Clinical trial results:
A Trial Investigating the Pharmacokinetic Properties of NN5401 (insulin degludec/insulin aspart) in Children, Adolescents and Adults with Type 1 Diabetes

Summary

EudraCT number	2009-016779-31
Trial protocol	DE
Global end of trial date	30 November 2010

Results information

Result version number	v1
This version publication date	16 March 2016
First version publication date	21 July 2015

Trial information

Trial identification

Sponsor protocol code	NN5401-1982

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01138488
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Allé, Bagsvaerd, Denmark, 2880
Public contact	Global Clinical Registry (GCR, 1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com
Scientific contact	Global Clinical Registry (GCR, 1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000479-PIP01-08
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 May 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 November 2010
Global end of trial reached?	Yes
Global end of trial date	30 November 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the total exposure of SIAC (insulin degludec/insulin aspart) in children, adolescents and adult subjects with type 1 diabetes

Protection of trial subjects:

Not applicable

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	07 June 2010
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	Germany: 38
Worldwide total number of subjects	38
EEA total number of subjects	38

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)	12
Adolescents (12-17 years)	13
Adults (18-64 years)	13
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Single centre in Germany

Pre-assignment

Screening details:

Not applicable

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Children

Arm description:

Children (6-11) : All subjects received one single dose of (100 U/mL) insulin degludec/insulin aspart (IDegAsp) (0.5 U/kg)

Arm type	Experimental
Investigational medicinal product name	IDegAsp
Investigational medicinal product code	IDegAsp
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

All subjects received one single dose of IDegAsp (0.5 U/kg) administered as a subcutaneous injection into a lifted skin fold of the lower abdominal wall above the inguinal area. The administration of trial occurred at approximately 8:00 hours in the morning on a single test day.

Arm title	Adolescents

Arm description:

Adolescents (12-17): All subjects received one single dose (100 U/mL) of IDegAsp (0.5 U/kg)

Arm type	Experimental
Investigational medicinal product name	IDegAsp
Investigational medicinal product code	IDegAsp
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

All subjects received one single dose of IDegAsp (0.5 U/kg) administered as a subcutaneous injection into a lifted skin fold of the lower abdominal wall above the inguinal area. The administration of trial occurred at approximately 8:00 hours in the morning on a single test day.

Arm title	Adults

Arm description:

Adults (18-65): All subjects received one single dose (100 U/mL) of IDegAsp (0.5 U/kg)

Arm type	Experimental

Investigational medicinal product name	IDegAsp
Investigational medicinal product code	IDegAsp
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

All subjects received one single dose of IDegAsp (0.5 U/kg) administered as a subcutaneous injection into a lifted skin fold of the lower abdominal wall above the inguinal area. The administration of trial occurred at approximately 8:00 hours in the morning on a single test day.

Number of subjects in period 1	Children	Adolescents	Adults
Started	12	13	13
Completed	12	13	13

Baseline characteristics

Reporting groups	
Reporting group title	Children
Reporting group description:	
Children (6-11) : All subjects received one single dose of (100 U/mL) insulin degludec/insulin aspart (IDegAsp) (0.5 U/kg)	
Reporting group title	Adolescents
Reporting group description:	
Adolescents (12-17): All subjects received one single dose (100 U/mL) of IDegAsp (0.5 U/kg)	
Reporting group title	Adults
Reporting group description:	
Adults (18-65): All subjects received one single dose (100 U/mL) of IDegAsp (0.5 U/kg)	

Reporting group values	Children	Adolescents	Adults
Number of subjects	12	13	13
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)	12	0	0
Adolescents (12-17 years)	0	13	0
Adults (18-64 years)	0	0	13
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	6	5	4
Male	6	8	9
Mean duration of diabetes			
Mean duration of diabetes			
Units: Years			
arithmetic mean	5.8	5.6	11.3
standard deviation	± 3	± 3.2	± 6.2
HbA1c			
Mean HbA1c%			
Units: Percentage			
arithmetic mean	7.7	7.6	7.7
standard deviation	± 1	± 0.9	± 0.9

Reporting group values	Total		
Number of subjects	38		
Age categorical Units: Subjects			
In utero	0		

Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	12		
Adolescents (12-17 years)	13		
Adults (18-64 years)	13		
From 65-84 years	0		
85 years and over	0		
Gender categorical			
Units: Subjects			
Female	15		
Male	23		
Mean duration of diabetes			
Mean duration of diabetes			
Units: Years			
arithmetic mean			
standard deviation	-		
HbA1c			
Mean HbA1c%			
Units: Percentage			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Children
Reporting group description:	
Children (6-11) : All subjects received one single dose of (100 U/mL) insulin degludec/insulin aspart (IDegAsp) (0.5 U/kg)	
Reporting group title	Adolescents
Reporting group description:	
Adolescents (12-17): All subjects received one single dose (100 U/mL) of IDegAsp (0.5 U/kg)	
Reporting group title	Adults
Reporting group description:	
Adults (18-65): All subjects received one single dose (100 U/mL) of IDegAsp (0.5 U/kg)	

Primary: AUCI454, 0-∞,SD, area under the serum insulin 454 (insulin degludec) concentration-time curve from 0 to infinity after single dose

End point title	AUCI454, 0-∞,SD, area under the serum insulin 454 (insulin degludec) concentration-time curve from 0 to infinity after single dose
End point description:	
End point type	Primary
End point timeframe:	
0 to infinity after single dose	

End point values	Children	Adolescents	Adults	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	13	13	
Units: pmol*h/L (CV%)				
geometric mean (geometric coefficient of variation)	121569 (± 69)	104895 (± 36)	85367 (± 24)	

Statistical analyses

Statistical analysis title	Mean ratio and CI
Comparison groups	Children v Adults
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	Mean ratio
Point estimate	1.42

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	2.16

Notes:

[1] - Mean ratio was calculated for Children/Adults

Statistical analysis title	Mean ratios and CI
Comparison groups	Adolescents v Adults
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	other[2]
Parameter estimate	Mean ratio
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.58

Notes:

[2] - Mean ratio was calculated for Adolescents/Adults

Primary: AUCIAsp,0-12h,SD, area under the serum insulin aspart concentration-time curve from 0 to 12 hours after a single dose

End point title	AUCIAsp,0-12h,SD, area under the serum insulin aspart concentration-time curve from 0 to 12 hours after a single dose

End point description:

End point type	Primary

End point timeframe:

0 to 12 hours after single dose

End point values	Children	Adolescents	Adults	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	13	13	
Units: pmol*h/L (CV%)				
geometric mean (geometric coefficient of variation)	1507 (± 66)	1013 (± 49)	892 (± 53)	

Statistical analyses

Statistical analysis title	AUCIAsp,0-12h,

Statistical analysis description:

AUCIAsp,0-12h,SD, area under the serum insulin aspart concentration-time curve from 0 to 12 hours after a single dose

Comparison groups	Children v Adults
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean ratio
Point estimate	1.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	2.8

Statistical analysis title	AUCIAsp,0-12h,

Statistical analysis description:

AUCIAsp,0-12h,SD, area under the serum insulin aspart concentration-time curve from 0 to 12 hours after a single dose

Comparison groups	Adolescents v Adults
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean ratio
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.69

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Onset after first trial product administration and no later than 7 days after the last trial product administration.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	Children
Reporting group description: -	
Reporting group title	Adolescents
Reporting group description: -	
Reporting group title	Adults

Reporting group description: -

Serious adverse events	Children	Adolescents	Adults
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Children	Adolescents	Adults
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 12 (41.67%)	1 / 13 (7.69%)	4 / 13 (30.77%)
Vascular disorders			
Phlebitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			

Headache			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	2 / 13 (15.38%)
occurrences (all)	0	1	2
Orthostatic intolerance			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Catheter site related reaction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Injection site haematoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	2 / 13 (15.38%)
occurrences (all)	0	1	2
Anal abscess			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 August 2010	• The BMI ranges for children were set too narrowly so that subjects with normal BMI could have been excluded from the trial. Thus, in order to ensure that children and adolescents with normal BMIs were included in the trial, BMI ranges were updated to be in accordance with the German guidelines of Association of obesity in childhood and adolescence. • The allowed minimum haemoglobin value for children and adolescents were set according to haemoglobin reference values for adults (minus approximately 10 percent). In order to follow local reference ranges of haemoglobin, values were adjusted to correspond to age specific reference ranges (minus 10 percent) in order to ensure that children and adolescents with normal haemoglobin levels were not excluded from the trial. • In addition other minor corrections and changes were included in the amendment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported