Clinical trial results:
GPPAD-POInT (Global Platform of Autoimmune Diabetes – Primary Oral Insulin Trial)
Oral Insulin Therapy for Prevention of Autoimmune Diabetes
A study of the Global Platform for the Prevention of Autoimmune Diabetes

Summary

EudraCT number	2017-003088-36
Trial protocol	SE GB PL DE BE
Global end of trial date	28 June 2024

Results information

Result version number	v1 (current)
This version publication date	04 December 2025
First version publication date	04 December 2025

Trial information

Trial identification

Sponsor protocol code	GPPAD-03-POInT

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03364868
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Technische Universität München, School of Medicine
Sponsor organisation address	Ismaninger Strasse 22, München, Germany, 81675
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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	26 August 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 June 2024
Global end of trial reached?	Yes
Global end of trial date	28 June 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether daily administration of oral insulin from age 4 months - 7 months until age 3.00 years to children with elevated genetic risk for type 1 diabetes reduces the cumulative incidence of beta-cell autoantibodies and diabetes in childhood.

Protection of trial subjects:

As part of the safety assessment , blood glucose was monitored before (-10 minutes) and at 30, 60 and 120 minutes after study drug intake at baseline, and at the visits 2, 4 and 8 months.
Adverse events were recorded and assessed until 60 days after end of treatment.
Local anesthetics (EMLA)was used to reduce pain during blood draws.

Background therapy:

No background therapy

Evidence for comparator:

No comparators

Actual start date of recruitment	07 February 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 504
Country: Number of subjects enrolled	Belgium: 80
Country: Number of subjects enrolled	Poland: 242
Country: Number of subjects enrolled	Sweden: 173
Country: Number of subjects enrolled	United Kingdom: 51
Worldwide total number of subjects	1050
EEA total number of subjects	999

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	1050

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Potential study subjects were identified through the GPPAD-02 study testing for type 1 diabetes risk in infancy.
In the GPPAD-02 study, testing for genetic risk of T1D was offered either at delivery (cord blood), together with the regular newborn screening, or at a pediatric baby-visit with collection of blood using GPPAD-02 filter paper cards.

Pre-assignment

Screening details:

Infants were tested for genetic risk of T1D based on risk scores derived from SNPs that defined HLA DR3, HLA DR4, and HLA DQ8 alleles, as well as SNPs from HLA class I and non-HLA T1D susceptibility genes, and from HLA class II protective alleles

Period 1

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

Blinding implementation details:

The IMP management including the blinding was done by a separate Interactive Web Remote System (IWRS).

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

The reference placebo (filling substance only: microcrystalline cellulose) is identical in appearance to the active medication.

Arm type	Placebo
Investigational medicinal product name	Microcrystalline Cellulose
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The reference placebo (filling substance only: microcrystalline cellulose) is identical in appearance to the active medication.

Arm title	Oral Insulin

Arm description:

Daily oral insulin / dose escalation:

7.5 mg for 2 months, followed by 22.5 mg for 2 months, followed by 67.5 mg until age 3.0 years

Arm type	Active comparator
Investigational medicinal product name	Oral Insulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Active ingredient:

Insulin provided as bulk human crystals filled in capsules.
Formulation of 7.5 mg, 22.5 mg and 67.5 mg insulin and microcrystalline cellulose as filling substance.

Number of subjects in period 1	Placebo	Oral Insulin
Started	522	528
Completed	479	485
Not completed	43	43
Adverse event, serious fatal	-	1
Consent withdrawn by subject	25	31
Adverse event, non-fatal	1	-
other	7	2
Lost to follow-up	10	9

Baseline characteristics

Reporting groups

Reporting group title	Placebo

Reporting group description:

The reference placebo (filling substance only: microcrystalline cellulose) is identical in appearance to the active medication.

Reporting group title	Oral Insulin

Reporting group description:

Daily oral insulin / dose escalation:

7.5 mg for 2 months, followed by 22.5 mg for 2 months, followed by 67.5 mg until age 3.0 years

Reporting group values	Placebo	Oral Insulin	Total
Number of subjects	522	528	1050
Age categorical			
Infants at median age of 6 months (range 4.0 - 7.0)			
Units: Subjects			
Infants at median age of 6 months (range 4.0 - 7.0	522	528	1050
Gender categorical Units: Subjects			
Female	260	259	519
Male	262	269	531

Subject analysis sets

Subject analysis set title	Full analysis set (ITT)
Subject analysis set type	Full analysis

Subject analysis set description:

Intention to treat: The intention-to-treat population includes all randomized children who received at least one dose of study medi-cation, according to the treatment they were randomized to receive

Subject analysis set title	Per protocol population
Subject analysis set type	Per protocol

Subject analysis set description:

The per-protocol population will be defined as all randomized children who were administered at least 85% of the expected number of capsules until either age 3 years or, for children who reached the study primary outcome prior to age 3 years, until the study visit when the child was defined as primary outcome positive (two or more islet au-toantibodies or diabetes).

Subject analysis set title	Full analysis set modified for primary outcome
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mITT population includes all randomized participants who received at least one dose of study medication, excluding those with two or more persistent confirmed islet autoantibodies at baseline. This population was used for the analysis of the primary outcome, in accordance with the Statistical Analysis Plan.

Subject analysis set title	Safety analysis
Subject analysis set type	Safety analysis

Subject analysis set description:

This population includes all randomized participants who received at least one dose of the investigational medicinal product (IMP). Safety outcomes were assessed during the treatment period and up to 60 days after treatment discontinuation. All adverse and serious adverse events were evaluated according to standard reporting guidelines.

Reporting group values	Full analysis set (ITT)	Per protocol population	Full analysis set modified for primary outcome
Number of subjects	1049	910	1048
Age categorical			
Infants at median age of 6 months (range 4.0 - 7.0)			
Units: Subjects			
Infants at median age of 6 months (range 4.0 - 7.0	1049	910	1048
Gender categorical Units: Subjects			
Female Male			

Reporting group values	Safety analysis		
Number of subjects	1050		
Age categorical			
Infants at median age of 6 months (range 4.0 - 7.0)			
Units: Subjects			
Infants at median age of 6 months (range 4.0 - 7.0	1050		
Gender categorical Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

The reference placebo (filling substance only: microcrystalline cellulose) is identical in appearance to the active medication.

Reporting group title	Oral Insulin

Reporting group description:

Daily oral insulin / dose escalation:

7.5 mg for 2 months, followed by 22.5 mg for 2 months, followed by 67.5 mg until age 3.0 years

Subject analysis set title	Full analysis set (ITT)
Subject analysis set type	Full analysis

Subject analysis set description:

Intention to treat: The intention-to-treat population includes all randomized children who received at least one dose of study medi-cation, according to the treatment they were randomized to receive

Subject analysis set title	Per protocol population
Subject analysis set type	Per protocol

Subject analysis set description:

The per-protocol population will be defined as all randomized children who were administered at least 85% of the expected number of capsules until either age 3 years or, for children who reached the study primary outcome prior to age 3 years, until the study visit when the child was defined as primary outcome positive (two or more islet au-toantibodies or diabetes).

Subject analysis set title	Full analysis set modified for primary outcome
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mITT population includes all randomized participants who received at least one dose of study medication, excluding those with two or more persistent confirmed islet autoantibodies at baseline. This population was used for the analysis of the primary outcome, in accordance with the Statistical Analysis Plan.

Subject analysis set title	Safety analysis
Subject analysis set type	Safety analysis

Subject analysis set description:

This population includes all randomized participants who received at least one dose of the investigational medicinal product (IMP). Safety outcomes were assessed during the treatment period and up to 60 days after treatment discontinuation. All adverse and serious adverse events were evaluated according to standard reporting guidelines.

Primary: Development of persistent confirmed multiple beta-cell autoantibodies or diagnosis of type 1 diabetes

End point title	Development of persistent confirmed multiple beta-cell autoantibodies or diagnosis of type 1 diabetes

End point description:

The primary outcome was the development of two or more islet autoantibodies, which were defined as confirmed autoantibodies to insulin (IAA), glutamic acid decarboxylase (GADA), insulinoma-associated antigen-2 (IA-2A), or zinc transporter-8 (ZnT8A) in two consecutive samples, and a second autoantibody in at least one sample . Participants who developed diabetes prior to two or more islet autoantibodies were also considered to have reached the primary outcome.

End point type	Primary

End point timeframe:

The primary endpoint was assessed from randomization (age 4–7 months) until diagnosis of type 1 diabetes or up to 54 months after end of treatment

End point values	Placebo	Oral Insulin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	522	526		
Units: Number of subjects	46	52		

Statistical analyses

Statistical analysis title	Two or More Islet AAB or Diabetes

Statistical analysis description:

Events, 5-year cumulative incidence and Hazard Ratio by study arm.
The primary analysis evaluated the time from randomisation to the development of persistent confirmed multiple beta-cell autoantibodies or clinical diagnosis of type 1 diabetes

Comparison groups	Placebo v Oral Insulin
Number of subjects included in analysis	1048
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.56
Method	Wald-test
Parameter estimate	Hazard ratio (HR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.67
Variability estimate	Standard deviation

Notes:

[1] - Superiority analysis was chosen to test whether oral insulin reduces the incidence of beta-cell autoimmunity compared to placebo.

Primary: Primary Outcome in the Sensitivity Analysis

End point title	Primary Outcome in the Sensitivity Analysis

End point description:

The primary outcome was the development of two or more islet autoantibodies, which were defined as confirmed autoantibodies to insulin (IAA), glutamic acid decarboxylase (GADA), insulinoma-associated antigen-2 (IA-2A), or zinc transporter-8 (ZnT8A) in two consecutive samples, and a second autoantibody in at least one sample . Participants who developed diabetes prior to two or more islet autoantibodies were also considered to have reached the primary outcome.

End point type	Primary

End point timeframe:

The primary endpoint was assessed from randomization (age 4-7 months) until diagnosis of type 1 diabetes or up to 54 months after end of treatment

End point values	Placebo	Oral Insulin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	522	527		
Units: Subjects	46	53		

Statistical analyses

Statistical analysis title	Sensitivity Analysis Dataset

Statistical analysis description:

Events, cumulative incidence and Hazard-Ration by study arm in the sensitivity analysis set.
Children, who have two or more islet autoantibodies at baseline, are included in a sensitivity analysis of the primary outcome.

Comparison groups	Placebo v Oral Insulin
Number of subjects included in analysis	1049
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5
Method	Wald-test
Parameter estimate	Log hazard ratio
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.7
Variability estimate	Standard deviation

Primary: Primary Outcome: per Protocol Population Dataset

End point title	Primary Outcome: per Protocol Population Dataset

End point description:

The primary outcome was the development of two or more islet autoantibodies, which were defined as confirmed autoantibodies to insulin (IAA), glutamic acid decarboxylase (GADA), insulinoma-associated antigen-2 (IA-2A), or zinc transporter-8 (ZnT8A) in two consecutive samples, and a second autoantibody in at least one sample . Participants who developed diabetes prior to two or more islet autoantibodies were also considered to have reached the primary outcome.

End point type	Primary

End point timeframe:

The primary endpoint was assessed from randomization (age4-7 months) until diagnosis of type 1 diabetes or up to 54 months after end of treatment

End point values	Placebo	Oral Insulin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	451	458		
Units: Subjects	45	49		

Statistical analyses

Statistical analysis title	Per Protocol Population Dataset

Statistical analysis description:

Events, cumulative incidence and Hazard Ration by study arm in the per protocol population dataset. The per-protocol population was defined as all randomized children who were administered at least 85% of the expected number of capsules until either age 3 years or, for children who reached the study primary outcome prior to age 3 years, until the study visit when the child was defined as primary outcome positive (two or more islet autoantibodies or diabetes).

Comparison groups	Placebo v Oral Insulin
Number of subjects included in analysis	909
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.72
Method	Wald-test
Parameter estimate	Hazard ratio (HR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.62
Variability estimate	Standard deviation

Secondary: One or more islet autoantibody

End point title	One or more islet autoantibody

End point description:

Time from randomisation to development of any persistent confirmed islet autoantibody (IAA, GADA, IA-2A, or ZnT8A), confirmed in two consecutive samples

End point type	Secondary

End point timeframe:

The secondary endpoint was assessed from randomization (age 4–7 months) until diagnosis of type 1 diabetes or up to 54 months after end of treatment

End point values	Placebo	Oral Insulin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	522	527		
Units: Subjects	55	68		

Statistical analyses

Statistical analysis title	One or more islet Autoantibodies
Statistical analysis description:	
Events, 5-year cumulative incidence and Hazard Ratio by study arm	
Comparison groups	Placebo v Oral Insulin
Number of subjects included in analysis	1049
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.25
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.76

Secondary: Persistent confirmed IAA

End point title	Persistent confirmed IAA
End point description:	
The secondary outcome was the elapsed time from random treatment assignment to the development of persistent confirmed IAA.	
End point type	Secondary
End point timeframe:	
The secondary endpoint was assessed from randomization (age 4–7 months) until diagnosis of type 1 diabetes or up to 54 months after end of treatment	

End point values	Placebo	Oral Insulin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	518	524		
Units: Subjects	44	55		

Statistical analyses

Statistical analysis title	Persistent Confirmed IAA
Statistical analysis description:	
Events, 5-year cumulative incidence and Hazard Ratio	
Comparison groups	Placebo v Oral Insulin
Number of subjects included in analysis	1042
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.28
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.85
Variability estimate	Standard deviation

Secondary: Persistent confirmed GADA	
End point title	Persistent confirmed GADA
End point description:	
The secondary outcome was the elapsed time from random treatment assignment to the development of persis-tent confirmed GADA.	
End point type	Secondary
End point timeframe:	
The secondary endpoint was assessed from randomization (age 4–7 months) until diagnosis of type 1 diabetes or up to 54 months after end of treatment	

End point values	Placebo	Oral Insulin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	521	526		
Units: Subjects	37	46		

Statistical analyses

Statistical analysis title	Persistent Confirmed GADA
Statistical analysis description:	
Events, 5-year cumulative incidence and Hazard Ratio by study arm	
Comparison groups	Placebo v Oral Insulin

Number of subjects included in analysis	1047
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.33
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.91
Variability estimate	Standard deviation

Secondary: Diabetes or dysglycemia

End point title	Diabetes or dysglycemia

End point description:

The secondary outcome was the elapsed time from random treatment assignment to the development of persis-tent dysglycemia or diabetes.

End point type	Secondary

End point timeframe:

The secondary endpoint was assessed from randomization (age 4–7 months) until diagnosis of type 1 diabetes or up to 54 months after end of treatment

End point values	Placebo	Oral Insulin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	522	527		
Units: Subjects	24	18		

Statistical analyses

Statistical analysis title	Diabetes or dysglycemia

Statistical analysis description:

Events, 5-year cumulative incidence and Hazard Ration by study arm

Comparison groups	Oral Insulin v Placebo
Number of subjects included in analysis	1049
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.34
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.74

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	1.37
Variability estimate	Standard deviation

Other pre-specified: Clinical Diabetes (Exploratory Outcome)

End point title	Clinical Diabetes (Exploratory Outcome)

End point description:

Exploratory outcome was the elapsed time from random treatment assignment to the development of clinical diabetes.
In children who did not reach the exploratory outcome, the elapsed time is the time from random treatment as-signment to the date of last contact .

End point type	Other pre-specified

End point timeframe:

The exploratory endpoint was assessed from randomization (age 4–7 months) until diagnosis of type 1 diabetes or up to 54 months after end of treatment

End point values	Placebo	Oral Insulin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	522	527		
Units: Subjects	24	18		

Statistical analyses

Statistical analysis title	Clinical Diabetes (Exploratory Outcome)

Statistical analysis description:

Events, 5-year cumulative incidence and Hazard Ratio by study arm

Comparison groups	Placebo v Oral Insulin
Number of subjects included in analysis	1049
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.32
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	1.36
Variability estimate	Standard deviation

Other pre-specified: Progression from Primary Outcome to Diabetes (Exploratory Outcome)

End point title	Progression from Primary Outcome to Diabetes (Exploratory Outcome)

End point description:

Exploratory outcome was the elapsed time from the date of primary outcome to the development of clinical dia-betes.
In children who did not reach the exploratory outcome, the elapsed time is the time from the date of primary out-come to the date of last contact.

End point type	Other pre-specified

End point timeframe:

The exploratory endpoint was assessed from randomization (age 4–7 months) until diagnosis of type 1 diabetes or up to 54 months after end of treatment

End point values	Placebo	Oral Insulin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	52		
Units: Subjects	24	17		

Statistical analyses

Statistical analysis title	Progression from Primary Outcome to Diabetes

Statistical analysis description:

Events, 5-year cumulative incidence and Hazard Ration by study arm

Comparison groups	Placebo v Oral Insulin
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.048
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	1.01

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were documented throughout the treatment period and for an additional 60 days following the last administration of the investigational medicinal product

Adverse event reporting additional description:

AEs were reported via eCRF.
Serious adverse events (SAEs) were reviewed and assessed by an external safety manager and reported to authorities where appropriate.
The evaluation of safety and tolerability included all children who received at least one dose of the investigational product.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

The reference placebo (filling substance only: microcrystalline cellulose) was identical in appeareance to active IMP

Reporting group title	Oral Insulin

Reporting group description:

Daily oral insulin capsules: / dose escalation 7.5 mg for 2 months followed by 22.5 mg for 2 months and 67.5mg followed until age 3.0 years

Serious adverse events	Placebo	Oral Insulin	
Total subjects affected by serious adverse events			
subjects affected / exposed	85 / 522 (16.28%)	90 / 528 (17.05%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasmas benign, malignant and unspecified			
subjects affected / exposed	1 / 522 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Vascular disorders			
subjects affected / exposed	1 / 522 (0.19%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Surgical and medical procedures			
Surgical and medical procedures			
subjects affected / exposed	1 / 522 (0.19%)	3 / 528 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
General disorders and administration site conditions			
subjects affected / exposed	1 / 522 (0.19%)	3 / 528 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Immune system disorders			
subjects affected / exposed	1 / 522 (0.19%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Reproductive System and Breast disorders			
subjects affected / exposed	0 / 522 (0.00%)	1 / 528 (0.19%)	
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			
Respiratory, thoracic and mediastinal disorders			
subjects affected / exposed	3 / 522 (0.57%)	4 / 528 (0.76%)	
occurrences causally related to treatment / all	0 / 3	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Investigations			
subjects affected / exposed	3 / 522 (0.57%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Injury, poisoning, and procedural complications			

subjects affected / exposed	11 / 522 (2.11%)	14 / 528 (2.65%)	
occurrences causally related to treatment / all	0 / 11	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Congenital, familial and genetic disorders			
subjects affected / exposed	3 / 522 (0.57%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Nervous system disorders			
subjects affected / exposed	8 / 522 (1.53%)	9 / 528 (1.70%)	
occurrences causally related to treatment / all	0 / 8	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal disorders			
subjects affected / exposed	6 / 522 (1.15%)	2 / 528 (0.38%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders			
subjects affected / exposed	0 / 522 (0.00%)	1 / 528 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infections and infestations			
subjects affected / exposed	59 / 522 (11.30%)	67 / 528 (12.69%)	
occurrences causally related to treatment / all	0 / 79	0 / 82	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Metabolism and nutritional disorders			
subjects affected / exposed	1 / 522 (0.19%)	0 / 528 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo	Oral Insulin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	500 / 522 (95.79%)	507 / 528 (96.02%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified			
subjects affected / exposed	3 / 522 (0.57%)	0 / 528 (0.00%)	
occurrences (all)	3	0	
Vascular disorders			
Vascular disorders			
subjects affected / exposed	2 / 522 (0.38%)	2 / 528 (0.38%)	
occurrences (all)	2	2	
Surgical and medical procedures			
Surgical and medical procedures			
subjects affected / exposed	11 / 522 (2.11%)	22 / 528 (4.17%)	
occurrences (all)	12	25	
General disorders and administration site conditions			
General disorders and administration site conditions			
subjects affected / exposed	245 / 522 (46.93%)	258 / 528 (48.86%)	
occurrences (all)	526	535	
Immune system disorders			
Immune system disorders			
subjects affected / exposed	23 / 522 (4.41%)	11 / 528 (2.08%)	
occurrences (all)	28	12	
Social circumstances			
Social circumstances			
subjects affected / exposed	0 / 522 (0.00%)	1 / 528 (0.19%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Reproductive system and breast disorders			
subjects affected / exposed	5 / 522 (0.96%)	5 / 528 (0.95%)	
occurrences (all)	6	5	
Respiratory, thoracic and mediastinal disorders			

Respiratory, thoracic and mediastinal disorders			
subjects affected / exposed	78 / 522 (14.94%)	86 / 528 (16.29%)	
occurrences (all)	111	131	
Psychiatric disorders			
Psychiatric disorders			
subjects affected / exposed	5 / 522 (0.96%)	6 / 528 (1.14%)	
occurrences (all)	5	6	
Hepatobiliary disorders			
Hepatobiliary disorders			
subjects affected / exposed	0 / 522 (0.00%)	1 / 528 (0.19%)	
occurrences (all)	0	1	
Investigations			
Investigations			
subjects affected / exposed	14 / 522 (2.68%)	6 / 528 (1.14%)	
occurrences (all)	16	6	
Injury, poisoning and procedural complications			
Injury. poisoning and procedural complications			
subjects affected / exposed	99 / 522 (18.97%)	88 / 528 (16.67%)	
occurrences (all)	166	142	
Congenital, familial and genetic disorders			
Congenital, familial and genetic disorders			
subjects affected / exposed	9 / 522 (1.72%)	4 / 528 (0.76%)	
occurrences (all)	9	5	
Cardiac disorders			
Cardiac disorders			
subjects affected / exposed	4 / 522 (0.77%)	2 / 528 (0.38%)	
occurrences (all)	6	2	
Nervous system disorders			
Nervous system disorders			
subjects affected / exposed	15 / 522 (2.87%)	17 / 528 (3.22%)	
occurrences (all)	16	23	
Blood and lymphatic system disorders			
Blood and lymphatic system disorders			
subjects affected / exposed	16 / 522 (3.07%)	11 / 528 (2.08%)	
occurrences (all)	16	12	
Ear and labyrinth disorders			

Ear and labyrynth disorders			
subjects affected / exposed	3 / 522 (0.57%)	15 / 528 (2.84%)	
occurrences (all)	6	15	
Eye disorders			
Eye disorders			
subjects affected / exposed	4 / 522 (0.77%)	10 / 528 (1.89%)	
occurrences (all)	4	10	
Gastrointestinal disorders			
Gastrointestinal disorders			
subjects affected / exposed	219 / 522 (41.95%)	233 / 528 (44.13%)	
occurrences (all)	429	435	
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders			
subjects affected / exposed	87 / 522 (16.67%)	75 / 528 (14.20%)	
occurrences (all)	108	87	
Renal and urinary disorders			
Renal and urinary disorders			
subjects affected / exposed	4 / 522 (0.77%)	3 / 528 (0.57%)	
occurrences (all)	4	3	
Endocrine disorders			
Endocrine disorders			
subjects affected / exposed	1 / 522 (0.19%)	0 / 528 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Muscoskeletal and connective tissue disorders			
subjects affected / exposed	5 / 522 (0.96%)	7 / 528 (1.33%)	
occurrences (all)	6	8	
Infections and infestations			
Infections and infestations			
subjects affected / exposed	488 / 522 (93.49%)	492 / 528 (93.18%)	
occurrences (all)	3677	3604	
Metabolism and nutrition disorders			
Metabolism and nutritional disorders			
subjects affected / exposed	17 / 522 (3.26%)	5 / 528 (0.95%)	
occurrences (all)	19	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 December 2018	Update IMPD and optimized manufacturing process
11 February 2022	Protocol Version 3.0 to Version 4.0 The amendment relates to the study duration (accrual was shorter than projected), a recalculation of power, and the interim analysis. In the original POINT protocol, study duration was estimated to last 7 years (including 3.5 years accrual, and 3.5 years follow-up, LPLV projected January 2025), and power was calculated accordingly. However enrollment was shorter and thus the study duration would be ~6.5 years (including 3.17 years accrual, and 3.25 years follow-up, LPLV June 2024). The statistician performed a new power calculation and confirmed that based on the true number of events and the current drop out rate, we still would have over 80% power despite a reduction of a median of 5 months observation time if we also drop the interim analysis

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/41237794