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ID: SYR-322_402 Cardiovascular Outcomes Study of Alogliptin in Patients With Type 2 Diabetes and Acute Coronary Syndrome

NCT00968708

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Results Preview[Close](#) [Hide All](#) **Participant Flow****Recruitment Details** Participants took part in the study at 898 investigative sites worldwide from 24 September 2009 to 18 June 2013.**Pre-Assignment Details** Participants with a diagnosis of type 2 diabetes mellitus and acute coronary syndrome were enrolled equally in 1 of 2 treatment groups, once a day placebo or alogliptin, in addition to receiving standard of care for cardiovascular disease and diabetes.

Arm/Group Title	Placebo	Alogliptin	Total (Not public)
Arm/Group Description	Alogliptin placebo matching tablets, orally, once daily. Participants continued to receive standard of care for cardiovascular disease and diabetes according to regional guidelines.	Alogliptin 25 mg, tablets, orally, once daily for participants with normal or mildly impaired renal function as defined by estimated glomerular filtration rate (eGFR) ≥ 60 mL/min). Alogliptin 12.5 mg, tablets, orally, once daily for participants with moderately impaired renal function (eGFR ≥ 30 and < 60 mL/min). Alogliptin 6.25 mg, tablets, orally, once daily for participants with severely impaired renal function or end stage renal disease (eGFR < 30 mL/min). Participants continued to receive standard of care for cardiovascular disease and diabetes according to regional guidelines.	

Period Title: Overall Study

Started	2679	2701	5380
Treated	2676	2698	5374
Completed	2361	2403	4764
Not Completed	318	298	616
<u>Reason Not Completed</u>			
Adverse Event	169	150	319
Major Protocol Deviation	0	1	1

Lost to Follow-up	19	11	30
Voluntary Withdrawal	104	101	205
Investigator Discretion	0	1	1
Other	26	34	60

 NOTE : "Other" is not sufficiently descriptive for "Other" Reason Not Completed. Please provide a more descriptive label.
(Not Public)

Not Completed = 318
Total from all reasons = 318

Not Completed = 298
Total from all reasons = 298

 **Baseline Characteristics**

Arm/Group Title	Placebo	Alogliptin	Total
 Arm/Group Description	Alogliptin placebo matching tablets, orally, once daily.	Alogliptin 25 mg, tablets, orally, once daily for participants with normal or mildly impaired renal function as defined by estimated glomerular filtration rate (eGFR) \geq 60 mL/min). Alogliptin 12.5 mg, tablets, orally, once daily for participants with moderately impaired renal function (eGFR \geq 30 and $<$ 60 mL/min). Alogliptin 6.25 mg, tablets, orally, once daily for participants with severely impaired renal function or end stage renal disease (eGFR $<$ 30 mL/min).	
Overall Number of Baseline Participants	2679	2701	5380
 Baseline Analysis Population Description	Full Analysis Set (FAS) - all randomized participants who signed informed consent.		
Age, Continuous Mean (Standard Deviation) Units: years	60.7 (9.88)	61.0 (9.96)	60.9 (9.92)
Gender, Male/Female Measure Type: Number Units: participants			
Female	856	873	1729
Male	1823	1828	3651
Race/Ethnicity, Customized Measure Type: Number Units: participants			
American Indian or Alaska Native	54	56	110
Asian	542	547	1089
Black or African American	115	101	216
Native Hawaiian or Other	5	6	11

Pacific Islander		
White 1943	1966	3909
More than one race 20	25	45
Race/Ethnicity, Customized		
Measure Type: Number		
Units: participants		
Hispanic or Latino 764	773	1537
Non-Hispanic or Latino 1915	1928	3843
Region of Enrollment		
Measure Type: Number		
Units: participants		
Argentina 136	136	272
Australia 7	8	15
Austria 8	8	16
Belgium 11	12	23
Brazil 179	181	360
Bulgaria 41	41	82
Canada 54	55	109
Chile 51	55	106
Colombia 15	13	28
Croatia 38	39	77
Czech Republic 13	13	26
Denmark 3	3	6
Egypt 7	7	14
Finland 12	10	22
France 11	11	22
Germany 26	27	53
Greece 0	1	1
Guatemala 25	24	49
Hong Kong 11	12	23
Hungary 60	59	119
India 165	165	330
Israel 100	101	201
Italy 25	25	50
Japan 105	104	209
Kuwait 2	3	5
Latvia 6	6	12
Lithuania 16	20	36
Malaysia 39	42	81
Mexico 192	191	383
New Zealand 13	13	26
Peru 79	81	160
Philippines 52	50	102
Poland 121	118	239
Portugal 13	16	29
Puerto Rico 16	19	35
Korea, Republic Of 61	62	123
Romania 40	38	78
Russian Federation 153	151	304
Serbia 35	35	70
Slovakia 46	49	95

South Africa	39	41	80
Spain	21	22	43
Sweden	16	16	32
Taiwan, Province Of China	14	13	27
Thailand	57	58	115
Ukraine	138	138	276
United Arab Emirates	3	3	6
United Kingdom	32	34	66
United States	372	372	744
Body Mass Index			
Mean (Standard Deviation)			29.48
Units: kg/m²	29.53 (5.758)	29.42 (5.422)	(5.591)
Duration of Type 2 Diabetes Mellitus			
Mean (Standard Deviation)			9.16
Units: years	9.18 (8.121)	9.13 (8.198)	(8.159)
Smoking History			
Measure Type: Number			
Units: participants			
Never smoked	1144	1158	2302
Current smoker	383	351	734
Ex-smoker	1152	1192	2344
Estimated Glomerular Filtration Rate (eGFR) [1]			
Mean (Standard Deviation)			70.93
Units: mL/min/1.73 m²	71.01 (21.541)	70.86 (21.297)	(21.417)
	[1] Calculated using the Modification of Diet in Renal Disease (MDRD) formula		
Renal Impairment Category [1]			
Measure Type: Number			
Units: participants			
Normal Renal Function	440	399	839
Mild Renal Impairment	1446	1530	2976
Moderate Renal Impairment	714	694	1408
Severe Renal Impairment/End-Stage Renal Disease	79	78	157
	[1] Normal renal function: eGFR ≥90 mL/min/1.73 m ² ; Mild renal impairment: eGFR ≥60 and <90 mL/min/1.73 m ² ; Moderate renal impairment: eGFR ≥30 and <60 mL/min/1.73 m ² ; Severe renal impairment: eGFR <30 mL/min/1.73 m ² ; End-stage renal disease (ESRD): eGFR <15 mL/min/1.73 m ²		
Index Acute Coronary Syndrome (ACS) Event Type [1]			
Measure Type: Number			
Units: participants			
Myocardial Infarction	2068	2084	4152
	NOTE : The sum of participants in all Categories for the Measure does not equal the Overall Number of Baseline	NOTE : The sum of participants in all Categories for the Measure does not equal the Overall Number of Baseline	

	Participants in the Arm/Group.	Participants in the Arm/Group.	
Unstable Angina	605	609	1214
	[1] Six participants in the placebo arm and 7 participants in the alogliptin arm are not included because they did not meet the ACS requirements for study inclusion.		

Time From Index ACS Event to Randomization [1]

Mean (Standard Deviation)			47.8
Units: days	48.0 (21.95)	47.6 (22.04)	(22.00)
	[1] Six participants in the placebo arm and 7 participants in the alogliptin arm are not included because they did not meet the ACS requirements for study inclusion.		

 Outcome Measures

1. Primary Outcome

Title: Percentage of Participants With Primary Major Adverse Cardiac Events (MACE)
 Primary Major Adverse Cardiac Events were defined as a composite of

 **Description:** cardiovascular death, nonfatal myocardial infarction and nonfatal stroke; these events were adjudicated by an independent cardiovascular endpoints committee.

Time Frame: From randomization until the adjudication cut-off date of May 31 2013 (maximum time on study was 41 months).

Safety Issue? No

 Outcome Measure Data 

 Analysis Population Description
 Full analysis set (all randomized participants)

Arm/Group Title	Placebo	Alogliptin
 Arm/Group Description:	Alogliptin placebo matching tablets, orally, once daily.	Alogliptin 25 mg, tablets, orally, once daily for participants with normal or mildly impaired renal function as defined by estimated glomerular filtration rate (eGFR) \geq 60 mL/min). Alogliptin 12.5 mg, tablets, orally, once daily for participants with moderately impaired renal function (eGFR \geq 30 and $<$ 60 mL/min). Alogliptin 6.25 mg, tablets, orally, once daily for participants with severely impaired renal function or end stage renal disease (eGFR $<$ 30 mL/min).
Number of Participants Analyzed	2679	2701
Measure Type: Number Units: percentage of participants	11.8	11.3

 Statistical Analysis 1 

**Statistical
Analysis
Overview**

**Comparison Groups
Comments**

Placebo, Alogliptin

Statistical analyses of the primary MACE composite endpoint was based on sequences of 1-sided repeated confidence intervals (CIs) to assess non-inferiority or statistical superiority with respect to the null hypotheses. Each sequence of repeated CIs was constructed using critical values from a 1-sided stopping boundary for a group sequential design (GSD), to preserve an overall false-rejection rate of 2.5%. Each sequence of 1-sided repeated CIs

had a simultaneous coverage probability of 97.5%.

Non-Inferiority or Equivalence Analysis?

Yes

Comments

If after accrual of 550 participants with MACE events, the upper bound of a 1-sided repeated CI for the hazard ratio (alogliptin to placebo) was <1.0 , superiority of alogliptin to placebo for the primary MACE composite would be concluded. If the upper bound of the 1-sided repeated CI for the hazard ratio of the primary MACE composite was <1.3 but ≥ 1.0 then non-inferiority but not superiority of alogliptin to placebo was to be concluded.

Statistical Test of Hypothesis

P-Value

0.315

Comments

[Not specified]

Method

Other [Cox proportional hazards]

Comments

[Not specified]

Method of Estimation

Estimation Parameter

Hazard Ratio (HR)

Estimated Value

0.962

Confidence Interval

(1-Sided) 97.5%
1.160

Estimation Comments

[Not specified]



Statistical Analysis 2



Statistical Analysis Overview

Comparison Groups

Placebo, Alogliptin

Comments

Stratified by endpoint renal function and geographic region

Non-Inferiority or Equivalence Analysis?

Yes

Comments

If after accrual of 550 participants with MACE events, the upper bound of a 1-sided repeated CI for the hazard ratio (alogliptin to placebo) was <1.0 , superiority of alogliptin to placebo for the primary MACE composite would be concluded. If the upper bound of the 1-sided repeated CI for the hazard ratio of the primary MACE composite was <1.3 but ≥ 1.0 then non-inferiority but not superiority of alogliptin to placebo was to be concluded.

Statistical Test of Hypothesis	P-Value	0.332
	Comments	Stratified by endpoint renal function (defined as the last observed postbaseline renal function (normal renal function/mild renal impairment vs moderate/severe renal impairment including end-stage renal disease)) and geographic region.
	Method	Other [Cox proportional hazards]
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.965
	Confidence Interval	(1-Sided) 97.5% 1.169
	Estimation Comments	[Not specified]

2. Secondary Outcome

Title: Percentage of Participants With Secondary Major Adverse Cardiac Events (MACE)

Description: Secondary MACE composite consisted of cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, or urgent revascularization due to unstable angina; these events were adjudicated by an independent cardiovascular endpoint committee.

Time Frame: From randomization until the adjudication cut-of date of May 31 2013 (maximum time on study was 41 months).

Safety Issue? No

 Outcome Measure Data 

 Analysis Population Description
Full analysis set

Arm/Group Title	Placebo	Alogliptin
 Arm/Group Description:	Alogliptin placebo matching tablets, orally, once daily.	Alogliptin 25 mg, tablets, orally, once daily for participants with normal or mildly impaired renal function as defined by estimated glomerular filtration rate (eGFR) \geq 60 mL/min). Alogliptin 12.5 mg, tablets, orally, once daily for participants with moderately impaired renal function (eGFR \geq 30 and $<$ 60 mL/min). Alogliptin 6.25 mg, tablets, orally, once daily for participants with severely impaired renal function or end

<p>Number of Participants Analyzed 2679</p> <p>Measure Type: Number</p> <p>Units: percentage of participants 13.4</p>	<p>stage renal disease (eGFR <30 mL/min).</p> <p>2701</p> <p>12.7</p>
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 Statistical Analysis 1 

<p>Statistical Analysis Overview</p>	<p>Comparison Groups</p> <p>Comments</p> <p>Non-Inferiority or Equivalence Analysis?</p> <p>Comments</p>	<p>Placebo, Alogliptin</p> <p>[Not specified]</p> <p>Yes</p> <p>If the upper bound of the confidence interval for the primary MACE composite was <1.0, then statistical superiority of alogliptin to placebo for the secondary MACE composite would be demonstrated.</p>
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Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.952
	Confidence Interval	(1-Sided) 97.5% 1.135
	Estimation Comments	[Not specified]

Adverse Events

Time Frame	From randomization until the adjudication cut-off date of May 31 2013 (maximum time on study was 41 months).
Additional Description	At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment.
Source Vocabulary Name	MedDRA Version 16.0
Assessment Type	Systematic Assessment

Arm/Group Title	Placebo	Alogliptin
 Arm/Group Description	Alogliptin placebo matching tablets, orally, once daily.	Alogliptin 25 mg, tablets, orally, once daily for participants with normal or mildly impaired renal function as defined by estimated glomerular filtration rate (eGFR) \geq 60 mL/min). Alogliptin 12.5 mg, tablets, orally, once daily for participants with moderately impaired renal function (eGFR \geq 30 and $<$ 60 mL/min). Alogliptin 6.25 mg, tablets, orally, once daily for participants with severely impaired renal function or end stage renal disease (eGFR $<$ 30 mL/min).

Serious Adverse Events

	Placebo Affected / at Risk (%)	Alogliptin Affected / at Risk (%)
Total	952/2679 (35.54%)	907/2701 (33.58%)
Blood and lymphatic system disorders		
Anaemia ^{† A}	17/2679 (0.63%)	16/2701 (0.59%)
Febrile neutropenia ^{† A}	0/2679 (0%)	1/2701 (0.04%)
Haemolytic anaemia ^{† A}	0/2679 (0%)	1/2701 (0.04%)
Iron deficiency anaemia ^{† A}	3/2679 (0.11%)	0/2701 (0%)
Leukocytosis ^{† A}	1/2679 (0.04%)	0/2701 (0%)
Lymphopenia ^{† A}	0/2679 (0%)	1/2701 (0.04%)

Microcytic anaemia † A	1/2679 (0.04%)	0/2701 (0%)
Neutropenia † A	1/2679 (0.04%)	0/2701 (0%)
Thrombocytopenia † A	1/2679 (0.04%)	0/2701 (0%)
Cardiac disorders		
Acute coronary syndrome † A	29/2679 (1.08%)	27/2701 (1%)
Acute left ventricular failure † A	0/2679 (0%)	2/2701 (0.07%)
Acute myocardial infarction † A	104/2679 (3.88%)	125/2701 (4.63%)
Angina pectoris † A	83/2679 (3.1%)	86/2701 (3.18%)
Angina unstable † A	142/2679 (5.3%)	117/2701 (4.33%)
Aortic valve stenosis † A	1/2679 (0.04%)	0/2701 (0%)
Arrhythmia † A	4/2679 (0.15%)	2/2701 (0.07%)
Arteriosclerosis coronary artery † A	1/2679 (0.04%)	1/2701 (0.04%)
Arteriospasm coronary † A	0/2679 (0%)	1/2701 (0.04%)
Atrial fibrillation † A	22/2679 (0.82%)	15/2701 (0.56%)
Atrial flutter † A	4/2679 (0.15%)	3/2701 (0.11%)
Atrial tachycardia † A	2/2679 (0.07%)	0/2701 (0%)
Atrioventricular block † A	0/2679 (0%)	1/2701 (0.04%)
Atrioventricular block complete † A	0/2679 (0%)	6/2701 (0.22%)
Atrioventricular block second degree † A	0/2679 (0%)	1/2701 (0.04%)
Bradyarrhythmia † A	1/2679 (0.04%)	0/2701 (0%)
Bradycardia † A	4/2679 (0.15%)	3/2701 (0.11%)
Cardiac arrest † A	11/2679 (0.41%)	14/2701 (0.52%)
Cardiac asthma † A	1/2679 (0.04%)	0/2701 (0%)
Cardiac discomfort † A	2/2679 (0.07%)	0/2701 (0%)
Cardiac failure † A	56/2679 (2.09%)	45/2701 (1.67%)
Cardiac failure acute † A	8/2679 (0.3%)	6/2701 (0.22%)
Cardiac failure chronic † A	7/2679 (0.26%)	7/2701 (0.26%)
Cardiac failure congestive † A	53/2679 (1.98%)	63/2701 (2.33%)
Cardiac valve disease † A	0/2679 (0%)	1/2701 (0.04%)
Cardio-respiratory arrest † A	9/2679 (0.34%)	6/2701 (0.22%)
Cardiogenic shock † A	5/2679 (0.19%)	14/2701 (0.52%)
Cardiomyopathy † A	1/2679 (0.04%)	4/2701 (0.15%)
Cardiopulmonary failure † A	1/2679 (0.04%)	3/2701 (0.11%)
Cardiorenal syndrome † A	1/2679 (0.04%)	1/2701 (0.04%)
Cardiovascular disorder † A	1/2679 (0.04%)	0/2701 (0%)
Cardiovascular insufficiency † A	0/2679 (0%)	1/2701 (0.04%)
Congestive cardiomyopathy † A	1/2679 (0.04%)	0/2701 (0%)
Cor pulmonale chronic † A	1/2679 (0.04%)	0/2701 (0%)
Coronary artery disease † A	34/2679 (1.27%)	35/2701 (1.3%)
Coronary artery dissection † A	1/2679 (0.04%)	0/2701 (0%)
Coronary artery insufficiency † A	0/2679 (0%)	2/2701 (0.07%)
Coronary artery occlusion † A	1/2679 (0.04%)	0/2701 (0%)
Coronary artery stenosis † A	17/2679 (0.63%)	20/2701 (0.74%)
Coronary artery thrombosis † A	1/2679 (0.04%)	0/2701 (0%)
Intracardiac thrombus † A	0/2679 (0%)	1/2701 (0.04%)
Ischaemic cardiomyopathy † A	4/2679 (0.15%)	9/2701 (0.33%)
Left ventricular dysfunction † A	1/2679 (0.04%)	1/2701 (0.04%)
	2/2679 (0.07%)	3/2701 (0.11%)

Left ventricular failure		
Mitral valve incompetence † A	2/2679 (0.07%)	1/2701 (0.04%)
Myocardial infarction † A	54/2679 (2.02%)	66/2701 (2.44%)
Myocardial ischaemia † A	19/2679 (0.71%)	20/2701 (0.74%)
Nodal rhythm † A	0/2679 (0%)	1/2701 (0.04%)
Palpitations † A	0/2679 (0%)	1/2701 (0.04%)
Postinfarction angina † A	2/2679 (0.07%)	0/2701 (0%)
Pulseless electrical activity † A	1/2679 (0.04%)	0/2701 (0%)
Right ventricular failure † A	1/2679 (0.04%)	1/2701 (0.04%)
Sick sinus syndrome † A	2/2679 (0.07%)	0/2701 (0%)
Silent myocardial infarction † A	2/2679 (0.07%)	1/2701 (0.04%)
Sinus bradycardia † A	0/2679 (0%)	1/2701 (0.04%)
Supraventricular tachycardia † A	4/2679 (0.15%)	7/2701 (0.26%)
Tachycardia † A	3/2679 (0.11%)	0/2701 (0%)
Tricuspid valve incompetence † A	1/2679 (0.04%)	1/2701 (0.04%)
Trifascicular block † A	1/2679 (0.04%)	0/2701 (0%)
Ventricular arrhythmia † A	0/2679 (0%)	1/2701 (0.04%)
Ventricular dysfunction † A	1/2679 (0.04%)	0/2701 (0%)
Ventricular dyskinesia † A	0/2679 (0%)	1/2701 (0.04%)
Ventricular extrasystoles † A	1/2679 (0.04%)	1/2701 (0.04%)
Ventricular fibrillation † A	6/2679 (0.22%)	5/2701 (0.19%)
Ventricular tachycardia † A	10/2679 (0.37%)	5/2701 (0.19%)
Congenital, familial and genetic disorders		
Congenital megaureter † A	0/2679 (0%)	1/2701 (0.04%)
Pyloric stenosis † A	1/2679 (0.04%)	0/2701 (0%)
Ear and labyrinth disorders		
Vertigo † A	2/2679 (0.07%)	3/2701 (0.11%)
Vertigo positional † A	2/2679 (0.07%)	3/2701 (0.11%)
Endocrine disorders		
Goitre † A	0/2679 (0%)	1/2701 (0.04%)
Hyperthyroidism † A	1/2679 (0.04%)	0/2701 (0%)
Eye disorders		
Amaurosis † A	1/2679 (0.04%)	0/2701 (0%)
Cataract † A	6/2679 (0.22%)	5/2701 (0.19%)
Cataract subcapsular † A	0/2679 (0%)	1/2701 (0.04%)
Dacryostenosis acquired † A	0/2679 (0%)	1/2701 (0.04%)
Diabetic retinopathy † A	1/2679 (0.04%)	1/2701 (0.04%)
Open angle glaucoma † A	0/2679 (0%)	1/2701 (0.04%)
Retinal detachment † A	0/2679 (0%)	1/2701 (0.04%)
Retinopathy † A	0/2679 (0%)	1/2701 (0.04%)
Vitreous haemorrhage † A	2/2679 (0.07%)	0/2701 (0%)
Gastrointestinal disorders		
Abdominal discomfort † A	1/2679 (0.04%)	0/2701 (0%)
Abdominal distension † A	1/2679 (0.04%)	0/2701 (0%)
Abdominal pain † A	3/2679 (0.11%)	6/2701 (0.22%)
Abdominal pain lower † A	1/2679 (0.04%)	0/2701 (0%)
Abdominal pain upper † A	1/2679 (0.04%)	1/2701 (0.04%)
Acute abdomen † A	1/2679 (0.04%)	0/2701 (0%)

Colitis ischaemic † A	1/2679 (0.04%)	0/2701 (0%)
Colitis ulcerative † A	0/2679 (0%)	1/2701 (0.04%)
Constipation † A	3/2679 (0.11%)	0/2701 (0%)
Crohn's disease † A	0/2679 (0%)	1/2701 (0.04%)
Dental caries † A	0/2679 (0%)	1/2701 (0.04%)
Diabetic gastroparesis † A	1/2679 (0.04%)	2/2701 (0.07%)
Diarrhoea † A	8/2679 (0.3%)	8/2701 (0.3%)
Diverticulitis intestinal haemorrhagic † A	0/2679 (0%)	1/2701 (0.04%)
Diverticulum intestinal haemorrhagic † A	1/2679 (0.04%)	1/2701 (0.04%)
Duodenal ulcer † A	2/2679 (0.07%)	1/2701 (0.04%)
Duodenal ulcer haemorrhage † A	0/2679 (0%)	1/2701 (0.04%)
Duodenitis † A	1/2679 (0.04%)	0/2701 (0%)
Dyspepsia † A	3/2679 (0.11%)	2/2701 (0.07%)
Dysphagia † A	1/2679 (0.04%)	0/2701 (0%)
Enteritis † A	0/2679 (0%)	1/2701 (0.04%)
Enterocolitis † A	0/2679 (0%)	1/2701 (0.04%)
Erosive duodenitis † A	1/2679 (0.04%)	0/2701 (0%)
Gastric haemorrhage † A	0/2679 (0%)	1/2701 (0.04%)
Gastric ulcer † A	3/2679 (0.11%)	2/2701 (0.07%)
Gastric ulcer haemorrhage † A	1/2679 (0.04%)	0/2701 (0%)
Gastritis † A	7/2679 (0.26%)	3/2701 (0.11%)
Gastritis erosive † A	4/2679 (0.15%)	2/2701 (0.07%)
Gastrointestinal angiodysplasia † A	0/2679 (0%)	1/2701 (0.04%)
Gastrointestinal haemorrhage † A	10/2679 (0.37%)	9/2701 (0.33%)
Gastrointestinal motility disorder † A	0/2679 (0%)	1/2701 (0.04%)
Gastrointestinal ulcer haemorrhage † A	1/2679 (0.04%)	0/2701 (0%)
Gastrooesophageal reflux disease † A	1/2679 (0.04%)	4/2701 (0.15%)
Gingival bleeding † A	1/2679 (0.04%)	0/2701 (0%)
Haemorrhoidal haemorrhage † A	1/2679 (0.04%)	0/2701 (0%)
Haemorrhoids † A	2/2679 (0.07%)	2/2701 (0.07%)
Hernial eventration † A	1/2679 (0.04%)	0/2701 (0%)
Impaired gastric emptying † A	0/2679 (0%)	3/2701 (0.11%)
Inguinal hernia † A	1/2679 (0.04%)	2/2701 (0.07%)
Inguinal hernia, obstructive † A	1/2679 (0.04%)	0/2701 (0%)
Intestinal angina † A	0/2679 (0%)	1/2701 (0.04%)
Intestinal infarction † A	0/2679 (0%)	1/2701 (0.04%)
Intestinal ischaemia † A	0/2679 (0%)	2/2701 (0.07%)
Intestinal obstruction † A	1/2679 (0.04%)	1/2701 (0.04%)
Irritable bowel syndrome † A	0/2679 (0%)	1/2701 (0.04%)
Large intestinal obstruction † A	0/2679 (0%)	1/2701 (0.04%)
Lip haematoma † A	0/2679 (0%)	1/2701 (0.04%)
Lower gastrointestinal haemorrhage † A	2/2679 (0.07%)	0/2701 (0%)
Mallory-Weiss syndrome † A	0/2679 (0%)	1/2701 (0.04%)
Oesophageal obstruction † A	1/2679 (0.04%)	0/2701 (0%)

Oesophageal pain † A	0/2679 (0%)	1/2701 (0.04%)
Oesophageal spasm † A	0/2679 (0%)	1/2701 (0.04%)
Oesophagitis † A	1/2679 (0.04%)	2/2701 (0.07%)
Pancreatic cyst † A	0/2679 (0%)	1/2701 (0.04%)
Pancreatic enlargement † A	1/2679 (0.04%)	0/2701 (0%)
Pancreatic mass † A	1/2679 (0.04%)	0/2701 (0%)
Pancreatitis † A	4/2679 (0.15%)	6/2701 (0.22%)
Pancreatitis acute † A	4/2679 (0.15%)	2/2701 (0.07%)
Pancreatitis chronic † A	1/2679 (0.04%)	2/2701 (0.07%)
Pancreatitis relapsing † A	0/2679 (0%)	3/2701 (0.11%)
Peptic ulcer † A	2/2679 (0.07%)	1/2701 (0.04%)
Peptic ulcer haemorrhage † A	1/2679 (0.04%)	0/2701 (0%)
Peritonitis sclerosing † A	0/2679 (0%)	1/2701 (0.04%)
Rectal haemorrhage † A	1/2679 (0.04%)	2/2701 (0.07%)
Retroperitoneal fibrosis † A	1/2679 (0.04%)	0/2701 (0%)
Retroperitoneal haematoma † A	1/2679 (0.04%)	0/2701 (0%)
Small intestinal obstruction † A	0/2679 (0%)	2/2701 (0.07%)
Upper gastrointestinal haemorrhage † A	4/2679 (0.15%)	6/2701 (0.22%)
Vomiting † A	2/2679 (0.07%)	1/2701 (0.04%)
General disorders		
Adverse drug reaction † A	0/2679 (0%)	2/2701 (0.07%)
Asthenia † A	3/2679 (0.11%)	0/2701 (0%)
Cardiac death † A	1/2679 (0.04%)	0/2701 (0%)
Chest discomfort † A	3/2679 (0.11%)	1/2701 (0.04%)
Chest pain † A	9/2679 (0.34%)	8/2701 (0.3%)
Death † A	6/2679 (0.22%)	6/2701 (0.22%)
Device battery issue † A	1/2679 (0.04%)	0/2701 (0%)
Device dislocation † A	0/2679 (0%)	1/2701 (0.04%)
Device failure † A	1/2679 (0.04%)	0/2701 (0%)
Device occlusion † A	2/2679 (0.07%)	2/2701 (0.07%)
General physical health deterioration † A	0/2679 (0%)	2/2701 (0.07%)
Hyperpyrexia † A	0/2679 (0%)	1/2701 (0.04%)
Impaired healing † A	1/2679 (0.04%)	0/2701 (0%)
Implant site pain † A	1/2679 (0.04%)	0/2701 (0%)
Multi-organ failure † A	2/2679 (0.07%)	3/2701 (0.11%)
Necrobiosis † A	1/2679 (0.04%)	0/2701 (0%)
Non-cardiac chest pain † A	54/2679 (2.02%)	40/2701 (1.48%)
Oedema † A	1/2679 (0.04%)	0/2701 (0%)
Oedema peripheral † A	1/2679 (0.04%)	3/2701 (0.11%)
Pseudoangina † A	1/2679 (0.04%)	0/2701 (0%)
Pyrexia † A	3/2679 (0.11%)	3/2701 (0.11%)
Sudden cardiac death † A	8/2679 (0.3%)	8/2701 (0.3%)
Sudden death † A	7/2679 (0.26%)	6/2701 (0.22%)
Hepatobiliary disorders		
Acute hepatic failure † A	1/2679 (0.04%)	0/2701 (0%)
Bile duct stone † A	2/2679 (0.07%)	0/2701 (0%)
Biliary colic † A	1/2679 (0.04%)	0/2701 (0%)

Biliary tract disorder † A	1/2679 (0.04%)	0/2701 (0%)
Cholangitis † A	1/2679 (0.04%)	0/2701 (0%)
Cholangitis acute † A	0/2679 (0%)	1/2701 (0.04%)
Cholecystitis † A	2/2679 (0.07%)	5/2701 (0.19%)
Cholecystitis acute † A	2/2679 (0.07%)	4/2701 (0.15%)
Cholecystitis chronic † A	3/2679 (0.11%)	0/2701 (0%)
Cholelithiasis † A	9/2679 (0.34%)	7/2701 (0.26%)
Hepatic cirrhosis † A	2/2679 (0.07%)	0/2701 (0%)
Hepatic function abnormal † A	0/2679 (0%)	2/2701 (0.07%)
Hepatitis acute † A	1/2679 (0.04%)	0/2701 (0%)
Jaundice cholestatic † A	0/2679 (0%)	2/2701 (0.07%)
Liver injury † A	1/2679 (0.04%)	0/2701 (0%)
Post cholecystectomy syndrome † A	1/2679 (0.04%)	0/2701 (0%)
Immune system disorders		
Anaphylactic reaction † A	3/2679 (0.11%)	1/2701 (0.04%)
Infections and infestations		
Abdominal sepsis † A	1/2679 (0.04%)	0/2701 (0%)
Abdominal wall infection † A	1/2679 (0.04%)	0/2701 (0%)
Abscess limb † A	6/2679 (0.22%)	1/2701 (0.04%)
Acinetobacter bacteraemia † A	0/2679 (0%)	1/2701 (0.04%)
Acute hepatitis B † A	1/2679 (0.04%)	0/2701 (0%)
Acute sinusitis † A	0/2679 (0%)	1/2701 (0.04%)
Anal abscess † A	0/2679 (0%)	1/2701 (0.04%)
Appendicitis † A	3/2679 (0.11%)	1/2701 (0.04%)
Appendicitis perforated † A	1/2679 (0.04%)	1/2701 (0.04%)
Arthritis bacterial † A	1/2679 (0.04%)	2/2701 (0.07%)
Atypical pneumonia † A	0/2679 (0%)	2/2701 (0.07%)
Bacteraemia † A	2/2679 (0.07%)	2/2701 (0.07%)
Bacterial diarrhoea † A	0/2679 (0%)	1/2701 (0.04%)
Bacterial pyelonephritis † A	0/2679 (0%)	1/2701 (0.04%)
Biliary tract infection † A	1/2679 (0.04%)	0/2701 (0%)
Breast abscess † A	1/2679 (0.04%)	0/2701 (0%)
Bronchitis † A	10/2679 (0.37%)	14/2701 (0.52%)
Bronchopneumonia † A	3/2679 (0.11%)	1/2701 (0.04%)
Carbuncle † A	0/2679 (0%)	2/2701 (0.07%)
Cellulitis † A	15/2679 (0.56%)	7/2701 (0.26%)
Cystitis † A	4/2679 (0.15%)	1/2701 (0.04%)
Cystitis escherichia † A	1/2679 (0.04%)	0/2701 (0%)
Dacryocanaliculitis † A	0/2679 (0%)	1/2701 (0.04%)
Dengue fever † A	0/2679 (0%)	1/2701 (0.04%)
Diabetic foot infection † A	0/2679 (0%)	1/2701 (0.04%)
Diabetic gangrene † A	0/2679 (0%)	1/2701 (0.04%)
Diarrhoea infectious † A	0/2679 (0%)	2/2701 (0.07%)
Diverticulitis † A	5/2679 (0.19%)	1/2701 (0.04%)
Endocarditis † A	2/2679 (0.07%)	2/2701 (0.07%)
Endocarditis bacterial † A	1/2679 (0.04%)	0/2701 (0%)
Enterocolitis infectious † A	1/2679 (0.04%)	0/2701 (0%)
Erysipelas † A	3/2679 (0.11%)	3/2701 (0.11%)

Escherichia sepsis † A	0/2679 (0%)	1/2701 (0.04%)
Escherichia urinary tract infection † A	1/2679 (0.04%)	0/2701 (0%)
Extradural abscess † A	0/2679 (0%)	1/2701 (0.04%)
Gangrene † A	4/2679 (0.15%)	4/2701 (0.15%)
Gas gangrene † A	1/2679 (0.04%)	0/2701 (0%)
Gastritis viral † A	1/2679 (0.04%)	0/2701 (0%)
Gastroenteritis † A	10/2679 (0.37%)	7/2701 (0.26%)
Gastroenteritis viral † A	2/2679 (0.07%)	1/2701 (0.04%)
Gastrointestinal infection † A	0/2679 (0%)	1/2701 (0.04%)
Genital infection † A	1/2679 (0.04%)	0/2701 (0%)
Groin abscess † A	1/2679 (0.04%)	0/2701 (0%)
HIV infection † A	1/2679 (0.04%)	0/2701 (0%)
Haematoma infection † A	1/2679 (0.04%)	0/2701 (0%)
Hepatitis B † A	1/2679 (0.04%)	0/2701 (0%)
Herpes zoster † A	2/2679 (0.07%)	1/2701 (0.04%)
Incision site infection † A	0/2679 (0%)	1/2701 (0.04%)
Infection † A	1/2679 (0.04%)	0/2701 (0%)
Influenza † A	1/2679 (0.04%)	0/2701 (0%)
Intervertebral discitis † A	1/2679 (0.04%)	0/2701 (0%)
Intestinal gangrene † A	1/2679 (0.04%)	1/2701 (0.04%)
Korean haemorrhagic fever † A	0/2679 (0%)	1/2701 (0.04%)
Liver abscess † A	0/2679 (0%)	1/2701 (0.04%)
Lobar pneumonia † A	3/2679 (0.11%)	1/2701 (0.04%)
Localised infection † A	2/2679 (0.07%)	3/2701 (0.11%)
Lower respiratory tract infection † A	5/2679 (0.19%)	3/2701 (0.11%)
Malaria † A	0/2679 (0%)	1/2701 (0.04%)
Mediastinitis † A	2/2679 (0.07%)	0/2701 (0%)
Meningitis † A	0/2679 (0%)	1/2701 (0.04%)
Meningitis viral † A	1/2679 (0.04%)	0/2701 (0%)
Orchitis † A	0/2679 (0%)	1/2701 (0.04%)
Osteomyelitis † A	1/2679 (0.04%)	5/2701 (0.19%)
Osteomyelitis acute † A	0/2679 (0%)	1/2701 (0.04%)
Osteomyelitis chronic † A	1/2679 (0.04%)	0/2701 (0%)
Periodontitis † A	0/2679 (0%)	1/2701 (0.04%)
Pharyngitis streptococcal † A	0/2679 (0%)	1/2701 (0.04%)
Pleural infection bacterial † A	0/2679 (0%)	1/2701 (0.04%)
Pneumonia † A	44/2679 (1.64%)	49/2701 (1.81%)
Pneumonia bacterial † A	1/2679 (0.04%)	0/2701 (0%)
Pneumonia influenzal † A	1/2679 (0.04%)	0/2701 (0%)
Pneumonia staphylococcal † A	1/2679 (0.04%)	0/2701 (0%)
Pneumonia viral † A	0/2679 (0%)	1/2701 (0.04%)
Post procedural cellulitis † A	0/2679 (0%)	1/2701 (0.04%)
Postoperative wound infection † A	5/2679 (0.19%)	4/2701 (0.15%)
Pseudomembranous colitis † A	1/2679 (0.04%)	0/2701 (0%)
Pyelonephritis † A	2/2679 (0.07%)	5/2701 (0.19%)
Pyelonephritis acute † A	4/2679 (0.15%)	1/2701 (0.04%)
Respiratory tract infection † A	2/2679 (0.07%)	1/2701 (0.04%)

Respiratory tract infection viral † A	1/2679 (0.04%)	0/2701 (0%)
Scrotal abscess † A	0/2679 (0%)	1/2701 (0.04%)
Scrub typhus † A	0/2679 (0%)	1/2701 (0.04%)
Sepsis † A	19/2679 (0.71%)	11/2701 (0.41%)
Septic shock † A	6/2679 (0.22%)	10/2701 (0.37%)
Serratia infection † A	1/2679 (0.04%)	0/2701 (0%)
Staphylococcal infection † A	0/2679 (0%)	1/2701 (0.04%)
Staphylococcal skin infection † A	1/2679 (0.04%)	0/2701 (0%)
Subcutaneous abscess † A	2/2679 (0.07%)	2/2701 (0.07%)
Thrombophlebitis septic † A	1/2679 (0.04%)	0/2701 (0%)
Tooth abscess † A	1/2679 (0.04%)	0/2701 (0%)
Tuberculosis † A	0/2679 (0%)	1/2701 (0.04%)
Upper respiratory tract infection † A	0/2679 (0%)	2/2701 (0.07%)
Urethritis † A	0/2679 (0%)	1/2701 (0.04%)
Urinary tract infection † A	14/2679 (0.52%)	10/2701 (0.37%)
Urosepsis † A	2/2679 (0.07%)	1/2701 (0.04%)
Viraemia † A	0/2679 (0%)	1/2701 (0.04%)
Viral infection † A	1/2679 (0.04%)	2/2701 (0.07%)
Wound infection † A	4/2679 (0.15%)	0/2701 (0%)
Wound infection staphylococcal † A	0/2679 (0%)	2/2701 (0.07%)
Injury, poisoning and procedural complications		
Accident † A	1/2679 (0.04%)	0/2701 (0%)
Alcohol poisoning † A	2/2679 (0.07%)	0/2701 (0%)
Anaemia postoperative † A	1/2679 (0.04%)	0/2701 (0%)
Ankle fracture † A	0/2679 (0%)	2/2701 (0.07%)
Arterial injury † A	0/2679 (0%)	1/2701 (0.04%)
Arterial restenosis † A	0/2679 (0%)	3/2701 (0.11%)
Arteriovenous fistula occlusion † A	1/2679 (0.04%)	0/2701 (0%)
Arteriovenous fistula site complication † A	0/2679 (0%)	1/2701 (0.04%)
Chemical poisoning † A	0/2679 (0%)	1/2701 (0.04%)
Chest injury † A	0/2679 (0%)	1/2701 (0.04%)
Concussion † A	1/2679 (0.04%)	0/2701 (0%)
Contusion † A	1/2679 (0.04%)	0/2701 (0%)
Coronary artery reocclusion † A	0/2679 (0%)	1/2701 (0.04%)
Coronary artery restenosis † A	17/2679 (0.63%)	19/2701 (0.7%)
Craniocerebral injury † A	0/2679 (0%)	1/2701 (0.04%)
Eyeball rupture † A	1/2679 (0.04%)	0/2701 (0%)
Fall † A	6/2679 (0.22%)	3/2701 (0.11%)
Fat embolism † A	1/2679 (0.04%)	0/2701 (0%)
Femoral neck fracture † A	1/2679 (0.04%)	1/2701 (0.04%)
Femur fracture † A	8/2679 (0.3%)	1/2701 (0.04%)
Foot fracture † A	2/2679 (0.07%)	1/2701 (0.04%)
Gun shot wound † A	1/2679 (0.04%)	0/2701 (0%)
Hand fracture † A	1/2679 (0.04%)	0/2701 (0%)
Head injury † A	1/2679 (0.04%)	2/2701 (0.07%)

Human bite † A	1/2679 (0.04%)	0/2701 (0%)
Inflammation of wound † A	0/2679 (0%)	1/2701 (0.04%)
Intentional overdose † A	1/2679 (0.04%)	0/2701 (0%)
Joint dislocation † A	0/2679 (0%)	1/2701 (0.04%)
Joint injury † A	1/2679 (0.04%)	0/2701 (0%)
Laceration † A	3/2679 (0.11%)	2/2701 (0.07%)
Ligament injury † A	1/2679 (0.04%)	0/2701 (0%)
Limb injury † A	2/2679 (0.07%)	0/2701 (0%)
Lower limb fracture † A	0/2679 (0%)	2/2701 (0.07%)
Lumbar vertebral fracture † A	1/2679 (0.04%)	0/2701 (0%)
Multiple fractures † A	1/2679 (0.04%)	0/2701 (0%)
Muscle rupture † A	0/2679 (0%)	1/2701 (0.04%)
Muscle strain † A	0/2679 (0%)	2/2701 (0.07%)
Open fracture † A	0/2679 (0%)	1/2701 (0.04%)
Overdose † A	1/2679 (0.04%)	1/2701 (0.04%)
Patella fracture † A	0/2679 (0%)	1/2701 (0.04%)
Post procedural haemorrhage † A	0/2679 (0%)	2/2701 (0.07%)
Post procedural myocardial infarction † A	1/2679 (0.04%)	0/2701 (0%)
Postoperative thoracic procedure complication † A	0/2679 (0%)	1/2701 (0.04%)
Postoperative wound complication † A	0/2679 (0%)	2/2701 (0.07%)
Pubis fracture † A	2/2679 (0.07%)	0/2701 (0%)
Radius fracture † A	1/2679 (0.04%)	0/2701 (0%)
Repetitive strain injury † A	1/2679 (0.04%)	0/2701 (0%)
Rib fracture † A	3/2679 (0.11%)	0/2701 (0%)
Road traffic accident † A	3/2679 (0.11%)	2/2701 (0.07%)
Spinal compression fracture † A	0/2679 (0%)	3/2701 (0.11%)
Subdural haematoma † A	1/2679 (0.04%)	1/2701 (0.04%)
Tendon rupture † A	0/2679 (0%)	1/2701 (0.04%)
Tibia fracture † A	0/2679 (0%)	1/2701 (0.04%)
Tobacco poisoning † A	1/2679 (0.04%)	0/2701 (0%)
Toxicity to various agents † A	2/2679 (0.07%)	1/2701 (0.04%)
Transfusion reaction † A	0/2679 (0%)	1/2701 (0.04%)
Traumatic haematoma † A	3/2679 (0.11%)	0/2701 (0%)
Traumatic intracranial haemorrhage † A	1/2679 (0.04%)	0/2701 (0%)
Ulna fracture † A	1/2679 (0.04%)	0/2701 (0%)
Vascular graft complication † A	1/2679 (0.04%)	1/2701 (0.04%)
Vascular graft occlusion † A	2/2679 (0.07%)	0/2701 (0%)
Vascular pseudoaneurysm † A	1/2679 (0.04%)	1/2701 (0.04%)
Wound dehiscence † A	1/2679 (0.04%)	1/2701 (0.04%)
Wound necrosis † A	1/2679 (0.04%)	0/2701 (0%)
Investigations		
Alanine aminotransferase increased † A	0/2679 (0%)	1/2701 (0.04%)
Amylase increased † A	0/2679 (0%)	2/2701 (0.07%)
Aspartate aminotransferase † A	0/2679 (0%)	1/2701 (0.04%)

increased

Blood creatine phosphokinase increased † A	0/2679 (0%)	1/2701 (0.04%)
Blood creatinine increased † A	0/2679 (0%)	1/2701 (0.04%)
Blood glucose increased † A	2/2679 (0.07%)	0/2701 (0%)
Blood potassium increased † A	1/2679 (0.04%)	0/2701 (0%)
Cardiac enzymes increased † A	2/2679 (0.07%)	0/2701 (0%)
Electrocardiogram ST segment depression † A	0/2679 (0%)	1/2701 (0.04%)
Gamma-glutamyltransferase increased † A	0/2679 (0%)	1/2701 (0.04%)
Haemoglobin decreased † A	3/2679 (0.11%)	0/2701 (0%)
Heart rate irregular † A	1/2679 (0.04%)	0/2701 (0%)
Hepatic enzyme increased † A	2/2679 (0.07%)	0/2701 (0%)
International normalised ratio increased † A	1/2679 (0.04%)	0/2701 (0%)
Lipase increased † A	2/2679 (0.07%)	1/2701 (0.04%)
Liver function test abnormal † A	0/2679 (0%)	1/2701 (0.04%)
Neutrophil count decreased † A	0/2679 (0%)	1/2701 (0.04%)
Oxygen saturation decreased † A	0/2679 (0%)	1/2701 (0.04%)
Pancreatic enzymes increased † A	1/2679 (0.04%)	0/2701 (0%)
Transaminases increased † A	1/2679 (0.04%)	0/2701 (0%)
Troponin increased † A	1/2679 (0.04%)	0/2701 (0%)
Metabolism and nutrition disorders		
Dehydration † A	4/2679 (0.15%)	1/2701 (0.04%)
Diabetes complicating pregnancy † A	1/2679 (0.04%)	0/2701 (0%)
Diabetes mellitus † A	11/2679 (0.41%)	6/2701 (0.22%)
Diabetes mellitus inadequate control † A	14/2679 (0.52%)	5/2701 (0.19%)
Diabetic ketoacidosis † A	1/2679 (0.04%)	0/2701 (0%)
Electrolyte imbalance † A	1/2679 (0.04%)	1/2701 (0.04%)
Failure to thrive † A	1/2679 (0.04%)	0/2701 (0%)
Fluid overload † A	2/2679 (0.07%)	1/2701 (0.04%)
Gout † A	4/2679 (0.15%)	3/2701 (0.11%)
Hyperglycaemia † A	11/2679 (0.41%)	5/2701 (0.19%)
Hyperglycaemic hyperosmolar nonketotic syndrome † A	1/2679 (0.04%)	0/2701 (0%)
Hyperkalaemia † A	2/2679 (0.07%)	5/2701 (0.19%)
Hyperlipasaemia † A	1/2679 (0.04%)	0/2701 (0%)
Hyperosmolar state † A	1/2679 (0.04%)	0/2701 (0%)
Hypertriglyceridaemia † A	2/2679 (0.07%)	0/2701 (0%)
Hypoalbuminaemia † A	1/2679 (0.04%)	0/2701 (0%)
Hypoglycaemia † A	16/2679 (0.6%)	18/2701 (0.67%)
Hypokalaemia † A	2/2679 (0.07%)	0/2701 (0%)
Hypomagnesaemia † A	1/2679 (0.04%)	0/2701 (0%)
Hyponatraemia † A	0/2679 (0%)	2/2701 (0.07%)
Hypophosphataemia † A	1/2679 (0.04%)	0/2701 (0%)
Hypovolaemia † A	1/2679 (0.04%)	0/2701 (0%)
Lactic acidosis † A	0/2679 (0%)	1/2701 (0.04%)

Metabolic acidosis † A	1/2679 (0.04%)	1/2701 (0.04%)
Obesity † A	1/2679 (0.04%)	1/2701 (0.04%)
Musculoskeletal and connective tissue disorders		
Arthralgia † A	0/2679 (0%)	1/2701 (0.04%)
Arthritis † A	0/2679 (0%)	1/2701 (0.04%)
Back pain † A	1/2679 (0.04%)	5/2701 (0.19%)
Bursitis † A	1/2679 (0.04%)	0/2701 (0%)
Chondrocalcinosis pyrophosphate † A	1/2679 (0.04%)	0/2701 (0%)
Costochondritis † A	0/2679 (0%)	1/2701 (0.04%)
Fibromyalgia † A	0/2679 (0%)	1/2701 (0.04%)
Flank pain † A	0/2679 (0%)	1/2701 (0.04%)
Haemarthrosis † A	0/2679 (0%)	1/2701 (0.04%)
Intervertebral disc disorder † A	1/2679 (0.04%)	2/2701 (0.07%)
Intervertebral disc protrusion † A	2/2679 (0.07%)	0/2701 (0%)
Lumbar spinal stenosis † A	1/2679 (0.04%)	0/2701 (0%)
Muscle contracture † A	1/2679 (0.04%)	0/2701 (0%)
Muscle haemorrhage † A	0/2679 (0%)	1/2701 (0.04%)
Muscle spasms † A	0/2679 (0%)	1/2701 (0.04%)
Muscle twitching † A	0/2679 (0%)	1/2701 (0.04%)
Muscular weakness † A	1/2679 (0.04%)	0/2701 (0%)
Musculoskeletal chest pain † A	14/2679 (0.52%)	16/2701 (0.59%)
Musculoskeletal discomfort † A	0/2679 (0%)	1/2701 (0.04%)
Musculoskeletal pain † A	0/2679 (0%)	1/2701 (0.04%)
Myalgia † A	0/2679 (0%)	1/2701 (0.04%)
Myopathy † A	1/2679 (0.04%)	1/2701 (0.04%)
Myositis † A	0/2679 (0%)	1/2701 (0.04%)
Neuropathic arthropathy † A	1/2679 (0.04%)	0/2701 (0%)
Osteoarthritis † A	3/2679 (0.11%)	3/2701 (0.11%)
Psoriatic arthropathy † A	1/2679 (0.04%)	0/2701 (0%)
Rhabdomyolysis † A	0/2679 (0%)	1/2701 (0.04%)
Rheumatoid arthritis † A	1/2679 (0.04%)	0/2701 (0%)
Rotator cuff syndrome † A	1/2679 (0.04%)	1/2701 (0.04%)
Spinal osteoarthritis † A	3/2679 (0.11%)	1/2701 (0.04%)
Tendon disorder † A	1/2679 (0.04%)	0/2701 (0%)
Tendonitis † A	1/2679 (0.04%)	0/2701 (0%)
Torticollis † A	0/2679 (0%)	1/2701 (0.04%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Adenocarcinoma gastric † A	0/2679 (0%)	2/2701 (0.07%)
Adenocarcinoma of colon † A	0/2679 (0%)	1/2701 (0.04%)
Basal cell carcinoma † A	0/2679 (0%)	1/2701 (0.04%)
Benign salivary gland neoplasm † A	0/2679 (0%)	1/2701 (0.04%)
Bladder cancer † A	2/2679 (0.07%)	2/2701 (0.07%)
Bladder papilloma † A	1/2679 (0.04%)	0/2701 (0%)
Breast cancer † A	2/2679 (0.07%)	3/2701 (0.11%)
Breast cancer stage III † A	0/2679 (0%)	1/2701 (0.04%)

Colon adenoma † A	1/2679 (0.04%)	0/2701 (0%)
Colon cancer † A	4/2679 (0.15%)	4/2701 (0.15%)
Colon cancer recurrent † A	1/2679 (0.04%)	0/2701 (0%)
Colon cancer stage II † A	1/2679 (0.04%)	0/2701 (0%)
Colon neoplasm † A	1/2679 (0.04%)	0/2701 (0%)
Colorectal adenocarcinoma † A	1/2679 (0.04%)	0/2701 (0%)
Endometrial cancer † A	1/2679 (0.04%)	0/2701 (0%)
Endometrial cancer stage I † A	1/2679 (0.04%)	0/2701 (0%)
Fibroadenoma of breast † A	1/2679 (0.04%)	0/2701 (0%)
Follicular thyroid cancer † A	1/2679 (0.04%)	0/2701 (0%)
Gallbladder cancer † A	0/2679 (0%)	1/2701 (0.04%)
Gastric cancer † A	1/2679 (0.04%)	2/2701 (0.07%)
Hepatic cancer † A	1/2679 (0.04%)	0/2701 (0%)
Hepatocellular carcinoma † A	0/2679 (0%)	1/2701 (0.04%)
Invasive ductal breast carcinoma † A	1/2679 (0.04%)	1/2701 (0.04%)
Lentigo maligna † A	0/2679 (0%)	1/2701 (0.04%)
Lip neoplasm † A	0/2679 (0%)	1/2701 (0.04%)
Lip squamous cell carcinoma † A	0/2679 (0%)	1/2701 (0.04%)
Lung adenocarcinoma † A	0/2679 (0%)	1/2701 (0.04%)
Lung cancer metastatic † A	0/2679 (0%)	1/2701 (0.04%)
Lung neoplasm † A	1/2679 (0.04%)	1/2701 (0.04%)
Lung neoplasm malignant † A	0/2679 (0%)	2/2701 (0.07%)
Malignant melanoma † A	0/2679 (0%)	1/2701 (0.04%)
Metastases to lymph nodes † A	1/2679 (0.04%)	0/2701 (0%)
Metastatic neoplasm † A	0/2679 (0%)	1/2701 (0.04%)
Non-Hodgkin's lymphoma † A	0/2679 (0%)	1/2701 (0.04%)
Oesophageal carcinoma † A	1/2679 (0.04%)	1/2701 (0.04%)
Osteoma † A	0/2679 (0%)	1/2701 (0.04%)
Ovarian neoplasm † A	0/2679 (0%)	1/2701 (0.04%)
Plasma cell myeloma † A	0/2679 (0%)	1/2701 (0.04%)
Prostate cancer † A	3/2679 (0.11%)	4/2701 (0.15%)
Rectal adenocarcinoma † A	1/2679 (0.04%)	0/2701 (0%)
Rectal cancer † A	0/2679 (0%)	1/2701 (0.04%)
Rectal cancer metastatic † A	0/2679 (0%)	1/2701 (0.04%)
Rectosigmoid cancer † A	1/2679 (0.04%)	0/2701 (0%)
Renal cancer † A	1/2679 (0.04%)	0/2701 (0%)
Renal cell carcinoma † A	1/2679 (0.04%)	2/2701 (0.07%)
Renal neoplasm † A	1/2679 (0.04%)	1/2701 (0.04%)
Signet-ring cell carcinoma † A	0/2679 (0%)	1/2701 (0.04%)
Spinal cord neoplasm † A	0/2679 (0%)	1/2701 (0.04%)
Squamous cell carcinoma † A	0/2679 (0%)	3/2701 (0.11%)
Squamous cell carcinoma of lung † A	0/2679 (0%)	2/2701 (0.07%)
Squamous cell carcinoma of skin † A	0/2679 (0%)	1/2701 (0.04%)
Uterine leiomyoma † A	1/2679 (0.04%)	1/2701 (0.04%)
Nervous system disorders		
Amyotrophic lateral sclerosis † A	1/2679 (0.04%)	0/2701 (0%)

Ataxia † A	1/2679 (0.04%)	0/2701 (0%)
Balance disorder † A	1/2679 (0.04%)	0/2701 (0%)
Brain hypoxia † A	1/2679 (0.04%)	0/2701 (0%)
Brain stem haemorrhage † A	0/2679 (0%)	1/2701 (0.04%)
Brain stem stroke † A	1/2679 (0.04%)	0/2701 (0%)
Carotid artery disease † A	0/2679 (0%)	2/2701 (0.07%)
Carotid artery occlusion † A	1/2679 (0.04%)	0/2701 (0%)
Carotid artery stenosis † A	5/2679 (0.19%)	3/2701 (0.11%)
Carotid sinus syndrome † A	1/2679 (0.04%)	0/2701 (0%)
Carpal tunnel syndrome † A	2/2679 (0.07%)	1/2701 (0.04%)
Cauda equina syndrome † A	1/2679 (0.04%)	1/2701 (0.04%)
Central pain syndrome † A	0/2679 (0%)	1/2701 (0.04%)
Cerebellar infarction † A	1/2679 (0.04%)	0/2701 (0%)
Cerebral arteriosclerosis † A	1/2679 (0.04%)	0/2701 (0%)
Cerebral infarction † A	4/2679 (0.15%)	4/2701 (0.15%)
Cerebrovascular accident † A	25/2679 (0.93%)	15/2701 (0.56%)
Cerebrovascular disorder † A	2/2679 (0.07%)	0/2701 (0%)
Cerebrovascular insufficiency † A	0/2679 (0%)	1/2701 (0.04%)
Cervicobrachial syndrome † A	1/2679 (0.04%)	1/2701 (0.04%)
Cognitive disorder † A	1/2679 (0.04%)	0/2701 (0%)
Coma † A	2/2679 (0.07%)	0/2701 (0%)
Convulsion † A	2/2679 (0.07%)	7/2701 (0.26%)
Diabetic ketoacidotic hyperglycaemic coma † A	1/2679 (0.04%)	0/2701 (0%)
Diabetic neuropathy † A	1/2679 (0.04%)	0/2701 (0%)
Dizziness † A	3/2679 (0.11%)	0/2701 (0%)
Embolic stroke † A	1/2679 (0.04%)	0/2701 (0%)
Encephalopathy † A	1/2679 (0.04%)	0/2701 (0%)
Epilepsy † A	3/2679 (0.11%)	2/2701 (0.07%)
Grand mal convulsion † A	0/2679 (0%)	1/2701 (0.04%)
Haemorrhage intracranial † A	1/2679 (0.04%)	0/2701 (0%)
Haemorrhagic stroke † A	4/2679 (0.15%)	0/2701 (0%)
Headache † A	2/2679 (0.07%)	0/2701 (0%)
Hemiparesis † A	1/2679 (0.04%)	1/2701 (0.04%)
Hypoaesthesia † A	0/2679 (0%)	1/2701 (0.04%)
Hypoglycaemic coma † A	0/2679 (0%)	1/2701 (0.04%)
Hypoglycaemic seizure † A	0/2679 (0%)	2/2701 (0.07%)
Hypoxic-ischaemic encephalopathy † A	2/2679 (0.07%)	1/2701 (0.04%)
Ischaemic cerebral infarction † A	0/2679 (0%)	1/2701 (0.04%)
Ischaemic stroke † A	7/2679 (0.26%)	15/2701 (0.56%)
Lacunar infarction † A	2/2679 (0.07%)	1/2701 (0.04%)
Lumbar radiculopathy † A	0/2679 (0%)	1/2701 (0.04%)
Metabolic encephalopathy † A	1/2679 (0.04%)	0/2701 (0%)
Migraine † A	0/2679 (0%)	2/2701 (0.07%)
Multiple sclerosis † A	1/2679 (0.04%)	0/2701 (0%)
Neuralgia † A	1/2679 (0.04%)	1/2701 (0.04%)
Neuritis cranial † A	2/2679 (0.07%)	0/2701 (0%)
Petit mal epilepsy † A	0/2679 (0%)	1/2701 (0.04%)

Polyneuropathy † A	2/2679 (0.07%)	0/2701 (0%)
Presyncope † A	2/2679 (0.07%)	2/2701 (0.07%)
Sciatica † A	2/2679 (0.07%)	2/2701 (0.07%)
Senile dementia † A	1/2679 (0.04%)	0/2701 (0%)
Spinal claudication † A	1/2679 (0.04%)	1/2701 (0.04%)
Subarachnoid haemorrhage † A	1/2679 (0.04%)	2/2701 (0.07%)
Syncope † A	9/2679 (0.34%)	9/2701 (0.33%)
Thrombotic cerebral infarction † A	0/2679 (0%)	1/2701 (0.04%)
Transient ischaemic attack † A	7/2679 (0.26%)	5/2701 (0.19%)
VIIth nerve paralysis † A	0/2679 (0%)	2/2701 (0.07%)
VIth nerve paralysis † A	1/2679 (0.04%)	0/2701 (0%)
Vascular dementia † A	0/2679 (0%)	1/2701 (0.04%)
Vertebrobasilar insufficiency † A	0/2679 (0%)	1/2701 (0.04%)
Pregnancy, puerperium and perinatal conditions		
Abortion spontaneous † A	1/2679 (0.04%)	0/2701 (0%)
Psychiatric disorders		
Abnormal behaviour † A	1/2679 (0.04%)	0/2701 (0%)
Agoraphobia † A	1/2679 (0.04%)	0/2701 (0%)
Alcohol abuse † A	0/2679 (0%)	1/2701 (0.04%)
Anxiety disorder † A	1/2679 (0.04%)	1/2701 (0.04%)
Bipolar disorder † A	1/2679 (0.04%)	0/2701 (0%)
Completed suicide † A	2/2679 (0.07%)	0/2701 (0%)
Confusional state † A	0/2679 (0%)	1/2701 (0.04%)
Depression † A	1/2679 (0.04%)	0/2701 (0%)
Major depression † A	1/2679 (0.04%)	2/2701 (0.07%)
Mental status changes † A	1/2679 (0.04%)	0/2701 (0%)
Mood altered † A	0/2679 (0%)	1/2701 (0.04%)
Schizophrenia, paranoid type † A	0/2679 (0%)	1/2701 (0.04%)
Stress † A	1/2679 (0.04%)	1/2701 (0.04%)
Renal and urinary disorders		
Acute prerenal failure † A	1/2679 (0.04%)	1/2701 (0.04%)
Azotaemia † A	3/2679 (0.11%)	1/2701 (0.04%)
Calculus bladder † A	0/2679 (0%)	1/2701 (0.04%)
Calculus ureteric † A	3/2679 (0.11%)	2/2701 (0.07%)
Calculus urinary † A	2/2679 (0.07%)	1/2701 (0.04%)
Cystitis haemorrhagic † A	0/2679 (0%)	1/2701 (0.04%)
Diabetic nephropathy † A	2/2679 (0.07%)	1/2701 (0.04%)
Haematuria † A	2/2679 (0.07%)	5/2701 (0.19%)
Hydronephrosis † A	1/2679 (0.04%)	1/2701 (0.04%)
Incontinence † A	1/2679 (0.04%)	0/2701 (0%)
Nephrolithiasis † A	2/2679 (0.07%)	4/2701 (0.15%)
Nephropathy † A	1/2679 (0.04%)	1/2701 (0.04%)
Obstructive uropathy † A	0/2679 (0%)	1/2701 (0.04%)
Prerenal failure † A	0/2679 (0%)	2/2701 (0.07%)
Renal artery stenosis † A	2/2679 (0.07%)	0/2701 (0%)
Renal colic † A	2/2679 (0.07%)	2/2701 (0.07%)
Renal embolism † A	1/2679 (0.04%)	0/2701 (0%)
Renal failure † A	13/2679 (0.49%)	12/2701 (0.44%)

Renal failure acute † A	36/2679 (1.34%)	43/2701 (1.59%)
Renal failure chronic † A	13/2679 (0.49%)	9/2701 (0.33%)
Renal impairment † A	7/2679 (0.26%)	8/2701 (0.3%)
Renal injury † A	0/2679 (0%)	1/2701 (0.04%)
Renal mass † A	1/2679 (0.04%)	0/2701 (0%)
Renal tubular necrosis † A	2/2679 (0.07%)	0/2701 (0%)
Ureteric obstruction † A	1/2679 (0.04%)	0/2701 (0%)
Urethral stenosis † A	1/2679 (0.04%)	1/2701 (0.04%)
Urinary incontinence † A	0/2679 (0%)	1/2701 (0.04%)
Urinary retention † A	0/2679 (0%)	6/2701 (0.22%)
Urinary tract obstruction † A	0/2679 (0%)	1/2701 (0.04%)
Reproductive system and breast disorders		
Benign prostatic hyperplasia † A	6/2679 (0.22%)	1/2701 (0.04%)
Gynaecomastia † A	1/2679 (0.04%)	0/2701 (0%)
Menorrhagia † A	1/2679 (0.04%)	0/2701 (0%)
Prostatism † A	1/2679 (0.04%)	0/2701 (0%)
Prostatitis † A	0/2679 (0%)	1/2701 (0.04%)
Scrotal mass † A	0/2679 (0%)	1/2701 (0.04%)
Uterine prolapse † A	1/2679 (0.04%)	0/2701 (0%)
Vaginal haemorrhage † A	2/2679 (0.07%)	1/2701 (0.04%)
Respiratory, thoracic and mediastinal disorders		
Acute pulmonary oedema † A	15/2679 (0.56%)	24/2701 (0.89%)
Acute respiratory distress syndrome † A	1/2679 (0.04%)	2/2701 (0.07%)
Acute respiratory failure † A	2/2679 (0.07%)	7/2701 (0.26%)
Asphyxia † A	0/2679 (0%)	1/2701 (0.04%)
Asthma † A	2/2679 (0.07%)	1/2701 (0.04%)
Bronchial hyperreactivity † A	0/2679 (0%)	1/2701 (0.04%)
Bronchiectasis † A	1/2679 (0.04%)	1/2701 (0.04%)
Bronchospasm † A	1/2679 (0.04%)	0/2701 (0%)
Bullous lung disease † A	0/2679 (0%)	1/2701 (0.04%)
Chronic obstructive pulmonary disease † A	19/2679 (0.71%)	13/2701 (0.48%)
Chronic respiratory failure † A	1/2679 (0.04%)	0/2701 (0%)
Cough † A	0/2679 (0%)	1/2701 (0.04%)
Dyspnoea † A	8/2679 (0.3%)	7/2701 (0.26%)
Epistaxis † A	2/2679 (0.07%)	1/2701 (0.04%)
Haemoptysis † A	1/2679 (0.04%)	1/2701 (0.04%)
Haemothorax † A	0/2679 (0%)	2/2701 (0.07%)
Hydrothorax † A	1/2679 (0.04%)	0/2701 (0%)
Hypoxia † A	0/2679 (0%)	2/2701 (0.07%)
Interstitial lung disease † A	1/2679 (0.04%)	3/2701 (0.11%)
Laryngeal oedema † A	0/2679 (0%)	1/2701 (0.04%)
Lung disorder † A	1/2679 (0.04%)	0/2701 (0%)
Pickwickian syndrome † A	1/2679 (0.04%)	0/2701 (0%)
Pleural effusion † A	1/2679 (0.04%)	4/2701 (0.15%)
Pleurisy † A	1/2679 (0.04%)	0/2701 (0%)

Pleuritic pain † A	1/2679 (0.04%)	0/2701 (0%)
Pneumonia aspiration † A	1/2679 (0.04%)	1/2701 (0.04%)
Pneumonitis † A	0/2679 (0%)	1/2701 (0.04%)
Pneumothorax † A	0/2679 (0%)	3/2701 (0.11%)
Pulmonary arterial hypertension † A	1/2679 (0.04%)	0/2701 (0%)
Pulmonary congestion † A	2/2679 (0.07%)	0/2701 (0%)
Pulmonary embolism † A	2/2679 (0.07%)	9/2701 (0.33%)
Pulmonary fibrosis † A	3/2679 (0.11%)	2/2701 (0.07%)
Pulmonary hypertension † A	4/2679 (0.15%)	4/2701 (0.15%)
Pulmonary mass † A	1/2679 (0.04%)	2/2701 (0.07%)
Pulmonary oedema † A	15/2679 (0.56%)	13/2701 (0.48%)
Pulmonary sarcoidosis † A	1/2679 (0.04%)	0/2701 (0%)
Respiratory arrest † A	0/2679 (0%)	1/2701 (0.04%)
Respiratory distress † A	0/2679 (0%)	1/2701 (0.04%)
Respiratory failure † A	8/2679 (0.3%)	8/2701 (0.3%)
Thoracic haemorrhage † A	1/2679 (0.04%)	0/2701 (0%)
Tracheal stenosis † A	0/2679 (0%)	1/2701 (0.04%)
Vocal cord polyp † A	0/2679 (0%)	1/2701 (0.04%)
Skin and subcutaneous tissue disorders		
Angioedema † A	1/2679 (0.04%)	1/2701 (0.04%)
Cutaneous lupus erythematosus † A	1/2679 (0.04%)	0/2701 (0%)
Decubitus ulcer † A	0/2679 (0%)	1/2701 (0.04%)
Dermatitis contact † A	1/2679 (0.04%)	0/2701 (0%)
Diabetic foot † A	4/2679 (0.15%)	7/2701 (0.26%)
Drug eruption † A	0/2679 (0%)	1/2701 (0.04%)
Dry gangrene † A	0/2679 (0%)	1/2701 (0.04%)
Erythema † A	1/2679 (0.04%)	0/2701 (0%)
Erythema nodosum † A	1/2679 (0.04%)	0/2701 (0%)
Pruritus † A	1/2679 (0.04%)	0/2701 (0%)
Rash † A	0/2679 (0%)	1/2701 (0.04%)
Skin necrosis † A	0/2679 (0%)	2/2701 (0.07%)
Skin ulcer † A	0/2679 (0%)	4/2701 (0.15%)
Surgical and medical procedures		
Hospitalisation † A	1/2679 (0.04%)	0/2701 (0%)
Implantable defibrillator insertion † A	1/2679 (0.04%)	0/2701 (0%)
Vascular disorders		
Accelerated hypertension † A	1/2679 (0.04%)	0/2701 (0%)
Angiodysplasia † A	1/2679 (0.04%)	0/2701 (0%)
Angiopathy † A	0/2679 (0%)	1/2701 (0.04%)
Aortic aneurysm † A	1/2679 (0.04%)	0/2701 (0%)
Aortic occlusion † A	1/2679 (0.04%)	0/2701 (0%)
Aortic stenosis † A	1/2679 (0.04%)	3/2701 (0.11%)
Aortic thrombosis † A	0/2679 (0%)	1/2701 (0.04%)
Arterial insufficiency † A	0/2679 (0%)	1/2701 (0.04%)
Arterial occlusive disease † A	2/2679 (0.07%)	0/2701 (0%)

† A

Arterial stenosis	1/2679 (0.04%)	0/2701 (0%)
Arteriosclerosis † A	1/2679 (0.04%)	0/2701 (0%)
Arteriovenous fistula † A	1/2679 (0.04%)	0/2701 (0%)
Circulatory collapse † A	2/2679 (0.07%)	0/2701 (0%)
Deep vein thrombosis † A	2/2679 (0.07%)	3/2701 (0.11%)
Femoral artery embolism † A	1/2679 (0.04%)	0/2701 (0%)
Femoral artery occlusion † A	1/2679 (0.04%)	1/2701 (0.04%)
Haematoma † A	1/2679 (0.04%)	0/2701 (0%)
Hypertension † A	16/2679 (0.6%)	8/2701 (0.3%)
Hypertensive crisis † A	10/2679 (0.37%)	5/2701 (0.19%)
Hypertensive emergency † A	2/2679 (0.07%)	3/2701 (0.11%)
Hypotension † A	7/2679 (0.26%)	6/2701 (0.22%)
Hypovolaemic shock † A	3/2679 (0.11%)	0/2701 (0%)
Iliac artery occlusion † A	1/2679 (0.04%)	1/2701 (0.04%)
Intermittent claudication † A	0/2679 (0%)	3/2701 (0.11%)
Malignant hypertension † A	2/2679 (0.07%)	2/2701 (0.07%)
Orthostatic hypotension † A	0/2679 (0%)	3/2701 (0.11%)
Peripheral arterial occlusive disease † A	9/2679 (0.34%)	9/2701 (0.33%)
Peripheral artery aneurysm † A	0/2679 (0%)	1/2701 (0.04%)
Peripheral artery stenosis † A	1/2679 (0.04%)	6/2701 (0.22%)
Peripheral artery thrombosis † A	0/2679 (0%)	1/2701 (0.04%)
Peripheral embolism † A	1/2679 (0.04%)	0/2701 (0%)
Peripheral ischaemia † A	2/2679 (0.07%)	2/2701 (0.07%)
Peripheral vascular disorder † A	4/2679 (0.15%)	3/2701 (0.11%)
Shock haemorrhagic † A	0/2679 (0%)	1/2701 (0.04%)
Subclavian artery stenosis † A	0/2679 (0%)	1/2701 (0.04%)
Thrombosis † A	0/2679 (0%)	1/2701 (0.04%)
Venous insufficiency † A	0/2679 (0%)	1/2701 (0.04%)
Venous occlusion † A	0/2679 (0%)	1/2701 (0.04%)

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA Version 16.0

Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events 2%

	Placebo Affected / at Risk (%)	Alogliptin Affected / at Risk (%)
Total	1493/2679 (55.73%)	1523/2701 (56.39%)
Blood and lymphatic system disorders		
Anaemia † A	96/2679 (3.58%)	130/2701 (4.81%)
Cardiac disorders		
Angina pectoris † A	133/2679 (4.96%)	122/2701 (4.52%)
Gastrointestinal disorders		
Constipation † A	66/2679 (2.46%)	70/2701 (2.59%)
Diarrhoea † A	99/2679 (3.7%)	122/2701 (4.52%)
Nausea † A	53/2679 (1.98%)	56/2701 (2.07%)

General disorders		
Oedema peripheral † A	104/2679 (3.88%)	101/2701 (3.74%)
Infections and infestations		
Bronchitis † A	68/2679 (2.54%)	81/2701 (3%)
Influenza † A	54/2679 (2.02%)	64/2701 (2.37%)
Nasopharyngitis † A	120/2679 (4.48%)	112/2701 (4.15%)
Upper respiratory tract infection † A	85/2679 (3.17%)	79/2701 (2.92%)
Urinary tract infection † A	94/2679 (3.51%)	102/2701 (3.78%)
Investigations		
Blood creatine phosphokinase increased † A	116/2679 (4.33%)	140/2701 (5.18%)
Blood creatinine increased † A	72/2679 (2.69%)	91/2701 (3.37%)
Creatinine renal clearance decreased † A	47/2679 (1.75%)	59/2701 (2.18%)
Glomerular filtration rate decreased † A	116/2679 (4.33%)	132/2701 (4.89%)
Lipase increased † A	83/2679 (3.1%)	81/2701 (3%)
Metabolism and nutrition disorders		
Diabetes mellitus † A	70/2679 (2.61%)	52/2701 (1.93%)
Dyslipidaemia † A	49/2679 (1.83%)	56/2701 (2.07%)
Hyperglycaemia † A	99/2679 (3.7%)	94/2701 (3.48%)
Hyperkalaemia † A	70/2679 (2.61%)	81/2701 (3%)
Hypertriglyceridaemia † A	71/2679 (2.65%)	55/2701 (2.04%)
Hypoglycaemia † A	159/2679 (5.94%)	167/2701 (6.18%)
Musculoskeletal and connective tissue disorders		
Arthralgia † A	64/2679 (2.39%)	68/2701 (2.52%)
Back pain † A	84/2679 (3.14%)	79/2701 (2.92%)
Pain in extremity † A	60/2679 (2.24%)	54/2701 (2%)
Nervous system disorders		
Dizziness † A	68/2679 (2.54%)	81/2701 (3%)
Headache † A	72/2679 (2.69%)	69/2701 (2.55%)
Renal and urinary disorders		
Diabetic nephropathy † A	68/2679 (2.54%)	62/2701 (2.3%)
Proteinuria † A	107/2679 (3.99%)	103/2701 (3.81%)
Renal impairment † A	174/2679 (6.49%)	203/2701 (7.52%)
Respiratory, thoracic and mediastinal disorders		
Cough † A	99/2679 (3.7%)	98/2701 (3.63%)
Dyspnoea † A	74/2679 (2.76%)	70/2701 (2.59%)
Vascular disorders		
Hypertension † A	198/2679 (7.39%)	193/2701 (7.15%)

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA Version 16.0

Limitations and Caveats

[Not Specified]

 More Information

Certain Agreements

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The first study related publication will be a multi-center publication submitted within 24 months after conclusion or termination of a study at all sites. After such multi site publication, all proposed site publications and presentations will be submitted to sponsor for review 60 days in advance of publication. Site will remove Sponsor confidential information unrelated to study results. Sponsor can delay a proposed publication for another 60 days to preserve intellectual property.

Results Point of Contact

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