



## 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
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#### 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
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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
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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
<b>Arm title</b>	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

<b>Arm title</b>	Saxagliptin 5mg + Dapagliflozin 10mg + Metformin
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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

<b>Number of subjects in period 1[1]</b>	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
<b>Arm title</b>	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

<b>Arm title</b>	Saxagliptin 5mg + Dapagliflozin 10mg + Metformin
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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

<b>Number of subjects in period 2<sup>[2]</sup></b>	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

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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

<b>Statistical analysis title</b>	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 <sup>[1]</sup>
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
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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
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End point timeframe:

From Baseline to Week 24

<b>End point values</b>	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

<b>Statistical analysis title</b>	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 <sup>[2]</sup>
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	

<b>End point values</b>	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

<b>Statistical analysis title</b>	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	

<b>End point values</b>	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

<b>Statistical analysis title</b>	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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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### Reporting groups

Reporting group title	Saxagliptin 5mg + Dapagliflozin 10mg + Metformin
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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
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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	
<b>Hepatobiliary disorders</b>			
<b>CHOLELITHIASIS</b>			
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	
<b>Skin and subcutaneous tissue disorders</b>			
<b>DIABETIC FOOT</b>			
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	
<b>SKIN ULCER</b>			
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	
<b>Musculoskeletal and connective tissue disorders</b>			
<b>RHABDOMYOLYSIS</b>			
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	
<b>Infections and infestations</b>			
<b>PYELONEPHRITIS</b>			
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 %

<b>Non-serious adverse events</b>	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:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported