



## Clinical trial results:

**A multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy, safety, tolerability, and pharmacokinetics of saxagliptin (BMS-477118) as monotherapy in pediatric patients with Type 2 diabetes.**

### Summary

EudraCT number	2010-020360-38
Trial protocol	BE Outside EU/EEA 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	CV181058
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#### 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, Södertälje, Sweden,
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)	EMA-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?	No

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:

To assess the safety and tolerability of saxagliptin monotherapy 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:

This study was conducted in accordance with Good Clinical Practice (GCP), as defined by the International Conference on Harmonization (ICH) and in accordance with the ethical principles underlying European Union Directive 2001/20/EC and the United States Code of Federal Regulations, Title 21, Part 50 (21CFR50).

The study was conducted in compliance with the protocol. The protocol and the amendment and the subject informed consent and assent forms was received Institutional Review Board/Independent Ethics Committee (IRB/IEC) approval/favorable opinion prior to initiation of the study.

Study personnel involved conducted this study was qualified by education, training, and experience to perform their respective tasks.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 April 2011
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	European Union: 1
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	8
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)	7
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

This is a multicenter, 52-week, randomized, prospective, double-blind, parallel-group study. Approximately 136 subjects not currently on pharmacologic therapy for diabetes with HbA1c  $\geq$  7.0% to  $\leq$  10.5% will be randomized 1:1 to receive oral blinded saxagliptin or blinded placebo.

### Pre-assignment

Screening details:

After obtaining informed consent, study procedures will be performed to confirm eligibility. Glucose levels confirmed during the screening process. Screening tests to exclude type 1 diabetes will be performed.

### 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	Investigator, Monitor, Carer, Subject, Data analyst, Assessor

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Saxagliptin

Arm description:

Saxagliptin 2.5 mg 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:

Saxagliptin 2.5 mg or 5 mg according to body weight once daily

<b>Arm title</b>	Placebo
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Arm description:

Placebo matching saxagliptin

Arm type	Placebo
Investigational medicinal product name	Placebo matching saxagliptin
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

<b>Number of subjects in period 1</b>	Saxagliptin	Placebo
Started	4	4
Double-blind treatment period	4	4
Completed	3	3
Not completed	1	1
Consent withdrawn by subject	1	-
Poor/non-compliance	-	1

## Baseline characteristics

### Reporting groups

Reporting group title	Saxagliptin
Reporting group description: Saxagliptin 2.5 mg 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	4	8
Age Categorical Units: number			
<= 18 years	4	4	8
Age continuous Units: years			
arithmetic mean	14.5	13.5	
standard deviation	± 0.5	± 1.8	-
Gender, Male/Female Units: participant			
Female	1	3	4
Male	3	1	4

### Subject analysis sets

Subject analysis set title	Saxagliptin
Subject analysis set type	Intention-to-treat
Subject analysis set description: Saxagliptin 2.5mg or 5 mg depending on body weight	
Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: Placebo matching saxagliptin	

Reporting group values	Saxagliptin	Placebo	
Number of subjects	4	4	
Age Categorical Units: number			
<= 18 years	4	4	
Age continuous Units: years			
arithmetic mean	14.5	13.5	
standard deviation	± 0.5	± 1.8	
Gender, Male/Female Units: participant			
Female	1	3	
Male	3	1	



## End points

### End points reporting groups

Reporting group title	Saxagliptin
Reporting group description: Saxagliptin 2.5 mg 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 2.5mg or 5 mg depending on body weight	
Subject analysis set title	Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: Placebo matching saxagliptin	

### Primary: Mean change in HbA1c from baseline to Week 16

End point title	Mean change in HbA1c from baseline to Week 16 <sup>[1]</sup>
End point description:	
End point type	Primary
End point timeframe: 16 week double-blind 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	Reporting group	Reporting group		
Number of subjects analysed	4	4		
Units: percentage				
arithmetic mean (standard deviation)	-0.7 (± 0.83)	0.6 (± 1.53)		

### Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

52 week

Adverse event reporting additional description:

16 week double-blind treatment period and 36 week long-term extension period

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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### Reporting groups

Reporting group title	Saxagliptin
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Reporting group description:

Saxagliptin 2.5 mg or 5 mg according to body weight

Reporting group title	Placebo
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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%)	1 / 4 (25.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	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	3 / 4 (75.00%)	3 / 4 (75.00%)	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	

Laceration subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 4 (25.00%) 1	
Thermal burn subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 4 (25.00%) 1	
Nervous system disorders Headache alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 2	1 / 4 (25.00%) 1	
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 4 (25.00%) 1	
General disorders and administration site conditions Peripheral swelling subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 4 (25.00%) 1	
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 4 (25.00%) 1	
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)  Diarrhoea subjects affected / exposed occurrences (all)  Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)  Vomiting subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0  1 / 4 (25.00%) 1  0 / 4 (0.00%) 0  1 / 4 (25.00%) 1  1 / 4 (25.00%) 1	1 / 4 (25.00%) 1  0 / 4 (0.00%) 0  1 / 4 (25.00%) 1  0 / 4 (0.00%) 0	
Respiratory, thoracic and mediastinal			

disorders			
Oropharyngeal pain			
alternative assessment type:			
Systematic			
subjects affected / exposed	2 / 4 (50.00%)	1 / 4 (25.00%)	
occurrences (all)	2	2	
cough			
alternative assessment type:			
Systematic			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	
occurrences (all)	1	1	
Epistaxis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Nasal congestion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Wheezing			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
erythema			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Hyperhidrosis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Onycholysis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			

Joint swelling subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 4 (25.00%) 1	
Infections and infestations			
Influenza subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 4 (25.00%) 1	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 4 (25.00%) 1	
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 4 (0.00%) 0	
Metabolism and nutrition disorders			
Hypernatraemia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 4 (0.00%) 0	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 September 2011	The exclusion criteria concerning monogenic etiology of Type 2 DM and secondary diabetes was expanded to include previous diagnosis of genetic disorders with strong associations with insulin resistance/diabetes and/or obesity such as Turner's Syndrome and Prader-Willi.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported