



Clinical trial results:

A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Phase 3 Trial to Evaluate the Safety and Efficacy of Triple Therapy with Saxagliptin added to Dapagliflozin in Combination with Metformin compared to Therapy with Placebo added to Dapagliflozin in combination with Metformin in Subjects with Type 2 Diabetes who have Inadequate Glycemic Control on Metformin and Dapagliflozin

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2011-006323-37 |
| Trial protocol | CZ HU PL |
| Global end of trial date | 12 January 2015 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 01 July 2016 |
| First version publication date | 01 July 2016 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | CV181-168 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01619059 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | AstraZeneca AB |
| Sponsor organisation address | Västra Mälarehamnen 9, Södertälje, Sweden, S-151851170 |
| Public contact | Eva Johnsson, AstraZeneca AB, 46 +46 31 7762484, Eva.Johnsson@astrazeneca.com |
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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? | No |

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 29 May 2015 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 12 January 2015 |
| Global end of trial reached? | Yes |
| Global end of trial date | 12 January 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to learn if BMS-477118 (Saxagliptin) as part of a triple combination therapy can improve (decrease) hemoglobin A1c in patients with type 2 diabetes after 24 weeks of treatment compared to a 2 drug oral antidiabetic therapy. The safety of this treatment will also be studied.

Protection of trial subjects:

Study eligibility was based on inclusion and exclusion criteria. Eligible subjects entered the 24-week, short-term, double-blind treatment period, and were randomly assigned by the Interactive Voice Response System (IVRS). Randomization schedules for both subject treatment and containers were generated and kept by the Randomization Center located within the Drug Supply Management Department at BMS and stored in a secure location with restricted access

Background therapy:

Dapagliflozin plus metformin

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 29 June 2012 |
| 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 | Canada: 90 |
| Country: Number of subjects enrolled | Czech Republic: 24 |
| Country: Number of subjects enrolled | Hungary: 15 |
| Country: Number of subjects enrolled | Mexico: 137 |
| Country: Number of subjects enrolled | Puerto Rico: 13 |
| Country: Number of subjects enrolled | Romania: 64 |
| Country: Number of subjects enrolled | Russian Federation: 133 |
| Country: Number of subjects enrolled | United States: 336 |
| Country: Number of subjects enrolled | Poland: 45 |
| Worldwide total number of subjects | 857 |
| EEA total number of subjects | 148 |

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) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 705 |
| From 65 to 84 years | 152 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Enrollment: 857 subjects

Pre-assignment

Screening details:

Open-label Period: 484 subjects Completed Open-label Period: 431 subjects Randomized to Short-Term (ST) Treatment Period: 315 subjects Entered Long-Term (LT) Treatment Period: 297 subjects

Period 1

| | |
|------------------------------|---|
| Period 1 title | Short-Term (ST) Treatment 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 |
| Arm title | Placebo + Dapagliflozin 10mg + Metformin |

Arm description:

Participants received Saxagliptin-matching placebo, dapagliflozin 10mg once daily plus open-label metformin for up to 52 weeks

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | Placebo + Dapagliflozin 10mg + Metformin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo + Dapagliflozin 10mg + Metformin

| | |
|------------------|--|
| Arm title | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin |
|------------------|--|

Arm description:

Participants received Saxagliptin 5mg, dapagliflozin 10mg once daily plus open-label metformin for up to 52 weeks

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Arm 2

| Number of subjects in period 1^[1] | Placebo + Dapagliflozin 10mg + Metformin | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin |
|---|--|--|
| Started | 162 | 153 |
| Completed | 156 | 142 |
| Not completed | 6 | 11 |
| Consent withdrawn by subject | 2 | 5 |
| Adverse event, non-fatal | 1 | - |
| Non-compliance, not Met Study Criteria | 1 | 2 |
| Lost to follow-up | 2 | 4 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Of 315 participants randomized, 298 completed Short-Term (ST) treatment period. Of 297 participants entered Long-Term (LT) treatment period, 280 completed.

Period 2

| | |
|------------------------------|---------------------------------|
| Period 2 title | Long-Term (LT) Treatment Period |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Single blind |
| Roles blinded | Subject |

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo + Dapagliflozin 10mg + Metformin |

Arm description:

Participants received Saxagliptin-matching placebo, dapagliflozin 10mg once daily plus open-label metformin for up to 52 weeks

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | Placebo + Dapagliflozin 10mg + Metformin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet, Tablet |
| Routes of administration | Oral use, Oral use |

Dosage and administration details:

Placebo + Dapagliflozin 10mg + Metformin

| | |
|------------------|--|
| Arm title | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin |
|------------------|--|

Arm description:

Participants received Saxagliptin 5mg, dapagliflozin 10mg once daily plus open-label metformin for up to 52 weeks

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Saxagliptin 5mg + Dapagliflozin 10mg + Metformin

| Number of subjects in period 2^[2] | Placebo + Dapagliflozin 10mg + Metformin | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin |
|---|--|--|
| Started | 155 | 142 |
| Completed | 147 | 133 |
| Not completed | 8 | 9 |
| Adverse event, serious fatal | 1 | - |
| Consent withdrawn by subject | 3 | 2 |
| Adverse event, non-fatal | 2 | 3 |
| Not Met Study Criteria | - | 1 |
| Lost to follow-up | 2 | 2 |
| Lack of efficacy | - | 1 |

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Of 315 participants randomized, 298 completed Short-Term (ST) treatment period. Of 297 participants entered Long-Term (LT) treatment period, 280 completed.

Baseline characteristics

Reporting groups

| | |
|--|--|
| Reporting group title | Placebo + Dapagliflozin 10mg + Metformin |
| Reporting group description: Participants received Saxagliptin-matching placebo, dapagliflozin 10mg once daily plus open-label metformin for up to 52 weeks | |
| Reporting group title | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin |
| Reporting group description: Participants received Saxagliptin 5mg, dapagliflozin 10mg once daily plus open-label metformin for up to 52 weeks | |

| Reporting group values | Placebo + Dapagliflozin 10mg + Metformin | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin | Total |
|---|--|--|-------|
| Number of subjects | 162 | 153 | 315 |
| Age categorical Units: Subjects | | | |
| Adults (<65 years) | 140 | 132 | 272 |
| Adults (>=65 years) | 22 | 21 | 43 |
| Age Continuous Units: YEARS arithmetic mean standard deviation | 54.5 ± 9.32 | 54.7 ± 9.83 | - |
| Gender, Male/Female Units: Participants | | | |
| FEMALE | 76 | 73 | 149 |
| MALE | 86 | 80 | 166 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| ASIAN | 8 | 5 | 13 |
| BLACK/AFRICAN AMERICAN | 9 | 11 | 20 |
| OTHER | 4 | 1 | 5 |
| WHITE | 141 | 136 | 277 |

Subject analysis sets

| | |
|---|--|
| Subject analysis set title | Randomized and Treated Subjects Data Set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Randomized and Treated Subjects Data Set | |

| Reporting group values | Randomized and Treated Subjects Data Set | | |
|------------------------------------|--|--|--|
| Number of subjects | 315 | | |
| Age categorical Units: Subjects | | | |
| Adults (<65 years) | 272 | | |
| Adults (>=65 years) | 43 | | |

| | | | |
|---|----------------------|--|--|
| Age Continuous Units: YEARS arithmetic mean standard deviation | 54.6 ± 9.56 | | |
| Gender, Male/Female Units: Participants | | | |
| FEMALE MALE | 166 149 | | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| ASIAN BLACK/AFRICAN AMERICAN OTHER WHITE | 13 20 5 277 | | |

End points

End points reporting groups

| | |
|--|--|
| Reporting group title | Placebo + Dapagliflozin 10mg + Metformin |
| Reporting group description: Participants received Saxagliptin-matching placebo, dapagliflozin 10mg once daily plus open-label metformin for up to 52 weeks | |
| Reporting group title | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin |
| Reporting group description: Participants received Saxagliptin 5mg, dapagliflozin 10mg once daily plus open-label metformin for up to 52 weeks | |
| Reporting group title | Placebo + Dapagliflozin 10mg + Metformin |
| Reporting group description: Participants received Saxagliptin-matching placebo, dapagliflozin 10mg once daily plus open-label metformin for up to 52 weeks | |
| Reporting group title | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin |
| Reporting group description: Participants received Saxagliptin 5mg, dapagliflozin 10mg once daily plus open-label metformin for up to 52 weeks | |
| Subject analysis set title | Randomized and Treated Subjects Data Set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Randomized and Treated Subjects Data Set | |

Primary: Adjusted Mean Change From Baseline in Hemoglobin A1C (HbA1c) at Week 24

| | |
|--|---|
| End point title | Adjusted Mean Change From Baseline in Hemoglobin A1C (HbA1c) at Week 24 |
| End point description: HbA1c was measured as percent of hemoglobin by a central laboratory. Baseline was defined as the last assessment on or prior to the date of the first dose of the double-blind study medication. HbA1c measurements were obtained at Week 24 in the double-blind period, including observations prior to rescue. | |
| End point type | Primary |
| End point timeframe: From Baseline to Week 24 | |

| End point values | Placebo + Dapagliflozin 10mg + Metformin | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin | | |
|-------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 149 | 139 | | |
| Units: Percent | | | | |
| least squares mean (standard error) | -0.16 (± 0.0605) | -0.51 (± 0.0624) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Mean Change From Baseline in HbA1C |
| Statistical analysis description: | |
| Adjusted Mean Change From Baseline in Hemoglobin A1C (HbA1c) at Week 24 | |
| Comparison groups | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin v Placebo + Dapagliflozin 10mg + Metformin |
| Number of subjects included in analysis | 288 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 ^[1] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.35 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.52 |
| upper limit | -0.18 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.087 |

Notes:

[1] - Tested at alpha=0.05

Secondary: Adjusted Mean Change From Baseline in 2-hour Post Prandial Glucose (PPG) from a Liquid Meal Tolerance Test (MTT) at Week 24

| | |
|-----------------|---|
| End point title | Adjusted Mean Change From Baseline in 2-hour Post Prandial Glucose (PPG) from a Liquid Meal Tolerance Test (MTT) at Week 24 |
|-----------------|---|

End point description:

Baseline was defined as the last assessment on or prior to the date of the first dose of the double-blind study medication. PPG measurements were obtained at Week 24 in the double-blind period, including observations prior to rescue.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Baseline to Week 24

| | | | | |
|-------------------------------------|--|--|--|--|
| End point values | Placebo + Dapagliflozin 10mg + Metformin | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 144 | 135 | | |
| Units: mg/dL | | | | |
| least squares mean (standard error) | -31.3 (± 3.182) | -37.1 (± 3.286) | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Mean Change From Baseline in PPG |
| Statistical analysis description: Adjusted Mean Change From Baseline in 2-hour Post Prandial Glucose (PPG) from a Liquid Meal Tolerance Test (MTT) at Week 24 | |
| Comparison groups | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin v Placebo + Dapagliflozin 10mg + Metformin |
| Number of subjects included in analysis | 279 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2014 ^[2] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -5.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14.9 |
| upper limit | 3.1 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.576 |

Notes:

[2] - Secondary endpoints were tested at alpha=0.05, applying the hierarchical order for the sequential testing procedure

Secondary: Adjusted Mean Change From Baseline in Fasting Plasma Glucose at Week 24

| | |
|---|---|
| End point title | Adjusted Mean Change From Baseline in Fasting Plasma Glucose at Week 24 |
| End point description: Baseline was defined as the last assessment on or prior to the date of the first dose of the double-blind study medication. FPG measurements were obtained at Week 24 in the double-blind period, including observations prior to rescue. | |
| End point type | Secondary |
| End point timeframe: From Baseline to Week 24 | |

| | | | | |
|-------------------------------------|--|--|--|--|
| End point values | Placebo + Dapagliflozin 10mg + Metformin | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 146 | 139 | | |
| Units: mg/dL | | | | |
| least squares mean (standard error) | -5.3 (± 2.59) | -9.1 (± 2.644) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Mean Change From Baseline in FPG |
| Statistical analysis description: | |
| Adjusted Mean Change From Baseline in Fasting Plasma Glucose at Week 24 | |
| Comparison groups | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin v Placebo + Dapagliflozin 10mg + Metformin |
| Number of subjects included in analysis | 285 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -3.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11 |
| upper limit | 3.6 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.713 |

Secondary: Percentage of Participants Achieving a Therapeutic Glycemic Response (Hemoglobin A1c [HbA1C]) <7.0% at Week 24 (Last Observation Carried Forward [LOCF])

| | |
|---|--|
| End point title | Percentage of Participants Achieving a Therapeutic Glycemic Response (Hemoglobin A1c [HbA1C]) <7.0% at Week 24 (Last Observation Carried Forward [LOCF]) |
| End point description: | |
| Therapeutic glycemic response is defined as HbA1c <7.0%. Data after rescue medication was excluded from this analysis. HbA1c was measured as a percent of hemoglobin. | |
| End point type | Secondary |
| End point timeframe: | |
| From Baseline to Week 24 | |

| | | | | |
|--------------------------------|--|--|--|--|
| End point values | Placebo + Dapagliflozin 10mg + Metformin | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 146 | 139 | | |
| Units: Percent of participants | | | | |
| number (confidence interval) | 23.1 (16.9 to 29.3) | 35.3 (28.2 to 42.4) | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Glycemic Response HbA1C <7.0% |
| Statistical analysis description: | |
| Percentage of Participants Achieving a Therapeutic Glycemic Response (Hemoglobin A1c [HbA1C]) <7.0% at Week 24 (Last Observation Carried Forward [LOCF]) | |
| Comparison groups | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin v Placebo + Dapagliflozin 10mg + Metformin |
| Number of subjects included in analysis | 285 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 12.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.4 |
| upper limit | 21 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.504 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Short-term + Long-term Treatment Period - Including Data After Rescue - Treated Subjects

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin |
|-----------------------|--|

Reporting group description:

Participants received Saxagliptin 5mg, dapagliflozin 10mg once daily plus open-label metformin for up to 52 weeks

| | |
|-----------------------|--|
| Reporting group title | Placebo + Dapagliflozin 10mg + Metformin |
|-----------------------|--|

Reporting group description:

Participants received Saxagliptin-matching placebo, dapagliflozin 10mg once daily plus open-label metformin for up to 52 weeks

| Serious adverse events | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin | Placebo + Dapagliflozin 10mg + Metformin | |
|---|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 7 / 153 (4.58%) | 11 / 162 (6.79%) | |
| number of deaths (all causes) | 0 | 1 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| HEPATIC CANCER | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 0 / 162 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| PERIPHERAL ARTERY THROMBOSIS | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 0 / 162 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PERIPHERAL VASCULAR DISORDER | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 0 / 162 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|-----------------|-----------------|--|
| General disorders and administration site conditions | | | |
| CHEST PAIN | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 162 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HERNIA | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 162 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| NON-CARDIAC CHEST PAIN | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 162 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| UTERINE HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 162 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| ASTHMA | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 162 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PULMONARY EMBOLISM | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 0 / 162 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| STAPHYLOCOCCUS TEST POSITIVE | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 162 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|-----------------|-----------------|--|
| FALL | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 162 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| ANGINA PECTORIS | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 162 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ATRIAL FIBRILLATION | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 162 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MYOCARDIAL INFARCTION | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 162 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Nervous system disorders | | | |
| SYNCOPE | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 0 / 162 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| RETINAL DETACHMENT | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 162 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| COLITIS | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 162 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTRITIS | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 162 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| CHOLELITHIASIS | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 0 / 162 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| DIABETIC FOOT | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 0 / 162 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SKIN ULCER | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 0 / 162 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| RHABDOMYOLYSIS | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 0 / 162 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| PYELONEPHRITIS | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 0 / 162 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| | | | |
|---|--|--|--|
| Non-serious adverse events | Saxagliptin 5mg + Dapagliflozin 10mg + Metformin | Placebo + Dapagliflozin 10mg + Metformin | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 37 / 153 (24.18%) | 37 / 162 (22.84%) | |

| | | | |
|---|---|--|--|
| Nervous system disorders HEADACHE subjects affected / exposed occurrences (all) | 9 / 153 (5.88%) 12 | 12 / 162 (7.41%) 13 | |
| Gastrointestinal disorders DIARRHOEA subjects affected / exposed occurrences (all) | 8 / 153 (5.23%) 8 | 6 / 162 (3.70%) 6 | |
| Infections and infestations NASOPHARYNGITIS subjects affected / exposed occurrences (all) URINARY TRACT INFECTION subjects affected / exposed occurrences (all) | 9 / 153 (5.88%) 10 11 / 153 (7.19%) 16 | 8 / 162 (4.94%) 8 11 / 162 (6.79%) 13 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|--|
| 24 April 2012 | The objective of this Amendment is to permit the collection and storage of blood samples |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported