Efficacy and safety of once weekly insulin icodec compared to once daily insulin degludec 100 units/mL, both in combination with insulin aspart, in adults with type 1 diabetes.;A 26-week, randomised, multicentre, open-label, active-controlled, parallel group, two armed, treat-to-target trial investigating the effect on glycaemic control and safety of treatment with once weekly insulin icodec compared to once daily insulin degludec, both in combination with insulin aspart in adults with type 1 di

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Primary objectiveTo confirm the effect on glycaemic control of once weekly insulin icodec in combination with insulin aspart, in subjects with T1D. This includes comparing the difference in change from baseline in HbA1c between once weekly insulin...

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

Summary

ID

NL-OMON52258

Source
ToetsingOnline

Brief title
ONWARDS 6

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
diabetes, Diabetes Mellitus type 1

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Diabetes type 1, Insulin icodec, Once weekly

Outcome measures

Primary outcome

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

Secondary outcome

Secondary efficacy endpoints

-Change in fasting plasma glucose (FPG) from baseline (week 0) to week 26

-Time in range 3.9-10.0 mmol/L (70-180 mg/dL) from week 22 to week 26

-Change in DTSQs (Diabetes Treatment Satisfaction Questionnaire) in total

treatment satisfaction from baseline (week 0) to week 26

-Change in HbA1c from baseline (week 0) to week 52

Secondary safety endpoints

-Number of severe hypoglycaemic episodes (level 3) from baseline (week 0) to week 26

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

-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) to week 26

-Number of severe hypoglycaemic episodes (level 3) from baseline (week 0) to week 57

-Number of clinically significant hypoglycaemic episodes (level 2) (<3.0 mmol/L (54 mg/dL), confirmed by BG meter) from baseline (week 0) to week 57

-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) to week 57

-Number of nocturnal 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) to week 26

-Number of nocturnal 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) to week 57

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

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

-Mean total weekly insulin dose from week 24 to week 26

-Mean total weekly insulin dose from week 50 to week 52

-Change in body weight from baseline (week 0) to week 26

Study description

Background summary

T1D is a heterogeneous disorder characterised by T cell-mediated autoimmune destruction of insulin-producing beta cells in the pancreas. The destruction of beta cell function leads to insulin deficiency and the requirement of lifelong administration of exogenous insulin. Results from the DCCT study and the follow-up study (EDIC) have demonstrated the importance of maintaining tight glycaemic control to reduce the risk of long-term complications associated with diabetes. As such, the fundamental principle for insulin treatment of T1D is to mimic normal physiological patterns as closely as possible. The current gold standard of care is based on intensive insulin therapy with multiple daily injections of prandial and basal insulin or continuous subcutaneous insulin infusion.

Study objective

Primary objective
To confirm the effect on glycaemic control of once weekly insulin icodec in combination with insulin aspart, in subjects with T1D. This includes comparing the difference in change from baseline in HbA1c between once weekly insulin icodec and once daily insulin degludec both in combination with insulin aspart after 26 weeks of treatment to a non-inferiority limit of 0.3%.

Secondary objective
To compare the safety and patient reported outcomes of once weekly insulin icodec versus once daily insulin degludec, both in combination with insulin aspart, in subjects with T1D.

Study design

This is a 26-week randomised, multicentre, multinational, open-label, active controlled, parallel group, two-armed, treat-to-target trial with two treatment arms. Subjects will be randomised (1:1) to receive either insulin icodec or once daily insulin degludec, both in combination with 2-4 daily bolus injections of insulin aspart. Randomisation of subjects will be stratified based on pre-trial basal insulin regimen and by HbA1c (either <8% or >= 8%) at

screening.

Intervention

Subjects will be randomised (1:1) to a treat-to-target basal-bolus insulin regimen with either once weekly insulin icodec or once daily insulin degludec, both in combination with insulin aspart.

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 risks identified in association with insulin icodec are justified by the anticipated benefits that may be afforded to subjects with diabetes mellitus.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-Male or female aged 18 years or more at the time of signing informed consent.
-Diagnosed with type 1 diabetes mellitus at least 1 year prior to the day of screening.
-Treated with multiple daily insulin injections (basal and bolus insulin analogue regimes) at least 1 year prior to the day of screening.
-HbA1c below 10% at screening visit based on analysis from central laboratory.

Exclusion criteria

- Myocardial infarction, stroke, hospitalization for unstable angina pectoris or transient ischaemic attack within 180 days prior to the day of screening.
-Chronic heart failure classified as New York Heart Association (NYHA) 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):	02-07-2021
Enrollment:	30
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	17-02-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	09-04-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-04-2021

Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	11-08-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-12-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-01-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-05-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-06-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-07-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-09-2022
Application type:	Amendment
Review commission:	METC NedMec

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	EUCTR2020-002374-27-NL
CCMO	NL76301.041.21
Other	UTN: U1111-1251-7315