Clinical trial results:
The effect of insulin degludec on risk of symptomatic nocturnal hypoglycaemia in subjects with type 1 diabetes and high risk of nocturnal severe hypoglycaemia

Summary

EudraCT number	2014-001942-24
Trial protocol	DK
Global end of trial date	01 March 2019

Results information

Result version number	v1 (current)
This version publication date	18 July 2021
First version publication date	18 July 2021
Summary attachment (see zip file)	Abstract sent to Diabetologia (Diabetologia_HypoDeg_Abstract_Juni_2021.pdf)

Trial information

Trial identification

Sponsor protocol code	HypoDeg

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02192450
WHO universal trial number (UTN)	-
Other trial identifiers	Regional Committee on Biomedical Research Ethics : #H-3-2014-101, Danish Medicines Agency : (#2014071615, Danish Data Protection Agency: I-suite no: 02945; #NOH-2014-018

Notes:

Sponsors

Sponsor organisation name	Nordsjællands Hospital
Sponsor organisation address	Dyrehavevej 29, Hilleroed, Denmark,
Public contact	Nordsjællands Hospital, Department of Cardiology, Nephrology and Endocrinology, +45 48294810, ulrik.pedersen-bjergaard@regionh.dk
Scientific contact	Nordsjællands Hospital, Department of Cardiology, Nephrology and Endocrinology, +45 48294810, ulrik.pedersen-bjergaard@regionh.dk

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	21 February 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 February 2019
Global end of trial reached?	Yes
Global end of trial date	01 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To test the hypothesis that insulin degludec, compared to insulin glargine, reduces the risk of symptomatic nocturnal hypoglycaemia in subjects with the greatest potential benefit from optimised insulin treatment - which is patients with type 1 diabetes and high risk of nocturnal severe hypoglycaemia.

Protection of trial subjects:

None. This was a pragmatic clinical trial, mimicking regular clinical practice.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2014
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	Denmark: 149
Worldwide total number of subjects	149
EEA total number of subjects	149

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)	149

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

HypoDeg trial was an investigator-initiated, two-year, cross-over study conducted in a PROBE (prospective, randomised, open, blinded endpoint) design, carried out at ten centres in Denmark. Recruitment Period: December 1st. 2015 - March 20th 2017.

Pre-assignment

Screening details:

Patients were eligible if they had been diagnosed clinically with type 1 diabetes for more than five years, were aged 18 years or older and had reported one or more episodes of nocturnal severe hypoglycaemia in the previous two years (defined by need for treatment assistance from another person).

Period 1

Period 1 title	First insulin
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	To receive insulin degludec first

Arm description: -

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

Dosage and administration details:

Once a day

Arm title	To receive insulin glargine U100 first

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Insulin glargine U100
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Once a day

Number of subjects in period 1	To receive insulin degludec first	To receive insulin glargine U100 first
Started	73	76
Completed	61	73
Not completed	12	3
Physician decision	2	-

Consent withdrawn by subject	-	2
Adverse event, non-fatal	2	-
Did not want to cross-over	4	-
Unknown	1	1
Non-comliance	3	-

Period 2

Period 2 title	Second insulin
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	To receive insulin glargine U100 second

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Insulin glargine U100
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Once a day

Arm title	To receive insulin degludec second

Arm description: -

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

Dosage and administration details:

Once a day

Number of subjects in period 2	To receive insulin glargine U100 second	To receive insulin degludec second
Started	61	73
Completed	56	72
Not completed	5	1
Consent withdrawn by subject	2	-
Fulfilled withdrawn criteria	1	-

Unknown	1	-
Died	1	1

Baseline characteristics

Reporting groups	
Reporting group title	First insulin

Reporting group description: -

Reporting group values	First insulin	Total	
Number of subjects	149	149	
Age categorical Units: Subjects			
Adults (18-64 years)	149	149	
Gender categorical Units: Subjects			
Female	44	44	
Male	105	105	

End points

End points reporting groups

Reporting group title	To receive insulin degludec first
Reporting group description: -	
Reporting group title	To receive insulin glargine U100 first
Reporting group description: -	
Reporting group title	To receive insulin glargine U100 second
Reporting group description: -	
Reporting group title	To receive insulin degludec second
Reporting group description: -	

Primary: Number of episodes of nocturnal symptomatic hypoglycaemia reported by the patients during the maintenance periods, i.e., the last nine months of each treatment arm

End point title	Number of episodes of nocturnal symptomatic hypoglycaemia reported by the patients during the maintenance periods, i.e., the last nine months of each treatment arm[1]

End point description:

End point type	Primary

End point timeframe:

Number of episodes of nocturnal symptomatic hypoglycaemia reported by the patients during the maintenance periods, i.e., the last nine months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No specification

End point values	To receive insulin degludec first	To receive insulin glargine U100 first		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	72		
Units: Episodes of nocturnal symptomatic hypogl	319	408		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of severe hypoglycaemia

End point title	Incidence of severe hypoglycaemia

End point description:

End point type	Secondary

End point timeframe:

incidence of severe hypoglycaemia (total, night-time, daytime) as defined by ADA as an event requiring assistance of another person to actively administer carbohydrates, glucagon, or take other corrective

End point values	To receive insulin degludec first	To receive insulin glargine U100 first		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	72		
Units: Episodes of severe hypoglycaemia	56	80		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: From randomization to one month after study end.	
Assessment type	Systematic

Dictionary used	
Dictionary name	Customized
Dictionary version	1

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

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 specification

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31337371