Clinical trial results:
A 26-week double blinded, multiregional trial comparing the effect and safety of once weekly insulin icodec and once daily insulin degludec 100 units/mL, both in combination with non-insulin anti-diabetic drugs, in insulin naive subjects with type 2 diabetes

Summary

EudraCT number	2020-000472-37
Trial protocol	CZ AT DK FR
Global end of trial date	23 June 2022

Results information

Result version number	v1 (current)
This version publication date	14 July 2023
First version publication date	14 July 2023

Trial information

Trial identification

Sponsor protocol code	NN1436-4479

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04795531
WHO universal trial number (UTN)	U1111-1247-5218

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Allé, Bagsvaerd, Denmark, 2880
Public contact	Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.com
Scientific contact	Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.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	25 August 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 June 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to demonstrate the effect on glycaemic control of once weekly insulin icodec, in combination with non-insulin anti-diabetic drugs, in insulin naïve subjects withtype 2 diabtetes mellitus (T2D).

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (64th World Medical Association (WMA) general Assembly; Oct 2013) and International Council for Harmonisation (ICH) Good Clinical Practice, including archiving of essential documents, (Current Step 4 version, Nov 2016) and 21 Code of Federal Regulations (CFR) 312.120.

Background therapy:

After randomisation subjects continued their pre-trial non-insulin anti-diabetic background medication throughout the entire trial except from sulfonylureas and glinides, which had to be reduced at randomisation by approximately 50% at the discretion of the investigator.

Evidence for comparator: -

Actual start date of recruitment	24 March 2021
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	Argentina: 55
Country: Number of subjects enrolled	Austria: 28
Country: Number of subjects enrolled	Brazil: 51
Country: Number of subjects enrolled	Canada: 54
Country: Number of subjects enrolled	China: 100
Country: Number of subjects enrolled	Czechia: 51
Country: Number of subjects enrolled	Denmark: 32
Country: Number of subjects enrolled	France: 31
Country: Number of subjects enrolled	Mexico: 46
Country: Number of subjects enrolled	Taiwan: 45
Country: Number of subjects enrolled	United States: 95
Worldwide total number of subjects	588
EEA total number of subjects	142

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)	411
From 65 to 84 years	177
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 89 sites in 11 countries as follows (number of sites that screened participants/ number of sites that randomised participants): Argentina (4/4), Austria (3/3), Brazil (4/4), Canada (14/13), China mainland (13/13), Czech Republic (6/6), Denmark (4/4), France (9/8), Mexico (2/2), Taiwan (5/5), United States (28/27).

Pre-assignment

Screening details:

After randomisation subjects continued their pre-trial non-insulin anti-diabetic background medication throughout the entire trial except from sulfonylureas and glinides, which had to be reduced at randomisation by approximately 50% at the discretion of the investigator.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Insulin icodec

Arm description:

Subjects were to receive once weekly subcutaneous (s.c.) injection of insulin icodec using PDS290 prefilled pen-injector at a starting dose of 70 units (U) and once weekly placebo for 26 weeks. The dose was then adjusted once weekly to reach the glycaemic target of 4.4-7.2 millimoles per liter (mmol/L) based on 3 pre-breakfast self-measured plasma glucose (SMPG) values measured on 2 previous days and on the day of the titration. If at least one pre-breakfast SMPG value was: < 4.4 mmol/L: dose reduced by 20 U; If the mean was: 4.4-7.2 mmol/L- no adjustment; > 7.2 mmol/L- dose increased by 20 U.

Arm type	Experimental
Investigational medicinal product name	Insulin icodec 700 U/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received once weekly placebo matched to insulin icodec subcutaneously at an initial dose of 70 U using 3 mL PDS290 pre-filled pen-injector for 26 weeks.

Investigational medicinal product name	Insulin icodec 700 U/mL PDS290
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were to receive once weekly subcutaneous (s.c.) injection of insulin icodec using PDS290 prefilled pen-injector at a starting dose of 70 units (U) and once weekly placebo for 26 weeks. The dose was then adjusted once weekly to reach the glycaemic target of 4.4-7.2 millimoles per liter (mmol/L) based on 3 pre-breakfast self-measured plasma glucose (SMPG) values measured on 2 previous days and on the day of the titration. If at least one pre-breakfast SMPG value was: < 4.4 mmol/L: dose reduced by 20 U; If the mean was: 4.4-7.2 mmol/L- no adjustment; > 7.2 mmol/L- dose increased by 20 U.

Arm title	Insulin degludec

Arm description:

Subjects were to receive once daily s.c. injection of insulin degludec using PDS290 prefilled pen-injector at a starting dose of 10 U and once daily placebo for 26 weeks. The dose was then adjusted once weekly to reach the glycaemic target of 4.4-7.2 millimoles per liter mmol/L based on 3 pre-breakfast values measured on 2 previous days and on the day of the titration. If at least one pre-breakfast SMPG value was: < 4.4 mmol/L: dose reduced by 3 U; If the mean was: 4.4-7.2 mmol/L- no adjustment; > 7.2 mmol/L- dose increased by 3 U.

Arm type	Experimental
Investigational medicinal product name	Tresiba 100 units/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received once daily placebo matched to insulin degludec subcutaneously at an initial dose of 10 U using 3 mL PDS290 pre-filled pen-injector for 26 weeks.

Investigational medicinal product name	Tresiba 100 units/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were to receive once daily s.c. injection of insulin degludec using PDS290 prefilled pen-injector at a starting dose of 10 U and once daily placebo for 26 weeks. The dose was then adjusted once weekly to reach the glycaemic target of 4.4-7.2 millimoles per liter mmol/L based on 3 pre-breakfast values measured on 2 previous days and on the day of the titration. If at least one pre-breakfast SMPG value was: < 4.4 mmol/L: dose reduced by 3 U; If the mean was: 4.4-7.2 mmol/L- no adjustment; > 7.2 mmol/L- dose increased by 3 U.

Number of subjects in period 1	Insulin icodec	Insulin degludec
Started	294	294
Full analysis set (FAS)	294	294
Safety analysis set (SAS)	293	294
Completed	288	286
Not completed	6	8
Consent withdrawn by subject	4	4
Physician decision	-	2
Death	2	1
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Insulin icodec
Reporting group description:	
Subjects were to receive once weekly subcutaneous (s.c.) injection of insulin icodec using PDS290 prefilled pen-injector at a starting dose of 70 units (U) and once weekly placebo for 26 weeks. The dose was then adjusted once weekly to reach the glycaemic target of 4.4-7.2 millimoles per liter (mmol/L) based on 3 pre-breakfast self-measured plasma glucose (SMPG) values measured on 2 previous days and on the day of the titration. If at least one pre-breakfast SMPG value was: < 4.4 mmol/L: dose reduced by 20 U; If the mean was: 4.4-7.2 mmol/L- no adjustment; > 7.2 mmol/L- dose increased by 20 U.	
Reporting group title	Insulin degludec
Reporting group description:	
Subjects were to receive once daily s.c. injection of insulin degludec using PDS290 prefilled pen-injector at a starting dose of 10 U and once daily placebo for 26 weeks. The dose was then adjusted once weekly to reach the glycaemic target of 4.4-7.2 millimoles per liter mmol/L based on 3 pre-breakfast values measured on 2 previous days and on the day of the titration. If at least one pre-breakfast SMPG value was: < 4.4 mmol/L: dose reduced by 3 U; If the mean was: 4.4-7.2 mmol/L- no adjustment; > 7.2 mmol/L- dose increased by 3 U.	

Reporting group values	Insulin icodec	Insulin degludec	Total
Number of subjects	294	294	588
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	210	201	411
From 65-84 years	84	93	177
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	57.70	58.56	
standard deviation	± 10.19	± 9.74	-
Gender Categorical Units: Subjects			
Female	109	110	219
Male	185	184	369

End points

End points reporting groups

Reporting group title	Insulin icodec

Reporting group description:

Subjects were to receive once weekly subcutaneous (s.c.) injection of insulin icodec using PDS290 prefilled pen-injector at a starting dose of 70 units (U) and once weekly placebo for 26 weeks. The dose was then adjusted once weekly to reach the glycaemic target of 4.4-7.2 millimoles per liter (mmol/L) based on 3 pre-breakfast self-measured plasma glucose (SMPG) values measured on 2 previous days and on the day of the titration. If at least one pre-breakfast SMPG value was: < 4.4 mmol/L: dose reduced by 20 U; If the mean was: 4.4-7.2 mmol/L- no adjustment; > 7.2 mmol/L- dose increased by 20 U.

Reporting group title	Insulin degludec

Reporting group description:

Subjects were to receive once daily s.c. injection of insulin degludec using PDS290 prefilled pen-injector at a starting dose of 10 U and once daily placebo for 26 weeks. The dose was then adjusted once weekly to reach the glycaemic target of 4.4-7.2 millimoles per liter mmol/L based on 3 pre-breakfast values measured on 2 previous days and on the day of the titration. If at least one pre-breakfast SMPG value was: < 4.4 mmol/L: dose reduced by 3 U; If the mean was: 4.4-7.2 mmol/L- no adjustment; > 7.2 mmol/L- dose increased by 3 U.

Primary: Change in glycated haemoglobin (HbA1c)

End point title	Change in glycated haemoglobin (HbA1c)

End point description:

Change in HbA1c from baseline week 0 (V2) to week 26 (V28) is presented. The endpoint data was evaluated based on the in-trial observation period. In-trial observation period started at randomisation and ended at the date of: The last direct subject-site contact, withdrawal for subjects who withdrew their informed consent, the last subject-investigator contact as defined by the investigator for subjects who were lost to follow-up (i.e., possibly an unscheduled phone visit) and death for subjects who died before any of the above. Full analysis set (FAS) included all randomised subjects.

End point type	Primary

End point timeframe:

From baseline week 0 (V2) to week 26 (V28)

End point values	Insulin icodec	Insulin degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294	294		
Units: Percentage (%) of HbA1c				
least squares mean (standard error)	-1.57 (± 0.05)	-1.36 (± 0.05)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The response and change from baseline in response after 26 weeks are analysed using an analysis of covariance (ANCOVA) model with treatment, region and SU/glinides use as fixed factors, and baseline response as covariate.

Comparison groups	Insulin icodec v Insulin degludec
Number of subjects included in analysis	588
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.34
upper limit	-0.08

Notes:

[1] - Non-inferiority of insulin icodec was considered confirmed if the upper limit of the two-sided 95% confidence interval (CI) for mean treatment difference (insulin icodec minus insulin degludec) was strictly below 0.3%.

Secondary: Number of clinically significant hypoglycaemic episodes (level 2) (less than [<] 3.0 mmol/L (54 milligrams per deciliter [mg/dL]), confirmed by blood glucose [BG] meter)

End point title	Number of clinically significant hypoglycaemic episodes (level 2) (less than [<] 3.0 mmol/L (54 milligrams per deciliter [mg/dL]), confirmed by blood glucose [BG] meter)

End point description:

Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 millimoles per liter [mmol/L] (54 mg/dL), confirmed by BG meter) is presented. Clinically significant hypoglycaemia (level 2) is defined as plasma glucose value of less than (<) 3.0 mmol/L (54 mg/dL) confirmed by BG meter. The endpoint data was evaluated based on on-treatment observation period. On-treatment period started at the date of first dose of trial product and ended at the first date of any of the following: End of trial visit (V30), Last date on trial product + 5 weeks for once daily insulin and + 6 weeks for once weekly insulin (corresponding to 5 weeks after the end of dosing interval for both treatment arms) and the end-date for in-trial observation period. The on-treatment period represented the time period in which a subject was considered exposed to trial product. Safety analysis set included all subjects who were randomly assigned to trial treatment and who took at least 1 dose of trial product.

End point type	Secondary

End point timeframe:

From baseline week 0 (V2) to week 31 (V30)

End point values	Insulin icodec	Insulin degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	293	294		
Units: Episodes				
number (not applicable)	53	23		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of severe hypoglycaemic episodes (level 3)

End point title	Number of severe hypoglycaemic episodes (level 3)

End point description:

Number of severe hypoglycaemic episodes (level 3) is presented. Severe hypoglycaemia (level 3) is defined as hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. The endpoint data was evaluated based on the on-treatment observation period. The on-treatment period started at the date of first dose of trial product as recorded on the electronic case report form (eCRF), and ended at the first date of any of the following: The end of trial visit (V30), the last date on trial product + 5 weeks for once daily insulin and + 6 weeks for once weekly insulin (corresponding to 5 weeks after the end of the dosing interval for both treatment arms) and the end-date for the in-trial observation period. The on-treatment period represented the time period in which a subject was considered exposed to trial product. Safety analysis set included all subjects who were randomly assigned to trial treatment and who took at least 1 dose of trial product.

End point type	Secondary

End point timeframe:

From baseline week 0 (V2) to week 31 (V30)

End point values	Insulin icodec	Insulin degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	293	294		
Units: Episodes				
number (not applicable)	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in fasting plasma glucose (FPG)

End point title	Change in fasting plasma glucose (FPG)

End point description:

Change in FPG from baseline week 0 (V2) to week 26 (V28) is presented. The endpoint data was evaluated based on the in-trial observation period. In-trial observation period started at randomisation and ended at the date of: The last direct subject-site contact, withdrawal for subjects who withdrew their informed consent, the last subject-investigator contact as defined by the investigator for subjects who were lost to follow-up (i.e., possibly an unscheduled phone visit) and death for subjects who died before any of the above. FAS included all randomised subjects. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline week 0 (V2) to week 26 (V28)

End point values	Insulin icodec	Insulin degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	284	290		
Units: millimoles per litre (mmol/L)				
least squares mean (standard error)	-3.01 (± 0.11)	-2.99 (± 0.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L (54 mg/dL), confirmed by BG meter) or severe hypoglycaemic episodes (level 3) from baseline week 0 (V2) to week 26 (V28)

End point title	Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L (54 mg/dL), confirmed by BG meter) or severe hypoglycaemic episodes (level 3) from baseline week 0 (V2) to week 26 (V28)

End point description:

Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L (54 mg/dL), confirmed by BG meter) or severe hypoglycaemic episodes (level 3) is presented. Clinically significant hypoglycaemia (level 2) is defined as plasma glucose value of < 3.0 mmol/L (54 mg/dL) confirmed by BG meter. Severe hypoglycaemia (level 3) is defined as hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. The endpoint data was evaluated based on on-treatment observation period. On-treatment period started at the date of first dose of trial product and ended at the first date of any of the following: The end of trial visit (V30), the last date on trial product + 5 weeks for once daily insulin and + 6 weeks for once weekly insulin and the end-date for in-trial observation period. Safety analysis set included all subjects who were randomly assigned to trial treatment and who took at least 1 dose of trial product.

End point type	Secondary

End point timeframe:

From baseline week 0 (V2) to week 26 (V28)

End point values	Insulin icodec	Insulin degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	293	294		
Units: Episodes				
number (not applicable)	50	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L (54 mg/dL), confirmed by BG meter) from baseline week 0 (V2) to week 26 (V28)

End point title	Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L (54 mg/dL), confirmed by BG meter) from baseline week 0 (V2) to week 26 (V28)

End point description:

Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L (54 mg/dL), confirmed

by BG meter) or severe hypoglycaemic episodes (level 3) is presented. Clinically significant hypoglycaemia (level 2) is defined as plasma glucose value of < 3.0 mmol/L (54 mg/dL) confirmed by BG meter. Severe hypoglycaemia (level 3) is defined as hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. The endpoint data was evaluated based on on-treatment observation period. On-treatment period started at the date of first dose of trial product and ended at the first date of any of the following: The end of trial visit (V30), the last date on trial product + 5 weeks for once daily insulin and + 6 weeks for once weekly insulin and the end-date for in-trial observation period. Safety analysis set included all subjects who were randomly assigned to trial treatment and who took at least 1 dose of trial product.

End point type	Secondary

End point timeframe:

From baseline week 0 (V2) to week 26 (V28)

End point values	Insulin icodec	Insulin degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	293	294		
Units: Episodes				
number (not applicable)	50	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L (54 mg/dL), confirmed by BG meter) or severe hypoglycaemic episodes (level 3)

End point title	Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L (54 mg/dL), confirmed by BG meter) or severe hypoglycaemic episodes (level 3)

End point description:

Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L (54 mg/dL), confirmed by BG meter) or severe hypoglycaemic episodes (level 3) is presented. Clinically significant hypoglycaemia (level 2) is defined as plasma glucose value of < 3.0 mmol/L (54 mg/dL) confirmed by BG meter. Severe hypoglycaemia (level 3) is defined as hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. The endpoint data was evaluated based on on-treatment observation period. On-treatment period started at the date of first dose of trial product and ended at the first date of any of the following: The end of trial visit (V30), the last date on trial product + 5 weeks for once daily insulin and + 6 weeks for once weekly insulin and the end-date for in-trial observation period. Safety analysis set included all subjects who were randomly assigned to trial treatment and who took at least 1 dose of trial product.

End point type	Secondary

End point timeframe:

From baseline week 0 (V2) to week 31 (V30)

End point values	Insulin icodec	Insulin degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	293	294		
Units: Episodes				
number (not applicable)	53	25		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of severe hypoglycaemic episodes (level 3) from baseline week 0 (V2) to week 26 (V28)

End point title	Number of severe hypoglycaemic episodes (level 3) from baseline week 0 (V2) to week 26 (V28)

End point description:

Number of severe hypoglycaemic episodes (level 3) is presented. Severe hypoglycaemia (level 3) is defined as hypoglycaemia with severe cognitive impairment requiring external assistance for recovery. Safety analysis set included all subjects who were randomly assigned to trial treatment and who took at least 1 dose of trial product.

End point type	Secondary

End point timeframe:

From baseline week 0 (V2) to week 26 (V28)

End point values	Insulin icodec	Insulin degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	293	294		
Units: Episodes				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in body weight

End point title	Change in body weight

End point description:

Change in body weight from baseline week 0 (V2) to week 26 (V28) is presented. The endpoint data was evaluated based on the in-trial observation period. In-trial observation period started at randomisation and ended at the date of: The last direct subject-site contact, withdrawal for subjects who withdrew their informed consent, the last subject-investigator contact as defined by the investigator for subjects who were lost to follow-up (i.e., possibly an unscheduled phone visit) and death for subjects who died before any of the above. Full analysis set included all randomised subjects.

End point type	Secondary

End point timeframe:

From baseline week 0 (V2) to week 26 (V28)

End point values	Insulin icodec	Insulin degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294	294		
Units: Kilograms (kg)				
least squares mean (standard error)	2.77 (± 0.22)	2.32 (± 0.24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean weekly insulin dose

End point title	Mean weekly insulin dose

End point description:

Estimated mean weekly insulin dose during the last 2 weeks of treatment (from week 24 to week 26) is presented. The endpoint data was evaluated based on the on-treatment observation period. The on-treatment period started at the date of first dose of trial product as recorded on the electronic case report form (eCRF), and ended at the first date of any of the following: The end of trial visit (V30), the last date on trial product + 5 weeks for once daily insulin and + 6 weeks for once weekly insulin (corresponding to 5 weeks after the end of the dosing interval for both treatment arms) and the end-date for the in-trial observation period. The on-treatment period represented the time period in which a subject was considered exposed to trial product. FAS included all randomised subjects.

End point type	Secondary

End point timeframe:

From week 24 (P26) to week 26 (V28)

End point values	Insulin icodec	Insulin degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294	294		
Units: Units (U) of insulin				
least squares mean (confidence interval 95%)	204.28 (189.44 to 220.29)	186.52 (173.06 to 201.02)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From week 0 to week 31

Adverse event reporting additional description:

All presented AEs are treatment-emergent adverse events (TEAEs). Adverse events were defined as treatment-emergent if the onset of event occurs in the on-treatment period (from week 0 to week 26). Results are based on safety analysis set which included all subjects randomly assigned to trial treatment and who took at least 1 dose of trial product.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24

Reporting groups

Reporting group title	Insulin degludec

Reporting group description:

Subjects were to receive once daily s.c. injection of insulin degludec using PDS290 prefilled pen-injector at a starting dose of 10 U and once daily placebo for 26 weeks. The dose was then adjusted once weekly to reach the glycaemic target of 4.4-7.2 millimoles per liter mmol/L based on 3 pre-breakfast values measured on 2 previous days and on the day of the titration. If at least one pre-breakfast SMPG value was: < 4.4 mmol/L: dose reduced by 3 U; If the mean was: 4.4-7.2 mmol/L- no adjustment; > 7.2 mmol/L- dose increased by 3 U.

Reporting group title	Insulin Icodec

Reporting group description:

Subjects were to receive once weekly subcutaneous (s.c.) injection of insulin icodec using PDS290 prefilled pen-injector at a starting dose of 70 units (U) and once weekly placebo for 26 weeks. The dose was then adjusted once weekly to reach the glycaemic target of 4.4-7.2 millimoles per liter (mmol/L) based on 3 pre-breakfast self-measured plasma glucose (SMPG) values measured on 2 previous days and on the day of the titration. If at least one pre-breakfast SMPG value was: < 4.4 mmol/L: dose reduced by 20 U; If the mean was: 4.4-7.2 mmol/L- no adjustment; > 7.2 mmol/L- dose increased by 20 U.

Serious adverse events	Insulin degludec	Insulin Icodec	
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 294 (5.10%)	15 / 293 (5.12%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colorectal cancer			
subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma pancreas			

subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	1 / 294 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	1 / 294 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic arteriosclerosis			
subjects affected / exposed	1 / 294 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	1 / 294 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 294 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 294 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	1 / 294 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural complication			
subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 294 (0.34%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure			

subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Diabetic neuropathy			
subjects affected / exposed	1 / 294 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinopathy hypertensive			
subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	1 / 294 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			

subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst			
subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 294 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 294 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	1 / 294 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cellulitis			
subjects affected / exposed	1 / 294 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 294 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 294 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 294 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urosepsis			
subjects affected / exposed	1 / 294 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 294 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Insulin degludec	Insulin Icodec	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 294 (9.86%)	52 / 293 (17.75%)	
Eye disorders			
Diabetic retinopathy			
subjects affected / exposed	6 / 294 (2.04%)	15 / 293 (5.12%)	
occurrences (all)	7	16	
Infections and infestations			
COVID-19			
subjects affected / exposed	14 / 294 (4.76%)	24 / 293 (8.19%)	
occurrences (all)	14	24	
Influenza			
subjects affected / exposed	9 / 294 (3.06%)	15 / 293 (5.12%)	
occurrences (all)	9	18	

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