Clinical trial results:
A multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of saxagliptin in combination with metformin IR or metformin XR in pediatric patients with type 2 diabetes who have inadequate glycemic control on metformin alone

Summary

EudraCT number	2010-024568-16
Trial protocol	BE Outside EU/EEA GB IT
Global end of trial date	22 April 2016

Results information

Result version number	v1 (current)
This version publication date	23 March 2017
First version publication date	23 March 2017

Trial information

Trial identification

Sponsor protocol code	CV181147

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB, S-151 85 Södertälje, Sweden
Sponsor organisation address	S-151 85 Södertälje, Sweden, Södertälje, Sweden, S-151 85
Public contact	Eva Johnsson, Clinical Science Lead, GLOBAL_MEDICINES_DEV, AstraZeneca AB, Eva.Johnsson@astrazeneca.com
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000200-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	14 November 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 April 2016
Global end of trial reached?	Yes
Global end of trial date	22 April 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The protocol-specified objectives presented in this synoptic report include the following:

- To assess the safety and tolerability of saxagliptin as add on to metformin therapy in pediatric subjects aged 10 to < 18 years when administered for up to 16 weeks of short term therapy and 52 weeks of total therapy.

Protection of trial subjects:

Freely given informed consent was obtained prior to clinical trial participation.
Minor's parents or legally acceptable representatives gasve fully informed written consent. Assent was obtained according to local regulations and if child is mentally capable.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 May 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 3
Country: Number of subjects enrolled	Mexico: 3
Worldwide total number of subjects	6
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)	1
Adolescents (12-17 years)	5
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of saxagliptin in combination with metformin IR or metformin XR in pediatric patients with type 2 diabetes who have inadequate glycemic control on metformin.

Pre-assignment

Screening details:

Approximately 236 subjects were planned to be randomized to study treatment (118 subjects per treatment group). Six subjects were randomized and treated in the study, and are included in the data analyses presented within this report.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Saxagliptin

Arm description:

Saxagliptin 2.5 or 5 mg according to body weight

Arm type	Experimental
Investigational medicinal product name	Saxagliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

2.5 mg or 5 mg according to body weight once daily

Arm title	Placebo

Arm description:

Placebo matching saxagliptin

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo matching saxagliptin once daily

Number of subjects in period 1	Saxagliptin	Placebo
Started	4	2
Completed	4	2

Baseline characteristics

Reporting groups	
Reporting group title	Saxagliptin
Reporting group description: Saxagliptin 2.5 or 5 mg according to body weight	
Reporting group title	Placebo
Reporting group description: Placebo matching saxagliptin	

Reporting group values	Saxagliptin	Placebo	Total
Number of subjects	4	2	6
Age Categorical Units: participants			
<=18 years	4	2	6
Between 18 and 65 years	0	0	0
>=65 years	0	0	0
Age continuous Units: years			
arithmetic mean	12.8	16	
standard deviation	± 1.1	± 1	-
Gender, Male/Female Units: participants			
Female	4	2	6
Male	0	0	0

Subject analysis sets	
Subject analysis set title	Saxagliptin
Subject analysis set type	Intention-to-treat
Subject analysis set description: Saxagliptin 2.5 mg or 5 mg according to the bodyweight	
Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: Saxagliptin matching placebo	

Reporting group values	Saxagliptin	Placebo	
Number of subjects	4	2	
Age Categorical Units: participants			
<=18 years	4	4	
Between 18 and 65 years	0	0	
>=65 years	0	0	
Age continuous Units: years			
arithmetic mean	12.8	16	
standard deviation	± 1.1	± 1	

Gender, Male/Female Units: participants			
Female	4	2	
Male	0	0	

End points

End points reporting groups

Reporting group title	Saxagliptin
Reporting group description: Saxagliptin 2.5 or 5 mg according to body weight	
Reporting group title	Placebo
Reporting group description: Placebo matching saxagliptin	
Subject analysis set title	Saxagliptin
Subject analysis set type	Intention-to-treat
Subject analysis set description: Saxagliptin 2.5 mg or 5 mg according to the bodyweight	
Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: Saxagliptin matching placebo	

Primary: Mean change in HbA1c from baseline to Week 16

End point title	Mean change in HbA1c from baseline to Week 16[1]
End point description:	
End point type	Primary
End point timeframe: 16 week short term treatment period	

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 statistical analysis has been performed for this end point due to a small number of subjects in the study

End point values	Saxagliptin	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	2		
Units: percentage				
arithmetic mean (standard deviation)	-1 (± 0.62)	0.9 (± 0.14)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 52 week	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0
Reporting groups	
Reporting group title	Saxagliptin
Reporting group description: Saxagliptin 2.5 or 5 mg according to body weight	
Reporting group title	Placebo
Reporting group description: Placebo matching saxagliptin	

Serious adverse events	Saxagliptin	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Saxagliptin	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	1 / 2 (50.00%)	
Investigations			
Urine output increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	0 / 4 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Nervous system disorders			

Headache			
subjects affected / exposed	2 / 4 (50.00%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Dizziness			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Stomach pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 4 (0.00%)	1 / 2 (50.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Pharyngitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Pharyngitis bacterial			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
pharyngitis streptococcal			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 October 2011	To clearly reflect that the randomization to study drugs saxagliptin and placebo will be stratified by metformin (XR or IR).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported