A 26-week trial comparing the effect and safety of once weekly insulin icodec and once daily insulin glargine 100 units/mL, both in combination with bolus insulin with or without non-insulin anti-diabetic drugs, in subjects with type 2 diabetes on a basal-bolus regimen.

Published: 21-10-2020
Last updated: 08-04-2024

Primary objectiveTo demonstrate the effect on glycaemic control of once weekly insulin icodec in combination with insulin aspart, with or without non-insulin anti-diabetic drugs, in subjects with T2D on a basal-bolus regimen. This includes comparing...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON54981

Source
ToetsingOnline

Brief title
ONWARDS 4

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
diabetes, Diabetes Mellitus type 2

Research involving
Human

Sponsors and support

Primary sponsor: Novo Nordisk
Source(s) of monetary or material Support: Novo Nordisk

Intervention

Keyword: Diabetes type 2, insulin icodec, Once weekly

Outcome measures

Primary outcome

Change in HbA1c (%) from baseline week 0 (V2) to week 26 (V28)

Secondary outcome

Secondary efficacy endpoints

* Change in fasting plasma glucose from baseline week 0 (V2) to week 26 (V28)

* Time in target-range 3.9*10.0 mmol/L (70-180 mg/dL) from week 22 (V24) to

week 26 (V28)

Secondary safety endpoints

* Number of severe hypoglycaemic episodes (level 3) from baseline week 0 (V2)

to week 31 (V30)

* 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 31

(V30) * 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 31 (V30)

* Time spent < 3.0 mmol/L (54 mg/dL) from week 22 (V24) to week 26 (V28)

* Time spent > 10 mmol/L (180 mg/dL) from week 22 (V24) to week 26 (V28)

* Mean weekly insulin dose from week 24 (V26) to week 26 (V28)

* Change in body weight from baseline week 0 (V2) to week 26 (V28)

Study description

Background summary

T2D is characterised by insulin resistance, impaired insulin secretion, increased hepatic glucose output due to glucagon dysregulation resulting in chronic hyperglycaemia. The pathogenesis is not fully understood but seems to be heterogeneous, involving environmental, lifestyle, and genetic factors leading to chronic hyperglycaemia caused by peripheral tissue insulin resistance, impaired insulin secretion due to abnormal beta-cell function and abnormal glucose metabolism in the liver. The current treatment cascade follows a stepwise approach comprising lifestyle changes in combination with pharmacological intervention. In many countries, metformin is recommended as initial pharmacological therapy, followed by combination therapy with other oral anti-diabetic drugs, glucagon-like peptide 1 receptor agonists (GLP-1 RA) and/or insulin as the disease progresses. On average, after failure of diet and exercise alone, subjects require a new intervention with glucose-lowering agents every 3-4 years in order to obtain/retain good glycaemic control. Clinical inertia, often resulting from a resistance to insulin initiation and intensification, is a major contributing factor to subjects with T2D who are not achieving recommended glycaemic targets. Increased convenience is believed to support timely insulin initiation and intensification in the treatment for T2D.

Study objective

Primary objective
To demonstrate the effect on glycaemic control of once weekly insulin icodec in combination with insulin aspart, with or without non-insulin anti-diabetic drugs, in subjects with T2D on a basal-bolus regimen. This includes comparing the difference in change from baseline in HbA1c between insulin icodec and insulin glargine after 26 weeks of treatment to a non-inferiority limit of 0.3%.

Secondary objective
To compare safety with once weekly insulin icodec versus once daily insulin glargine, both in combination with insulin aspart, with or without non-insulin anti-diabetic drugs, in subjects with T2D on a basal-bolus regimen.

Study design

A 26-week trial comparing the effect and safety of once weekly insulin icodec and once daily insulin glargine 100 units/mL, both in combination with bolus insulin with or without non-insulin anti-diabetic drugs, in subjects with type 2 diabetes on a basal-bolus regimen.

Intervention

Subjects will be randomised (1:1) to receive once weekly insulin icodec or once daily insulin glargine, both in combination with 2-4 times daily injections of insulin aspart. Insulin icodec, insulin glargine and insulin aspart are all administered as a subcutaneous injection.

Study burden and risks

Insulin icodec is efficacious at clinically relevant doses. Titration guidance for phase 3a trials aims to achieve good glycaemic control without increasing the risk of hypoglycaemic events.
No new significant safety information that changes the current benefit*risk profile of insulin icodec emerged from the ongoing and completed clinical trials. The safety profile of insulin icodec remains in line with the cumulative experience.
As an overall assessment, Novo Nordisk evaluates that the benefit*risk balance of insulin icodec remains favourable.
Considering the measures taken to minimise risk to subjects participating in this trial, the potential risks identified in association with insulin icodec are justified by the anticipated benefits that may be afforded to subjects with diabetes mellitus.

Contacts

Public
Novo Nordisk

Flemingweg 8
Alphen aan den Rijn 2408AV
NL
Scientific
Novo Nordisk

Flemingweg 8
Alphen aan den Rijn 2408AV
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Male or female aged above or equal to 18 years at the time of signing informed consent.
- Diagnosed with T2D * 180 days prior to the day of screening.
- HbA1c from 7.0-10.0% (53.0-85.8 mmol/mol) both inclusive at screening confirmed by central laboratory analysis.
- Treated with once daily basal insulin (neutral protamine hagedorn insulin, insulin degludec, insulin detemir, insulin glargine 100 units/mL, or insulin glargine 300 units/mL) and 2-4 daily injections of bolus insulin analog (insulin aspart, faster acting insulin aspart, insulin lispro, faster acting insulin lispro, insulin glulisine) * 90 days prior to the day of screening with or without any of the following anti-diabetic drugs/regimens with stable doses * 90 days prior to screening:
* Metformin
* Sulfonylureas
* Meglitinides (glinides)
* DPP-4 inhibitors
* SGLT2 inhibitors
* Thiazolidinediones
* Alpha-glucosidase inhibitors
* Oral combination products (for the allowed individual oral anti-diabetic drugs)
* Oral or injectable GLP-1 RAs
- Body mass index (BMI) * 40.0 kg/m2

Exclusion criteria

- Any episodes (as declared by the subject or in the medical records) of

diabetic ketoacidosis within 90 days prior to the day of screening.
- Myocardial infarction, stroke, hospitalisation for unstable angina pectoris or transient ischaemic attack within 180 days prior to the day of screening.
- Chronic heart failure classified as being in New York Heart Association Class IV at screening.
- Anticipated initiation or change in concomitant medications (for more than 14 consecutive days) known to affect weight or glucose metabolism (e.g. treatment with orlistat, thyroid hormones, or corticosteroids).
- Uncontrolled and potentially unstable diabetic retinopathy or maculopathy. Verified by a fundus examination performed within the past 90 days prior to screening or in the period between screening and randomisation. Pharmacological pupil-dilation is a requirement unless using a digital fundus photography camera specified for non-dilated examination.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-06-2021
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Lantus
Generic name:	glargine

Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	nog niet bekend
Generic name:	icodec

Ethics review

Approved WMO Date:	21-10-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-11-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-11-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-01-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-01-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-06-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2020-000474-16-NL
CCMO	NL75121.018.20