



## 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 |
|-----------------------|----------|

#### 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,<br>GLOBAL_MEDICINES_DEV, AstraZeneca AB,<br>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 |
|------------------|---------|

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:<br>Saxagliptin 2.5 mg or 5 mg according to body weight |             |
| Reporting group title                                                               | Placebo     |
| Reporting group description:<br>Placebo matching saxagliptin                        |             |

| Reporting group values                    | Saxagliptin | Placebo | Total |
|-------------------------------------------|-------------|---------|-------|
| Number of subjects                        | 4           | 4       | 8     |
| Age Categorical<br>Units: number          |             |         |       |
| <= 18 years                               | 4           | 4       | 8     |
| Age continuous<br>Units: years            |             |         |       |
| arithmetic mean                           | 14.5        | 13.5    |       |
| standard deviation                        | ± 0.5       | ± 1.8   | -     |
| Gender, Male/Female<br>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:<br>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:<br>Placebo matching saxagliptin                       |                    |

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



## End points

### End points reporting groups

|                                                                                         |                    |
|-----------------------------------------------------------------------------------------|--------------------|
| Reporting group title                                                                   | Saxagliptin        |
| Reporting group description:<br>Saxagliptin 2.5 mg or 5 mg according to body weight     |                    |
| Reporting group title                                                                   | Placebo            |
| Reporting group description:<br>Placebo matching saxagliptin                            |                    |
| Subject analysis set title                                                              | Saxagliptin        |
| Subject analysis set type                                                               | Intention-to-treat |
| Subject analysis set description:<br>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:<br>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:<br>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 |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

### 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

| 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<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                                                                        | 0 / 4 (0.00%)<br>0                                                                                                            | 1 / 4 (25.00%)<br>1                                                                                |  |
| Thermal burn<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                                                                      | 0 / 4 (0.00%)<br>0                                                                                                            | 1 / 4 (25.00%)<br>1                                                                                |  |
| Nervous system disorders<br>Headache<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                | 1 / 4 (25.00%)<br>2                                                                                                           | 1 / 4 (25.00%)<br>1                                                                                |  |
| Blood and lymphatic system disorders<br>Lymphadenopathy<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                           | 0 / 4 (0.00%)<br>0                                                                                                            | 1 / 4 (25.00%)<br>1                                                                                |  |
| General disorders and administration<br>site conditions<br>Peripheral swelling<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                    | 0 / 4 (0.00%)<br>0                                                                                                            | 1 / 4 (25.00%)<br>1                                                                                |  |
| Eye disorders<br>Vision blurred<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                                                   | 0 / 4 (0.00%)<br>0                                                                                                            | 1 / 4 (25.00%)<br>1                                                                                |  |
| Gastrointestinal disorders<br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Gastrooesophageal reflux disease<br>subjects affected / exposed<br>occurrences (all)<br><br>Vomiting<br>subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0<br><br>1 / 4 (25.00%)<br>1<br><br>0 / 4 (0.00%)<br>0<br><br>1 / 4 (25.00%)<br>1<br><br>1 / 4 (25.00%)<br>1 | 1 / 4 (25.00%)<br>1<br><br>0 / 4 (0.00%)<br>0<br><br>1 / 4 (25.00%)<br>1<br><br>0 / 4 (0.00%)<br>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<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 4 (0.00%)<br>0  | 1 / 4 (25.00%)<br>1 |  |
| Infections and infestations                                                                 |                     |                     |  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 4 (0.00%)<br>0  | 1 / 4 (25.00%)<br>1 |  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)       | 1 / 4 (25.00%)<br>1 | 1 / 4 (25.00%)<br>1 |  |
| Viral upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 4 (25.00%)<br>1 | 0 / 4 (0.00%)<br>0  |  |
| Metabolism and nutrition disorders                                                          |                     |                     |  |
| Hypernatraemia<br>subjects affected / exposed<br>occurrences (all)                          | 1 / 4 (25.00%)<br>1 | 0 / 4 (0.00%)<br>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