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

Summary

EudraCT number	2011-006324-20
Trial protocol	GB CZ PL
Global end of trial date	19 February 2015

Results information

Result version number	v1 (current)
This version publication date	29 July 2016
First version publication date	29 July 2016

Trial information

Trial identification

Sponsor protocol code	MB102-129

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01646320
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca Pharmaceuticals
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	10 July 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 February 2015
Global end of trial reached?	Yes
Global end of trial date	19 February 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-512148 (dapagliflozin) 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:

Prior to the beginning of the study, the investigator must have had the IRB/IEC's written approval/favorable opinion of the written informed consent form and any other information to be provided to the subjects. Freely given written informed consent was obtained from each subject or, in those situations where consent could not be given by the subject, their legally acceptable representatives, prior to study participation, including informed consent for any screening procedures conducted to establish subject eligibility in the study.

Background therapy:

Stable metformin therapy alone for at least 8 weeks prior to screening visit at a dose ≥ 1500 mg per day. Saxagliptin 5 mg was added during the open label treatment period of 8-16 weeks.

Evidence for comparator: -

Actual start date of recruitment	21 September 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	United States: 148
Country: Number of subjects enrolled	Czech Republic: 13
Country: Number of subjects enrolled	Mexico: 166
Country: Number of subjects enrolled	Poland: 17
Country: Number of subjects enrolled	Puerto Rico: 6
Country: Number of subjects enrolled	Romania: 25
Country: Number of subjects enrolled	Russian Federation: 89
Country: Number of subjects enrolled	United Kingdom: 19
Worldwide total number of subjects	483
EEA total number of subjects	74

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)	415
From 65 to 84 years	68
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Phase 3 Trial with Dapagliflozin 10 mg added to Saxagliptin 5 mg in Combination with Metformin ≥ 1500 mg compared to placebo added to Saxagliptin in combination with Metformin in Subjects with Type 2 Diabetes who have Inadequate Glycemic Control on Metformin and Saxagliptin

Pre-assignment

Screening details:

Arm1: Dapagliflozin (10 mg) + Saxagliptin (5 mg) + Metformin ≥ 1500 mg IR Arm 2: Placebo + Saxagliptin (5 mg) + Metformin IR

Period 1

Period 1 title	Short-term period (Day 1 to Week 24)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Dapa+Saxa+Met

Arm description:

Participants received dapagliflozin, 10 mg, and open-label saxagliptin 5 mg and metformin ≥1500 mg per day for up to 52 weeks

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

Dosage and administration details:

Saxagliptin Tablets, Oral, 5mg , Once daily, 24 weeks: Metformin XR Tablets, Oral, ≥ 1500mg/≤ 2000mg, Once daily, 24 weeks Other Names: Glucophage XR Drug: Dapagliflozin Tablet, Oral, 10mg, Once daily, 24 weeks

Arm title	Pla+Saxa+Met

Arm description:

Participants received dapagliflozin matching placebo and open-label saxagliptin 5 mg and metformin ≥1500 mg per day for up to 52 weeks

Arm type	Placebo
Investigational medicinal product name	Placebo + Saxagliptin (5 mg) + Metformin IR
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Saxagliptin Tablets, Oral, 5mg , Once daily, 24 weeks: Metformin XR Tablets, Oral, ≥ 1500mg/≤ 2000mg, Once daily, 24 weeks Other Names: Glucophage XR: Placebo matching with Dapagliflozin Tablets, Oral, 0mg, Once daily, 24 weeks

Number of subjects in period 1[1]	Dapa+Saxa+Met	Pla+Saxa+Met
Started	160	160
Completed	148	153
Not completed	12	7
Consent withdrawn by subject	2	-
Adverse event, non-fatal	3	-
Not reported	2	2
Not specified	1	-
No longer meets study criteria	-	1
Lost to follow-up	4	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 320 participants randomized, 301 completed Short-Term (ST) treatment period. Of 294 participants entered Long-Term (LT) treatment period, 281 completed

Period 2

Period 2 title	Long-term Period (Weeks 24 to 52)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Dapa+Saxa+Met

Arm description:

Participants received dapagliflozin, 10 mg, and open-label saxagliptin 5 mg and metformin ≥1500 mg per day for up to 52 weeks

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

Dosage and administration details:

Saxagliptin Tablets, Oral, 5mg , Once daily, 52 weeks: Metformin XR Tablets, Oral, ≥ 1500mg/≤ 2000mg, Once daily, 52 weeks Other Names: Glucophage XR Drug: Dapagliflozin Tablet, Oral, 10mg, Once daily, 52 weeks

Arm title	Pla+Saxa+Met

Arm description:

Participants received dapagliflozin matching placebo and open-label saxagliptin 5 mg and metformin ≥1500 mg per day for up to 52 weeks

Arm type	Placebo
Investigational medicinal product name	Placebo + Saxagliptin (5 mg) + Metformin IR
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Saxagliptin Tablets, Oral, 5mg , Once daily, 52 weeks: Metformin XR Tablets, Oral, ≥ 1500mg/≤ 2000mg, Once daily, 52 weeks Other Names: Glucophage XR: Placebo matching with Dapagliflozin Tablets, Oral, 0mg, Once daily, 52 weeks

Number of subjects in period 2[2]	Dapa+Saxa+Met	Pla+Saxa+Met
Started	147	147
Completed	141	140
Not completed	6	7
Consent withdrawn by subject	-	2
Adverse event, non-fatal	4	2
Lost to follow-up	-	2
Subject no longer meets study criteria	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 320 participants randomized, 301 completed Short-Term (ST) treatment period. Of 294 participants entered Long-Term (LT) treatment period, 281 completed

Baseline characteristics

Reporting groups	
Reporting group title	Dapa+Saxa+Met
Reporting group description:	
Participants received dapagliflozin, 10 mg, and open-label saxagliptin 5 mg and metformin ≥1500 mg per day for up to 52 weeks	
Reporting group title	Pla+Saxa+Met
Reporting group description:	
Participants received dapagliflozin matching placebo and open-label saxagliptin 5 mg and metformin ≥1500 mg per day for up to 52 weeks	

Reporting group values	Dapa+Saxa+Met	Pla+Saxa+Met	Total
Number of subjects	160	160	320
Age categorical Units: Subjects			
Adults (18-64 years)	137	132	269
Greater than or equal to 65 years	23	28	51
Age Continuous | Units: YEARS			
arithmetic mean	55.2	55	
standard deviation	± 8.61	± 9.6	-
Gender, Male/Female Units: Participants			
FEMALE	90	84	174
MALE	70	76	146
Age, Customized Units: Subjects			
< 65	137	132	269
>= 65	23	28	51

End points

End points reporting groups

Reporting group title	Dapa+Saxa+Met
Reporting group description:	
Participants received dapagliflozin, 10 mg, and open-label saxagliptin 5 mg and metformin ≥1500 mg per day for up to 52 weeks	
Reporting group title	Pla+Saxa+Met
Reporting group description:	
Participants received dapagliflozin matching placebo and open-label saxagliptin 5 mg and metformin ≥1500 mg per day for up to 52 weeks	
Reporting group title	Dapa+Saxa+Met
Reporting group description:	
Participants received dapagliflozin, 10 mg, and open-label saxagliptin 5 mg and metformin ≥1500 mg per day for up to 52 weeks	
Reporting group title	Pla+Saxa+Met
Reporting group description:	
Participants received dapagliflozin matching placebo and open-label saxagliptin 5 mg and metformin ≥1500 mg per day for up to 52 weeks	

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. HbA1c values recorded after rescue treatment or recorded more than 8 days after last dose date were excluded from this analysis. Baseline was defined as the last assessment prior to the start date and time of the first dose of the double-blind study medication. In cases where time of the first dose or time of the assessment was not available, 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 during the qualification and lead-in periods and on Day 1 and Weeks 6, 12, 18, and 24 in the double-blind period.	
End point type	Primary
End point timeframe:	
From Baseline to Week 24	

End point values	Dapa+Saxa+Met	Pla+Saxa+Met		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	158		
Units: Percentage				
least squares mean (standard error)	-0.82 (± 0.0686)	-0.1 (± 0.0704)		

Statistical analyses

Statistical analysis title	Primary Analysis
Statistical analysis description:	
Longitudinal repeated measures analysis	
Comparison groups	Dapa+Saxa+Met v Pla+Saxa+Met
Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [1]
Method	Longitudinal Repeated Measures Analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.91
upper limit	-0.53
Variability estimate	Standard error of the mean
Dispersion value	0.0964

Notes:

[1] - Tested at alpha=0.05

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:

Data after rescue medication was excluded from this analysis. Baseline was defined as the last assessment prior to the start date and time of the first dose of the double-blind study medication. In cases where time of the first dose or time of the assessment was not available, 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 during the qualification and lead-in periods and on Day 1 and Weeks 6, 12, 18, and 24 in the double-blind period

End point type	Secondary

End point timeframe:

From Baseline to Week 24

End point values	Dapa+Saxa+Met	Pla+Saxa+Met		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	157		
Units: mg/dL				
least squares mean (standard error)	-32.7 (± 2.821)	-5.3 (± 2.968)		

Statistical analyses

Statistical analysis title	Secondary Analysis

Statistical analysis description:	
Longitudinal repeated measures analysis of FPG	
Comparison groups	Dapa+Saxa+Met v Pla+Saxa+Met
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [2]
Method	Longitudinal Repeated Measures Analysis
Parameter estimate	Mean difference (final values)
Point estimate	-27.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.4
upper limit	-19.6
Variability estimate	Standard error of the mean
Dispersion value	4.015

Notes:

[2] - Secondary end points are tested following a sequential testing procedure at alpha=0.05

Secondary: Adjusted mean change from baseline in 120-minute postprandial glucose (PPG) at Week 24

End point title	Adjusted mean change from baseline in 120-minute postprandial glucose (PPG) at Week 24

End point description:

2-hour postprandial glucose (PPG) from a liquid meal tolerance test (2-h MTT) Subject must be fasted for at least 8 hrs prior to the MTT.

End point type	Secondary

End point timeframe:

From Baseline to Week 24

End point values	Dapa+Saxa+Met	Pla+Saxa+Met		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	132		
Units: mg/dL				
least squares mean (standard error)	-73.5 (± 4.055)	-38 (± 4.104)		

Statistical analyses

Statistical analysis title	Secondary analysis

Statistical analysis description:

ANCOVA analysis of change from baseline in 2-hour postprandial glucose during a MTT at Week 24

Comparison groups	Dapa+Saxa+Met v Pla+Saxa+Met

Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [3]
Method	Longitudinal Repeated Measures Analysis
Parameter estimate	Mean difference (final values)
Point estimate	-35.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-46.3
upper limit	-24.7
Variability estimate	Standard error of the mean
Dispersion value	5.493

Notes:

[3] - Secondary end points are tested following a sequential testing procedure at alpha=0.05

Secondary: Adjusted mean change from baseline in body weight at week 24

End point title	Adjusted mean change from baseline in body weight at week 24

End point description:

Data after rescue medication was excluded from this analysis. Baseline was defined as the last assessment prior to the start date and time of the first dose of the double-blind study medication. In cases where time of the first dose or time of the assessment was not available, baseline was defined as the last assessment on or prior to the date of the first dose of the double-blind study medication. Body weights were measured during the qualification and lead-in periods and on Day 1 and Weeks 6, 12, 18, and 24 in the double-blind period.

End point type	Secondary

End point timeframe:

From baseline to Week 24

End point values	Dapa+Saxa+Met	Pla+Saxa+Met		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	158		
Units: kg				
least squares mean (standard error)	-1.91 (± 0.2191)	-0.41 (± 0.227)		

Statistical analyses

Statistical analysis title	Secondary analysis

Statistical analysis description:

Longitudinal repeated measures model analysis of change from baseline in Total body weight at week 24

Comparison groups	Dapa+Saxa+Met v Pla+Saxa+Met

Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [4]
Method	Longitudinal Repeated Measures Analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.12
upper limit	-0.89
Variability estimate	Standard error of the mean
Dispersion value	0.3126

Notes:

[4] - Secondary endpoints are tested following a sequential testing procedure at alpha=0.05

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

End point title	Percentage of Subjects Achieving a Therapeutic Glycemic Response (Hemoglobin A1c [HbA1C]) <7.0% at Week 24 (Last Observation Carried Forward [LOCF])

End point description:

Percent adjusted for baseline HbA1c. Therapeutic glycemic response is defined as HbA1c <7.0%. Data after rescue medication was excluded from this analysis.

End point type	Secondary

End point timeframe:

From baseline to week 24

End point values	Dapa+Saxa+Met	Pla+Saxa+Met		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	158		
Units: Percentage				
number (not applicable)	36.7	13.3		

Statistical analyses

Statistical analysis title	Secondary analysis

Statistical analysis description:

Analysis of the proportion of subjects achieving a therapeutic glycemic response (defined as HbA1c < 7.0%) at Week 24 (LOCF) using a logistic regression based on the methodology of Zhang, Tsiatis and Davidian and Tsiatis, Davidian, Zhang and Lu, with the adjustment for baseline HbA1c and stratum.

Comparison groups	Dapa+Saxa+Met v Pla+Saxa+Met

Number of subjects included in analysis	316
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [5]
Method	Modified logistic regression
Parameter estimate	Mean difference (final values)
Point estimate	25.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	16.7
upper limit	34.4

Notes:

[5] - Secondary end points are tested following a sequential testing procedure at alpha=0.05

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From baseline to week 52	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	PLA + SAXA + MET
Reporting group description:	
Participants received dapagliflozin matching placebo and open-label saxagliptin 5 mg and metformin ≥1500 mg per day for up to 52 weeks	
Reporting group title	DAPA + SAXA + MET
Reporting group description:	
Participants received dapagliflozin, 10 mg, and open-label saxagliptin 5 mg and metformin ≥1500 mg per day for up to 52 weeks	

Serious adverse events	PLA + SAXA + MET	DAPA + SAXA + MET	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 160 (2.50%)	7 / 160 (4.38%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events			
Investigations			
LIVER FUNCTION TEST ABNORMAL			
subjects affected / exposed	1 / 160 (0.63%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
INVASIVE DUCTAL BREAST CARCINOMA			
subjects affected / exposed	0 / 160 (0.00%)	1 / 160 (0.63%)	
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			
ANKLE FRACTURE			

subjects affected / exposed	1 / 160 (0.63%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 160 (0.00%)	1 / 160 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
ANGINA UNSTABLE			
subjects affected / exposed	0 / 160 (0.00%)	1 / 160 (0.63%)	
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 / 160 (0.00%)	1 / 160 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC FAILURE			
subjects affected / exposed	0 / 160 (0.00%)	1 / 160 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC FAILURE ACUTE			
subjects affected / exposed	0 / 160 (0.00%)	1 / 160 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 160 (0.00%)	1 / 160 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 160 (0.00%)	1 / 160 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

GASTRIC ULCER			
subjects affected / exposed	1 / 160 (0.63%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 160 (0.00%)	1 / 160 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
ABSCESS LIMB			
subjects affected / exposed	1 / 160 (0.63%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
APPENDICITIS			
subjects affected / exposed	0 / 160 (0.00%)	1 / 160 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GANGRENE			
subjects affected / exposed	1 / 160 (0.63%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
POSTOPERATIVE WOUND INFECTION			
subjects affected / exposed	0 / 160 (0.00%)	1 / 160 (0.63%)	
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: 2 %

Non-serious adverse events	PLA + SAXA + MET	DAPA + SAXA + MET	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	112 / 160 (70.00%)	103 / 160 (64.38%)	
Injury, poisoning and procedural complications			

CONTUSION			
subjects affected / exposed	4 / 160 (2.50%)	1 / 160 (0.63%)	
occurrences (all)	4	1	
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	0 / 160 (0.00%)	6 / 160 (3.75%)	
occurrences (all)	0	6	
HEADACHE			
subjects affected / exposed	13 / 160 (8.13%)	11 / 160 (6.88%)	
occurrences (all)	15	16	
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	4 / 160 (2.50%)	1 / 160 (0.63%)	
occurrences (all)	5	1	
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	3 / 160 (1.88%)	4 / 160 (2.50%)	
occurrences (all)	3	4	
DIARRHOEA			
subjects affected / exposed	9 / 160 (5.63%)	7 / 160 (4.38%)	
occurrences (all)	11	7	
DYSPEPSIA			
subjects affected / exposed	4 / 160 (2.50%)	2 / 160 (1.25%)	
occurrences (all)	4	2	
NAUSEA			
subjects affected / exposed	8 / 160 (5.00%)	4 / 160 (2.50%)	
occurrences (all)	9	4	
Hepatobiliary disorders			
HEPATIC STEATOSIS			
subjects affected / exposed	4 / 160 (2.50%)	1 / 160 (0.63%)	
occurrences (all)	4	1	
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	3 / 160 (1.88%)	5 / 160 (3.13%)	
occurrences (all)	3	5	
Skin and subcutaneous tissue disorders			

RASH			
subjects affected / exposed	4 / 160 (2.50%)	0 / 160 (0.00%)	
occurrences (all)	4	0	
Psychiatric disorders			
DEPRESSION			
subjects affected / exposed	5 / 160 (3.13%)	0 / 160 (0.00%)	
occurrences (all)	5	0	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	2 / 160 (1.25%)	4 / 160 (2.50%)	
occurrences (all)	2	4	
BACK PAIN			
subjects affected / exposed	10 / 160 (6.25%)	5 / 160 (3.13%)	
occurrences (all)	10	5	
MUSCLE SPASMS			
subjects affected / exposed	6 / 160 (3.75%)	2 / 160 (1.25%)	
occurrences (all)	6	2	
MUSCULOSKELETAL PAIN			
subjects affected / exposed	4 / 160 (2.50%)	3 / 160 (1.88%)	
occurrences (all)	4	4	
PAIN IN EXTREMITY			
subjects affected / exposed	6 / 160 (3.75%)	3 / 160 (1.88%)	
occurrences (all)	6	3	
Infections and infestations			
INFLUENZA			
subjects affected / exposed	12 / 160 (7.50%)	12 / 160 (7.50%)	
occurrences (all)	14	14	
NASOPHARYNGITIS			
subjects affected / exposed	8 / 160 (5.00%)	5 / 160 (3.13%)	
occurrences (all)	9	5	
PHARYNGITIS			
subjects affected / exposed	3 / 160 (1.88%)	6 / 160 (3.75%)	
occurrences (all)	3	6	
URINARY TRACT INFECTION			
subjects affected / exposed	16 / 160 (10.00%)	15 / 160 (9.38%)	
occurrences (all)	19	19	

VULVOVAGINAL MYCOTIC INFECTION			
subjects affected / exposed	1 / 160 (0.63%)	7 / 160 (4.38%)	
occurrences (all)	1	9	
Metabolism and nutrition disorders			
DYSLIPIDAEMIA			
subjects affected / exposed	3 / 160 (1.88%)	7 / 160 (4.38%)	
occurrences (all)	3	7	
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	9 / 160 (5.63%)	5 / 160 (3.13%)	
occurrences (all)	10	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported