresiba (Insulin Degludec, 100 U/ml) SC injection, once daily in the morning before breakfast for 12 weeks on top of rapid acting insulin analog.

Reporting group values	Toujeo	Tresiba	Total
Number of subjects	172	171	343
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	42.9 ± 13.53	42.8 ± 13.05	-
Gender categorical Units: Subjects			
Female	86	74	160
Male	86	97	183

End points

End points reporting groups

Reporting group title	Toujeo
Reporting group description: Toujeo (Insulin Glargine, 300 U/ml) subcutaneous (SC) injection, once daily in the morning before breakfast for 12 weeks on top of rapid acting insulin analog.	
Reporting group title	Tresiba
Reporting group description: Tresiba (Insulin Degludec, 100 U/ml) SC injection, once daily in the morning before breakfast for 12 weeks on top of rapid acting insulin analog.	

Primary: Percentage of Time of Glucose Concentration Within the Target Range of Greater Than or Equal to (\geq) 70 to Less Than or Equal to (\leq) 180 Milligrams Per Decilitre: Non-inferiority Analysis

End point title	Percentage of Time of Glucose Concentration Within the Target Range of Greater Than or Equal to (\geq) 70 to Less Than or Equal to (\leq) 180 Milligrams Per Decilitre: Non-inferiority Analysis
End point description: The Continuous Glucose Monitoring (CGM) system combined frequent interstitial glucose measurements (every 5 minutes) with ability to analyse glucose levels in real time. Adjusted least square (LS) means and standard error (SE) were obtained using analysis of covariance (ANCOVA) model on data obtained from the multiple imputations during Week 10 to Week 12. Analysis was performed on intent-to-treat (ITT) population which included all randomised subjects (who signed the informed consent form and were allocated to a treatment group before the first investigational medicinal product [IMP] administration and recorded in the IRT database), irrespective of the treatment actually received and were analysed according to the treatment group allocated by randomisation. Here, 'number of subjects analysed' = subjects evaluable for this endpoint.	
End point type	Primary
End point timeframe: During Week 10 up to Week 12	

End point values	Toujeo	Tresiba		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	151		
Units: percentage of time				
least squares mean (standard error)	52.74 (\pm 0.859)	55.09 (\pm 0.893)		

Statistical analyses

Statistical analysis title	Toujeo versus Tresiba
Statistical analysis description: Analysis was performed using ANCOVA model including the fixed categorical effect of treatment groups and randomisation stratum of screening HbA1c ($<8.0\%$, $\geq 8.0\%$) and the continuous fixed covariate of Baseline percent time in range value.	
Comparison groups	Toujeo v Tresiba

Number of subjects included in analysis	309
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[1]
P-value	= 0.0067 ^[2]
Method	ANCOVA
Parameter estimate	Least square mean difference
Point estimate	3.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	5.44

Notes:

[1] - Non-inferiority was based on a relative margin of 10%. Since higher time in range means better outcome, non-inferiority was demonstrated if the lower bound of the two-sided 95% confidence interval (CI) of the difference between Toujeo LS mean and 90% of Tresiba LS mean at Week 12 was >0.

[2] - Threshold of significance at <0.05.

Secondary: Glucose Total Coefficient of Variation (CV%)

End point title	Glucose Total Coefficient of Variation (CV%)
-----------------	--

End point description:

CV% was a measure of spread of variability relative to mean of population. For CGM glucose values, CV% was measure of glycemic variability across 20 days and calculated as ratio of standard deviation of glucose values to mean of glucose values. LS means and SE were obtained using ANCOVA model using fixed categorical effects of treatment groups (Toujeo, Tresiba), randomisation stratum of screening HbA1c (<8.0% versus >=8.0%), and the continuous fixed covariate of Baseline value. Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this endpoint.

End point type	Secondary
----------------	-----------

End point timeframe:

During Week 10 up to Week 12

End point values	Toujeo	Tresiba		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	151		
Units: percentage of mean glucose level				
least squares mean (standard error)	39.91 (± 0.360)	41.22 (± 0.373)		

Statistical analyses

Statistical analysis title	Toujeo versus Tresiba
----------------------------	-----------------------

Statistical analysis description:

A hierarchical step-down testing procedure was used to control type I error. The hierarchical testing was then performed sequentially only when the previous primary endpoint demonstrated non-inferiority. Analysis was performed using ANCOVA model including the fixed categorical effect of treatment groups and randomisation stratum of screening HbA1c (<8.0%, >=8.0%) and the continuous fixed covariate of Baseline percent time in range value.

Comparison groups	Toujeo v Tresiba
-------------------	------------------

Number of subjects included in analysis	309
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[3]
P-value	< 0.0001 ^[4]
Method	ANCOVA
Parameter estimate	Least square mean difference
Point estimate	-5.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.5
upper limit	-4.38

Notes:

[3] - Non-inferiority was based on a relative margin of 10%. Since lower CV means better outcome, non-inferiority was demonstrated if the upper bound of the two-sided 95% CI of the difference between Toujeo LS mean and 110% of Tresiba LS mean at Week 12 was <0.

[4] - Threshold of significance at <0.05.

Secondary: Percentage of Time of Glucose Concentration Within the Target Range of ≥ 70 to ≤ 180 Milligrams Per Decilitre: Superiority Analysis

End point title	Percentage of Time of Glucose Concentration Within the Target Range of ≥ 70 to ≤ 180 Milligrams Per Decilitre: Superiority Analysis
-----------------	---

End point description:

The CGM system combined frequent interstitial glucose measurements (every 5 minutes) with ability to analyse glucose levels in real time. Adjusted LS means and SE were obtained using ANCOVA model on data obtained from the multiple imputations during Week 10 to Week 12. Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this endpoint.

End point type	Secondary
----------------	-----------

End point timeframe:

During Week 10 up to Week 12

End point values	Toujeo	Tresiba		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	151		
Units: percentage of time				
least squares mean (standard error)	52.74 (\pm 0.859)	55.09 (\pm 0.893)		

Statistical analyses

Statistical analysis title	Toujeo versus Tresiba
----------------------------	-----------------------

Statistical analysis description:

A hierarchical step-down testing procedure was used to control type I error. The hierarchical testing was then performed sequentially when the primary endpoint and the secondary endpoint of total CV demonstrated non-inferiority. Analysis was performed using ANCOVA model including the fixed categorical effect of treatment groups and randomisation stratum of screening HbA1c (<8.0%, \geq 8.0%) and the continuous fixed covariate of Baseline percent time in range value.

Comparison groups	Toujeo v Tresiba
-------------------	------------------

Number of subjects included in analysis	309
Analysis specification	Pre-specified
Analysis type	superiority ^[5]
P-value	= 0.0548 ^[6]
Method	ANCOVA
Parameter estimate	Least square mean difference
Point estimate	-2.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.75
upper limit	0.05

Notes:

[5] - Superiority was demonstrated if the lower bound of the two-sided 95% CI of the adjusted difference estimate of Toujeo and Tresiba at Week 12 was > 0.

[6] - Threshold of significance at <0.05.

Secondary: Glucose Within-day CV% and Between-day CV%

End point title	Glucose Within-day CV% and Between-day CV%
-----------------	--

End point description:

CV% was a measure of spread of variability relative to mean of population. For CGM glucose values, CV% was measure of glycemic variability across 20 days and calculated within day and between days as ratio of standard deviation of glucose values to mean of glucose values. LS mean and SE were obtained from ANCOVA model including fixed categorical effects of treatment groups (TOUJEO, TRESIBA), randomisation stratum of screening HbA1c (<8.0% versus >=8.0%), and as well as, the continuous fixed covariate of Baseline value. Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this endpoint.

End point type	Secondary
----------------	-----------

End point timeframe:

During Week 10 up to Week 12

End point values	Toujeo	Tresiba		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	151		
Units: percentage of mean glucose level				
least squares mean (standard error)				
Within-day CV%	33.48 (± 0.342)	34.37 (± 0.351)		
Between-day CV%	17.23 (± 0.404)	18.08 (± 0.415)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Glycated Hemoglobin A1c (HbA1c) at Week 12

End point title	Change From Baseline in Glycated Hemoglobin A1c (HbA1c) at Week 12
-----------------	--

End point description:

Change in HbA1c at Week 12 was analysed using an ANCOVA model including the fixed categorical effects of treatment groups (Toujeo, Tresiba), and the continuous fixed covariate of Baseline HbA1c value. Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this endpoint.

End point type Secondary

End point timeframe:

Baseline, Week 12

End point values	Toujeo	Tresiba		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	153		
Units: percentage of HbA1c				
least squares mean (standard error)	-0.75 (\pm 0.058)	-0.92 (\pm 0.057)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Fasting Plasma Glucose (FPG) at Week 12

End point title Change From Baseline in Fasting Plasma Glucose (FPG) at Week 12

End point description:

Change in FPG was analysed using an ANCOVA model including the fixed categorical effects of treatment groups (Toujeo, Tresiba) and the randomisation stratum of HbA1c at screening (<8.0%, \geq 8.0%) and the continuous fixed covariate of Baseline FPG value. Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this endpoint.

End point type Secondary

End point timeframe:

Baseline, Week 12

End point values	Toujeo	Tresiba		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	151		
Units: milligrams per decilitre				
least squares mean (standard error)	-16.05 (\pm 5.455)	-34.55 (\pm 5.523)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Time With Glucose Level <70 Milligrams Per Decilitre (All Time and During the Night)

End point title	Percentage of Time With Glucose Level <70 Milligrams Per Decilitre (All Time and During the Night)
-----------------	--

End point description:

The CGM system combined frequent interstitial glucose measurements (every 5 minutes) with ability to analyse glucose levels in real time. "All time" represent the time between 00.00 hour to 23.59 hours and "night" represent the time between 00.00 hour to 05.59 hours. LS means and SE were obtained using ANCOVA model using fixed categorical effects of treatment groups (Toujeo, Tresiba), randomisation stratum of screening HbA1c (<8.0% versus >=8.0%), and the continuous fixed covariate of Baseline value. Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this endpoint.

End point type	Secondary
----------------	-----------

End point timeframe:

During Week 10 up to Week 12

End point values	Toujeo	Tresiba		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	151		
Units: percentage of time				
least squares mean (standard error)				
All time	5.55 (± 0.353)	6.49 (± 0.362)		
Night	6.32 (± 0.511)	6.26 (± 0.524)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Hours Per Day With Glucose Level <70 Milligrams Per Decilitre (All Time and During the Night)

End point title	Mean Hours Per Day With Glucose Level <70 Milligrams Per Decilitre (All Time and During the Night)
-----------------	--

End point description:

"All time" represent the time between 00.00 hour to 23.59 hours and "night" represent the time between 00.00 hour to 05.59 hours. Mean hours per day with glucose level <70 milligrams per decilitre during "all time" and only "during night" for the duration of Week 10 to Week 12 is reported in this endpoint. Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this endpoint.

End point type	Secondary
----------------	-----------

End point timeframe:

During Week 10 up to Week 12

End point values	Toujeo	Tresiba		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	151		
Units: hours per day				
least squares mean (standard error)				
All time	1.33 (± 0.085)	1.56 (± 0.087)		
Night	0.38 (± 0.031)	0.38 (± 0.031)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Time With Glucose Level >180 Milligrams Per Decilitre

End point title	Percentage of Time With Glucose Level >180 Milligrams Per Decilitre
-----------------	---

End point description:

The CGM system combined frequent interstitial glucose measurements (every 5 minutes) with ability to analyse glucose levels in real time. LS means and SE were obtained using ANCOVA model using fixed categorical effects of treatment groups (Toujeo, Tresiba), randomisation stratum of screening HbA1c (<8.0% versus ≥8.0%), and the continuous fixed covariate of Baseline value. Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this endpoint.

End point type	Secondary
----------------	-----------

End point timeframe:

During Week 10 up to Week 12

End point values	Toujeo	Tresiba		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	151		
Units: percentage of time				
least squares mean (standard error)	41.52 (± 0.975)	38.31 (± 1.002)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Hours Per Day With Glucose Level >180 Milligrams Per Decilitre

End point title	Mean Hours Per Day With Glucose Level >180 Milligrams Per Decilitre
-----------------	---

End point description:

Mean hours per day with glucose level >180 milligrams per decilitre for the duration of Week 10 to Week 12 is reported in this endpoint. Analysis was performed on ITT population. Here, 'number of subjects analysed' = subjects evaluable for this endpoint.

End point type	Secondary
----------------	-----------

End point timeframe:

During Week 10 up to Week 12

End point values	Toujeo	Tresiba		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	151		
Units: hours per day				
least squares mean (standard error)	9.96 (± 0.234)	9.19 (± 0.240)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With at Least One Hypoglycemic Event During the On-treatment Period

End point title	Number of Subjects With at Least One Hypoglycemic Event During the On-treatment Period
-----------------	--

End point description:

Severe hypoglycemia was an event in which the subject required the assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions, because the subject was not capable of helping self. Documented symptomatic hypoglycemia was an event during which typical symptoms of hypoglycemia were accompanied by a measured plasma glucose concentration of <3.9 millimoles per litre (mmol/L) (<70 milligrams per decilitre). On-treatment period was defined as the time from the first injection of IMP (included) up to 2 days after the last injection of IMP. Analysis was performed on safety population that included all randomised subjects who had received at least one dose or part of a dose of IMP and were analysed according to the treatment actually received.

End point type	Secondary
----------------	-----------

End point timeframe:

From the first injection of IMP up to 2 days after the last injection of IMP (i.e., up to 86 days)

End point values	Toujeo	Tresiba		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172	171		
Units: subjects				
Any hypoglycemia	165	166		
Severe hypoglycemia	8	10		
Documented symptomatic hypoglycemia	136	134		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Hypoglycemic Events Per Subject Year During the On-treatment Period

End point title	Number of Hypoglycemic Events Per Subject Year During the On-treatment Period
-----------------	---

End point description:

Number of hypoglycemia events (any, severe and documented) per subject-year of exposure were reported. Severe hypoglycemia was an event in which the subject required the assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions, because the subject was not capable of helping self. Documented symptomatic hypoglycemia was an event during which typical symptoms of hypoglycemia were accompanied by a measured plasma glucose concentration of <3.9 mmol/L (<70 milligrams per decilitre). On-treatment period was defined as the time from the first injection of IMP (included) up to 2 days after the last injection of IMP. Total subject years = The sum of the duration of exposure for all subject, expressed in subject years. Analysis was performed on safety population.

End point type	Secondary
----------------	-----------

End point timeframe:

From the first injection of IMP up to 2 days after the last injection of IMP (i.e., up to 86 days)

End point values	Toujeo	Tresiba		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172	171		
Units: events per subject-year				
number (not applicable)				
Any hypoglycemia	109.4	114.9		
Severe hypoglycemia	0.2	0.3		
Documented symptomatic hypoglycemia	67.1	66.9		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

From the first injection of IMP up to 2 days after the last injection of IMP (i.e., up to 86 days)

Adverse event reporting additional description:

Reported AEs were TEAEs that developed/worsened or became serious during on-treatment period (defined as the time from the first injection of IMP to the last injection of IMP + 2 days). Analysis was performed on safety population.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	24.0
--------------------	------

Reporting groups

Reporting group title	Toujeo
-----------------------	--------

Reporting group description:

Toujeo (Insulin Glargine, 300 U/ml) SC injection, before meals once daily in the morning for 12 weeks on top of rapid acting insulin analog.

Reporting group title	Tresiba
-----------------------	---------

Reporting group description:

Tresiba (Insulin Degludec, 100 U/ml) SC injection, before meals once daily in the morning for 12 weeks on top of rapid acting insulin analog.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No non-serious adverse events were reported at the frequency threshold of 5%.

Serious adverse events	Toujeo	Tresiba	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 172 (4.07%)	8 / 171 (4.68%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	0 / 172 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Hypoglycaemic Seizure			
subjects affected / exposed	2 / 172 (1.16%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic Unconsciousness			

subjects affected / exposed	4 / 172 (2.33%)	2 / 171 (1.17%)	
occurrences causally related to treatment / all	1 / 4	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic Intolerance			
subjects affected / exposed	1 / 172 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Failure			
subjects affected / exposed	0 / 172 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 172 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetic Ketoacidosis			
subjects affected / exposed	0 / 172 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 172 (0.00%)	4 / 171 (2.34%)	
occurrences causally related to treatment / all	0 / 0	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Toujeo	Tresiba	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 172 (0.00%)	0 / 171 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported