Clinical trial results:
A Study of Effectiveness and Safety of Apidra in Combination With Lantus Therapy in Basal-bolus Insulin Regimen in Inadequately Controlled Children and Adolescents With Type 1 Diabetes in the Russian Federation.

Summary

EudraCT number	2014-004639-38
Trial protocol	Outside EU/EEA
Global end of trial date	18 October 2012

Results information

Result version number	v1 (current)
This version publication date	01 April 2016
First version publication date	26 July 2015

Trial information

Trial identification

Sponsor protocol code	APIDR_L_04884

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01202474
WHO universal trial number (UTN)	U1111-1116-8645

Notes:

Sponsors

Sponsor organisation name	Sanofi-aventis Russia
Sponsor organisation address	Tverskaya str., 22, "Summit Business Centre" , Moscow, Russian Federation, 125009
Public contact	Trial Transparency Team, Sanofi Aventis Recherche & Developpement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi Aventis Recherche & Developpement, Contact-US@sanofi.com

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 March 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 October 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the percentage of subjects achieving glycosylated hemoglobin (HbA1c) level < 8% (in subjects of 6-12 years old) and HbA1c level < 7.5% (in subjects of 13-17 year old) at 6 and 12 months of treatment.

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of pediatric subjects. The parent(s) or guardian(s) as well as the children were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time. In addition to the consent form for the parent(s)/guardian(s), an assent form in child-appropriate language was provided and explained to the child. Repeated invasive procedures were minimized. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight. A topical anesthesia may have been used to minimize distress and discomfort.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 May 2011
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	Russian Federation: 90
Worldwide total number of subjects	90
EEA total number of subjects	0

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)	32
Adolescents (12-17 years)	58
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was performed at 8 centers in the Russian Federation. A total of 100 subjects were screened between 17 May 2011 to 13 Oct 2011.

Pre-assignment

Screening details:

Of 100 screened subjects, 90 subjects were treated. 10 subjects were excluded due to protocol noncompliance linked to the Investigational product

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Insulin Glulisine + Insulin Glargine

Arm description:

Insulin Glulisine in combination with insulin Glargine for 12 month.

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

Dosage and administration details:

Insulin Glargine, according to recommendations of treatment in children and adolescents once a daily.

Investigational medicinal product name	Insulin Glulisine
Investigational medicinal product code	
Other name	Apidra®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Insulin Glulisine, as per Physician's practice, before meal (0-15) minutes, or within 20 minutes after a meal start.

Number of subjects in period 1	Insulin Glulisine + Insulin Glargine
Started	90
Treated	90
Completed	89
Not completed	1
Consent withdrawn by subject	1

Baseline characteristics

Reporting groups	
Reporting group title	Insulin Glulisine + Insulin Glargine

Reporting group description:

Insulin Glulisine in combination with insulin Glargine for 12 month.

Reporting group values	Insulin Glulisine + Insulin Glargine	Total	
Number of subjects	90	90	
Age categorical Units: Subjects			
Children (2-11 years)	32	32	
Adolescents (12-17 years)	58	58	
Gender categorical Units: Subjects			
Female	44	44	
Male	46	46	
Body weight index			
Number of subjects analysed for this parameter was 89.			
Units: kg/m2			
arithmetic mean	19.54		
standard deviation	± 3.19	-	

End points

End points reporting groups

Reporting group title	Insulin Glulisine + Insulin Glargine

Reporting group description:

Insulin Glulisine in combination with insulin Glargine for 12 month.

Primary: Percentage of Subject Who Achieved HbA1c Level < 8% in Subjects 6-12 Years Old

End point title	Percentage of Subject Who Achieved HbA1c Level < 8% in Subjects 6-12 Years Old[1]

End point description:

Analysis was performed in efficacy population included all treated subjects. Number of subjects analysed = subjects from efficacy population at age 6-12 years.

End point type	Primary

End point timeframe:

At 6 and 12 month

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: Single arm study

End point values	Insulin Glulisine + Insulin Glargine			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: Percentage of subjects				
number (not applicable)				
6-12 years old: month 6 6-12 years old: Month 12	48.9 51.1			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Who Achieved HbA1c Level < 7,5% in Subjects 13 - 17 Years Old

End point title	Percentage of Subjects Who Achieved HbA1c Level < 7,5% in Subjects 13 - 17 Years Old[2]

End point description:

Analysis was performed in efficacy population. Number of subjects analysed = subjects from efficacy population at age 13-17 years.

End point type	Primary

End point timeframe:

At 6 and 12 month

Notes:

[2] - 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: Single arm study

End point values	Insulin Glulisine + Insulin Glargine			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: Percentage of subjects				
number (not applicable)				
13-17 years old: month 6	22.2			
13-17 years old: month 12	31.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in HbA1c

End point title	Change in HbA1c
End point description:	
Analysis was performed on efficacy population.	
End point type	Secondary
End point timeframe:	
Baseline, month 6, month 12	

End point values	Insulin Glulisine + Insulin Glargine			
Subject group type	Reporting group			
Number of subjects analysed	90			
Units: Percentage Heamoglobin				
arithmetic mean (standard deviation)				
HbA1c level: baseline	8.8 (± 0.6)			
HbA1c level: month 6	8.3 (± 1.2)			
HbA1c level: month 12	8 (± 1.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Daily Dose of Insuline Glargine and Glulisine

End point title	Change in Daily Dose of Insuline Glargine and Glulisine

End point description:

Analysis was performed on efficacy population.

End point type	Secondary

End point timeframe:

Baseline, month 6, month 12

End point values	Insulin Glulisine + Insulin Glargine			
Subject group type	Reporting group			
Number of subjects analysed	90			
Units: international unit(s)				
arithmetic mean (standard deviation)				
Insulin Glargine dose: at baseline	17 (± 8.2)			
Insulin Glulisine dose: at baseline	23.8 (± 10.3)			
Insulin Glargine dose: month 6	17.9 (± 8.1)			
Insulin Glulisine dose: month 6	24.5 (± 11.4)			
Insulin Glargine dose: month 12	18.4 (± 8.2)			
Insulin Glulisine dose: month 12	25.9 (± 11.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of Hypoglycemia Per Subject

End point title	Rate of Hypoglycemia Per Subject

End point description:

Hypoglycemia episodes in three categories: symptomatic, symptom-free and severe hypoglycemia. Analysis was carried out on safety population included all subjects who received at least one dose of insulin glargine.

End point type	Secondary

End point timeframe:

From baseline up to 12 month

End point values	Insulin Glulisine + Insulin Glargine			
Subject group type	Reporting group			
Number of subjects analysed	90			
Units: average number of episodes				
number (not applicable)	20.73			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form up to the final visit (12 month) regardless of seriousness or relationship to investigational product. Analysis was performed on safety population.

Adverse event reporting additional description:

Reported adverse events are treatment-emergent adverse events that is AEs that developed/worsened during the 'on treatment period' (after the first study drug intake until 24 hrs after last drug).

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.3

Reporting groups

Reporting group title	Insulin Glulisine + Insulin Glargine

Reporting group description:

Insulin Glulisine in combination with insulin Glargine for 12 month.

Serious adverse events	Insulin Glulisine + Insulin Glargine		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 90 (4.44%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 90 (1.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral motor neuropathy			
subjects affected / exposed	1 / 90 (1.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	2 / 90 (2.22%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		

Diabetic ketoacidosis			
subjects affected / exposed	1 / 90 (1.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Insulin Glulisine + Insulin Glargine		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 90 (48.89%)		
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 90 (10.00%)		
occurrences (all)	16		
General disorders and administration site conditions			
Flu-like symptoms			
subjects affected / exposed	39 / 90 (43.33%)		
occurrences (all)	83		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 January 2011	To use insulin glulisin (Apidra®) as the studied therapy making use of the prefilled disposable syringe SoloStar® 100 U/ml instead of the earlier planned reusable syringe OptiClick®. To change the date to conduct the study due to the later beginning of the subjects enrollment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported