Home > Record Summary > Results Section

ID: SYR-322-OLE-012 | Long-term Safety of Alogliptin in Patients With Type 2 Diabetes Mellitus | NCT00306384

Results Preview

Close

Hide All

Participant Flow

Recruitment Details	Patients who completed 1 of the following 7 studies took part in the study at 423 investigative sites worldwide: SYR-322-PLC-010 (NCT00286455); SYR-322-SULF-007 (NCT00286468); SYR-322-MET-008 (NCT00286442); SYR-322-TZD-009 (NCT00286494); SYR-322-INS-011 (NCT00286429); 01-05-TL-322OPI-001 (NCT00328627); 01-06-TL-322OPI-002 (NCT00395512).
Pre-Assignment Details	Patients who had previously completed 1 of 7 double-blind alogliptin studies were randomized (1:1) to either 12.5 or 25 mg once daily alogliptin. Patients who were rescued during their previous double-blind study in response to protocol-defined hyperglycemic rescue criteria were assigned to alogliptin 25 mg.

Arm/Group Title	**Alogliptin 12.5 mg**	**Alogliptin 25 mg**	**Rescued: Alogliptin 25 mg**	Total (Not public)
Arm/Group Description	Participants who completed the previous double-blind study received alogliptin 12.5 tablet, orally, once daily for up to 4 years.	Participants who completed the previous double-blind study received alogliptin 25 mg tablets orally, once daily for up to 4 years.	Participants rescued from the previous double-blind study received alogliptin 25 mg tablets, orally once daily for up to 4 years.	
Period Title: Overall Study				
Started	1396	1399	528	3323
Safety Set	1395 [1]	1398 [2]	527 [3]	3320
Completed	854	891	251	1996
Not Completed	542	508	277	1327
Reason Not Completed				
Adverse Event	103	87	40	230
Major protocol deviation	43	51	18	112
Lost to Follow-up	57	41	35	133
Voluntary withdrawal	199	187	91	477
Study termination	1	0	1	2
Pregnancy	3	1	1	5
Lack of Efficacy	26	40	38	104
Investigator discretion	28	31	21	80
Other	80	70	32	182
NOTE : "Other" is not sufficiently descriptive for "Other" Reason Not Completed. Please provide a more descriptive label.				
Site closure (Not Public)	2	0	0	2
	Not Completed = 542 Total from all reasons = 542	Not Completed = 508 Total from all reasons = 508	Not Completed = 277 Total from all reasons = 277	

[1] Patients who received at least one dose of study drug
[2] Patients who received at least one dose of study drug
[3] Patients who received at least one dose of study drug

Baseline Characteristics

Arm/Group Title	**Alogliptin 12.5 mg**	**Alogliptin 25 mg**	**Rescued: Alogliptin 25 mg**	**Total**
Arm/Group Description	Participants who completed the previous double-blind study received alogliptin 12.5 tablet, orally, once daily for	Participants who completed the previous double-blind study received alogliptin 25 mg tablets orally, once daily	Participants rescued from the previous double-blind study received alogliptin 25 mg tablets, orally once daily for	

	up to 4 years.	for up to 4 years.	up to 4 years.	
Overall Number of Baseline Participants	1396	1399	528	**3323**
Baseline Analysis Population Description	[Not specified]			
Age, Continuous				
Mean (Standard Deviation)				
Units: years	55.8 (9.92)	55.1 (10.21)	53.0 (10.06)	55.0 (10.11)
Age, Customized				
Measure Type: Number				
Units: participants				
<65 years	1134	1134	461	2729
≥65 years	262	265	67	594
Gender, Male/Female				
Measure Type: Number				
Units: participants				
Female	699	730	289	1718
Male	697	669	239	1605
Race/Ethnicity, Customized				
Measure Type: Number				
Units: participants				
American Indian or Alaska Native	8	3	2	13
Asian	120	108	32	260
Native Hawaiian or Other Pacific Islander	2	0	1	3
Black or African American	65	88	34	187
White	1025	1007	390	2422
Other	176	193	69	438
Body Mass Index (BMI)				
Mean (Standard Deviation)				
Units: kg/m^2	31.42 (5.370)	31.71 (5.266)	32.20 (5.704)	31.66 (5.386)
Diabetes duration				
Mean (Standard Deviation)				
Units: years	6.56 (5.446)	6.92 (5.824)	8.35 (6.325)	6.99 (5.784)
Previous double-blind study treatment [1]				
Measure Type: Number				
Units: participants				
Placebo	118	110	135	363
Alogliptin 12.5 mg	274	262	105	641
Alogliptin 25 mg	243	262	99	604
Study 01-05-TL-322OPI-001	546	548	146	1240
Study 01-06-TL-322OPI-002	215	217	43	475

[1] Patients from coadministration Studies 01-05-TL-322OPI-001 and 01-06-TL-322OPI-002 are presented separately; due to the complexity of treatment assignments, they were not included in the subgroups of patients previously randomized to placebo, alogliptin 12.5 mg, or alogliptin 25 mg.

Outcome Measures

1. Primary Outcome

Title: Percentage of Participants With Treatment-emergent Adverse Events (TEAEs)

Description: Safety was assessed by physical examinations, clinical laboratory parameters, electrocardiogram (ECG) readings, vital sign measurements, oral temperature, and hypoglycemic events. Changes in laboratory values or ECG parameters were considered to be adverse events if they were judged to be clinically significant. A TEAE was any event that started on or after the first dose of open-label study drug and within 14 days after the last dose.

Time Frame: 4 years

Safety Issue? Yes

Outcome Measure Data

Analysis Population Description

Safety set

Arm/Group Title	Alogliptin 12.5 mg	Alogliptin 25 mg	Rescued: Alogliptin 25 mg
Arm/Group Description:	Participants who completed the previous double-blind study received alogliptin 12.5 tablet, orally, once daily for up to 4 years.	Participants who completed the previous double-blind study received alogliptin 25 mg tablets orally, once daily for up to 4 years.	Participants rescued from the previous double-blind study received alogliptin 25 mg tablets, orally once daily for up to 4 years.
Number of Participants Analyzed	1394	1399	527
Measure Type: Number Units: percentage of participants			
Any treatment emergent adverse event (TEAE)	87.2	87.1	84.6
Study drug-related TEAE	25.6	22.7	24.9
TEAE leading to discontinuation	7.0	6.1	7.6
Treatment emergent serious AE	16.7	16.3	15.7
Study drug-related serious AE	2.6	2.1	1.9
Treatment-emergent deaths	1.4	1.0	0.9

2. Secondary Outcome

Title: Change From Baseline Over Time in Glycosylated Hemoglobin

Description: The change from Baseline in glycosylated hemoglobin (HbA1c; the concentration of glucose bound to hemoglobin as a percent of the absolute maximum that can be bound) during the study. Endpoint was defined as the last postbaseline observation collected within 7 days after the last dose of open-label study drug.

Time Frame: Baseline and Month 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42 and 45.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Safety set where data were available.

Arm/Group Title	Alogliptin 12.5 mg	Alogliptin 25 mg	Rescued: Alogliptin 25 mg
Arm/Group Description:	Participants who completed the previous double-blind study received alogliptin 12.5 tablet, orally, once daily for up to 4 years.	Participants who completed the previous double-blind study received alogliptin 25 mg tablets orally, once daily for up to 4 years.	Participants rescued from the previous double-blind study received alogliptin 25 mg tablets, orally once daily for up to 4 years.
Number of Participants Analyzed	1395	1398	527
Mean (Standard Deviation) Units: percent glycosylated hemoglobin			

Baseline (n=1362, 1359, 501)	7.21 (0.815)	7.22 (0.814)	9.30 (0.900)
Week 12 change from Baseline (n=1290, 1286, 463)	0.18 (0.635)	0.14 (0.632)	-0.52 (1.064)
Month 6 change from Baseline (n= 1236, 1252, 433)	0.31 (0.859)	0.26 (0.848)	-0.73 (1.285)
Month 9 change from Baseline (n=1217, 1231, 413)	0.34 (0.969)	0.33 (0.894)	-0.78 (1.282)
Month 12 change from Baseline (1175, 1182, 388)	0.41 (1.010)	0.41 (0.952)	-0.78 (1.309)
Month 15 change from Baseline (n=1119, 1133, 374)	0.47 (0.990)	0.48 (1.068)	-0.75 (1.332)
Month 18 change from Baseline (n=1111, 1095, 350)	0.50 (1.082)	0.50 (1.047)	-0.70 (1.320)
Month 21 change from Baseline (n=1061, 1071, 338)	0.52 (1.096)	0.51 (1.070)	-0.75 (1.389)
Month 24 change from Baseline (n=1027, 1039, 320)	0.53 (1.111)	0.58 (1.107)	-0.69 (1.417)
Month 27 change from Baseline (n=991, 1002, 300)	0.58 (1.124)	0.58 (1.159)	-0.71 (1.349)
Month 30 change from Baseline (n=944, 955, 281)	0.57 (1.127)	0.57 (1.167)	-0.78 (1.361)
Month 33 change from Baseline (n=923, 941, 276)	0.55 (1.181)	0.57 (1.196)	-0.73 (1.418)
Month 36 change from Baseline (n=882, 931, 274)	0.54 (1.215)	0.55 (1.141)	-0.80 (1.411)
Month 39 change from Baseline (n=886, 913, 259)	0.56 (1.223)	0.56 (1.216)	-0.73 (1.431)
Month 42 change from Baseline (n=854, 891, 252)	0.59 (1.225)	0.54 (1.221)	-0.78 (1.492)
Month 45 change from Baseline (n=866, 902, 253)	0.61 (1.250)	0.56 (1.242)	-0.70 (1.398)
Endpoint change from Baseline (n=1362, 1359, 501)	1.63 (1.310)	0.61 (1.261)	-0.42 (1.448)

3. Secondary Outcome

Title: Change From Baseline in Fasting Plasma Glucose

Description: The change from Baseline in fasting plasma glucose (FPG) at the last post-baseline observation, collected within 7 days after the last dose of open-label study drug.

Time Frame: Baseline and Year 4

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Safety set where data were available.

Arm/Group Title	**Alogliptin 12.5 mg**	**Alogliptin 25 mg**	**Rescued: Alogliptin 25 mg**
Arm/Group Description:	Participants who completed the	Participants who completed the	Participants rescued from the

	previous double-blind study received alogliptin 12.5 tablet, orally, once daily for up to 4 years.	previous double-blind study received alogliptin 25 mg tablets orally, once daily for up to 4 years.	previous double-blind study received alogliptin 25 mg tablets, orally once daily for up to 4 years.
Number of Participants Analyzed	1388	1386	517
Mean (Standard Deviation) Units: mg/dL			
Baseline	144.4 (41.64)	142.6 (39.41)	215.3 (60.25)
Change from Baseline	14.8 (56.25)	14.9 (53.46)	-26.4 (84.51)

4. Secondary Outcome

Title: Percentage of Participants With Marked Hyperglycemia

Description: Marked Hyperglycemia is defined as fasting plasma glucose greater than or equal to 200 mg/dL (≥11.10 mmol/L).
The Month 42 to Month 45 interval includes all marked hyperglycemic episodes occurring on or after Day 1247 (a 203-day visit window).

Time Frame: Randomization up to 4 years.

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Safety set where data were available.

Arm/Group Title	**Alogliptin 12.5 mg**	**Alogliptin 25 mg**	**Rescued: Alogliptin 25 mg**
Arm/Group Description:	Participants who completed the previous double-blind study received alogliptin 12.5 tablet, orally, once daily for up to 4 years.	Participants who completed the previous double-blind study received alogliptin 25 mg tablets orally, once daily for up to 4 years.	Participants rescued from the previous double-blind study received alogliptin 25 mg tablets, orally once daily for up to 4 years.
Number of Participants Analyzed	1395	1398	527
Measure Type: Number Units: percentage of participants			
Day 1 to <Week 2 (n=1299, 1290, 481)	9.1	8.0	55.5
Week 2 to <Week 4 (n=1286, 1306, 481)	11.5	10.2	45.9
Week 4 to <Week 8 (n=1303, 1331, 490)	9.2	11.0	46.1
Week 8 to <Week 12 (n=1331, 1347, 495)	11.5	10.8	41.0
Week 12 to <Month 6 (n=1329, 1338, 480)	12.0	11.6	39.4
Month 6 to <Month 9 (n=1286, 1289, 448)	12.8	10.7	36.8

Month 9 to <Month 12 (n=1252, 1260, 425)	11.4	12.9	32.5
Month 12 to <Month 15 (n=1210, 1217, 409)	13.1	13.0	29.3
Month 15 to <Month 18 (n=1157, 1166, 389)	12.7	13.8	27.8
Month 18 to <Month 21 (n=1128, 1128, 365)	11.7	11.6	26.8
Month 21 to <Month 24 (n=1094,1099, 357)	11.2	11.5	26.3
Month 24 to <Month 27 (n=1046, 1066, 334)	11.6	12.3	24.9
Month 27 to <Month 30 (n=1010, 1028, 316)	12.6	11.8	24.7
Month 30 to <Month 33 (n=981, 988, 299)	11.6	11.7	19.7
Month 33 to <Month 36 (n=945, 959, 289)	11.5	12.3	23.5
Month 36 to <Month 39 (n=920, 949, 281)	13.2	12.5	21.0
Month 39 to <Month 42 (n=899, 934, 267)	13.7	13.1	19.5
Month 42 to Month 45 (n=889, 921, 261)	25.5	23.9	39.1
Overall (n= 1389, 1392, 518)	49.7	50.7	87.6

5. Secondary Outcome

Title: Change From Baseline in Proinsulin Level

Description: Proinsulin is a precursor to insulin, and was measured as an indicator of pancreatic function. The change from Baseline in fasting proinsulin to the last post-baseline observation, collected within 7 days after the last dose of open-label study drug.
Note: A transcription error occurred in the reporting of 1 proinsulin value for a patient in the alogliptin 25 mg completed group, for whom a partial patient ID number was mistakenly entered as an end-of-treatment proinsulin level.

Time Frame: Baseline and Year 4

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Safety set where data were available.

Arm/Group Title	**Alogliptin 12.5 mg**	**Alogliptin 25 mg**	**Rescued: Alogliptin 25 mg**
Arm/Group Description:	Participants who completed the previous double-blind study received alogliptin 12.5 tablet, orally, once daily for up to 4 years.	Participants who completed the previous double-blind study received alogliptin 25 mg tablets orally, once daily for up to 4 years.	Participants rescued from the previous double-blind study received alogliptin 25 mg tablets, orally once daily for up to 4 years.
Number of Participants Analyzed	1277	1263	393
Mean (Standard Deviation) Units: pmol/L			
Baseline	26.1 (25.99)	25.4 (30.28)	40.2 (36.47)
Change from Baseline	4.1 (27.09)	39.7 (1243.37)	-3.3 (31.45)

6. Secondary Outcome

Title: Change From Baseline in Insulin Level

Description: The change from Baseline in fasting insulin at the last post-baseline observation, collected within 7 days after the last dose of open-label study drug.

Time Frame: Baseline and Year 4

Safety Issue? No

Outcome Measure Data

Analysis Population Description
Safety set where data was available. Does not include patients enrolled in Protocol 01-05-TL-OPI322-001 or Protocol 01-06-TL-OPI322-002.

Arm/Group Title	**Alogliptin 12.5 mg**	**Alogliptin 25 mg**	**Rescued: Alogliptin 25 mg**
Arm/Group Description:	Participants who completed the previous double-blind study received alogliptin 12.5 tablet, orally, once daily for up to 4 years.	Participants who completed the previous double-blind study received alogliptin 25 mg tablets orally, once daily for up to 4 years.	Participants rescued from the previous double-blind study received alogliptin 25 mg tablets, orally once daily for up to 4 years.
Number of Participants Analyzed	537	526	212
Mean (Standard Deviation) Units: µIU/mL			
Baseline	15.19 (9.898)	15.50 (12.608)	18.64 (15.845)
Change from Baseline	2.45 (42.706)	2.13 (16.496)	5.62 (23.197)

7. Secondary Outcome

Title: Change From Baseline in C-peptide Level

Description: C-peptide is a byproduct created when the hormone insulin is produced and is measured by a blood test. Change from Baseline to the last post-baseline observation, collected within 7 days after the last dose of open-label study drug.

Time Frame: Baseline and Year 4
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Safety set where data was available. Patients enrolled in Protocol 01-05-TL-OPI322-001 or Protocol 01-06-TL-OPI322-002 are not included.

Arm/Group Title	**Alogliptin 12.5 mg**	**Alogliptin 25 mg**	**Rescued: Alogliptin 25 mg**
Arm/Group Description:	Participants who completed the previous double-blind study received alogliptin 12.5 tablet, orally, once daily for up to 4 years.	Participants who completed the previous double-blind study received alogliptin 25 mg tablets orally, once daily for up to 4 years.	Participants rescued from the previous double-blind study received alogliptin 25 mg tablets, orally once daily for up to 4 years.
Number of Participants Analyzed	615	615	322
Mean (Standard Deviation) Units: ng/mL			
Baseline	3.406 (1.5115)	3.323 (1.5945)	3.572 (1.7531)
Change from Baseline	-0.471 (1.6464)	-0.439 (1.2783)	-0.641 (1.5804)

8. Secondary Outcome

Title: Change From Baseline in Body Weight
Description: Change from Baseline in body weight to the last post-baseline observation collected within 7 days after the last dose of open-label study drug.
Time Frame: Baseline and Year 4
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Safety set for whom data was available.

Arm/Group Title	**Alogliptin 12.5 mg**	**Alogliptin 25 mg**	**Rescued: Alogliptin 25 mg**
Arm/Group Description:	Participants who completed the previous double-blind study received alogliptin 12.5 tablet, orally, once daily for up to 4 years.	Participants who completed the previous double-blind study received alogliptin 25 mg tablets orally, once daily for up to 4 years.	Participants rescued from the previous double-blind study received alogliptin 25 mg tablets, orally once daily for up to 4 years.
Number of Participants Analyzed	1387	1385	518
Mean (Standard Deviation) Units: kg			
Baseline	86.12 (19.376)	86.61 (19.185)	88.62 (20.947)
Change from Baseline	-0.64 (5.283)	-0.61 (5.428)	0.25 (5.036)

9. Secondary Outcome

Title: Percentage of Participants With a Clinical Response
Description: Clinical response was defined based on the absolute value of HbA1c meeting one of two clinical targets at any post-baseline visit:

- HbA1c ≤6.5%;
- HbA1c ≤7.0%.

Time Frame: Weeks 2, 4, 8, 12, every 3 months up to 4 years, and 1 Day after final dose.
Safety Issue? No

Outcome Measure Data

Analysis Population Description
Safety set.

Arm/Group Title	**Alogliptin 12.5 mg**	**Alogliptin 25 mg**	**Rescued: Alogliptin 25 mg**
Arm/Group Description:	Participants who completed the previous double-blind study received alogliptin 12.5 tablet, orally, once daily for up to 4 years.	Participants who completed the previous double-blind study received alogliptin 25 mg tablets orally, once daily for up to 4 years.	Participants rescued from the previous double-blind study received alogliptin 25 mg tablets, orally once daily for up to 4 years.
Number of Participants Analyzed	1395	1398	527
Measure Type: Number Units: percentage of participants			
HbA1c ≤6.5%	34.8	34.1	11.0
HbA1c ≤7.0%	64.1	65.5	27.1

Adverse Events

Time Frame	Treatment-emergent adverse events (AEs) were defined as any AEs that started on or after the date of the first dose of open-label study drug and within 14 days after the date of the last dose of open-label study drug.
Additional Description	At each study visit, the investigator assessed whether any events had occurred. Participants could report events at any other time during the study.
Source Vocabulary Name	MedDRA (12.0)
Assessment Type	Systematic Assessment

Arm/Group Title	Alogliptin 12.5 mg	Alogliptin 25 mg	Rescued: Alogliptin 25 mg
Arm/Group Description	Participants who completed the previous double-blind study received alogliptin 12.5 tablet, orally, once daily for up to 4 years.	Participants who completed the previous double-blind study received alogliptin 25 mg tablets orally, once daily for up to 4 years.	Participants rescued from the previous double-blind study received alogliptin 25 mg tablets, orally once daily for up to 4 years.

Serious Adverse Events

	Alogliptin 12.5 mg Affected / at Risk (%)	**Alogliptin 25 mg** Affected / at Risk (%)	**Rescued: Alogliptin 25 mg** Affected / at Risk (%)
Total	233/1394 (16.71%)	228/1399 (16.3%)	83/527 (15.75%)
Blood and lymphatic system disorders			
Anaemia † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Iron deficiency anaemia † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Cardiac disorders			
Acute coronary syndrome † A	2/1394 (0.14%)	1/1399 (0.07%)	2/527 (0.38%)
Acute myocardial infarction † A	7/1394 (0.5%)	11/1399 (0.79%)	4/527 (0.76%)
Angina pectoris † A	5/1394 (0.36%)	5/1399 (0.36%)	2/527 (0.38%)
† A			

Angina unstable	6/1394 (0.43%)	3/1399 (0.21%)	2/527 (0.38%)
Aortic valve stenosis † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Arteriosclerosis coronary artery † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Atrial fibrillation † A	1/1394 (0.07%)	4/1399 (0.29%)	1/527 (0.19%)
Atrioventricular block complete † A	2/1394 (0.14%)	0/1399 (0%)	0/527 (0%)
Atrioventricular block second degree † A	2/1394 (0.14%)	0/1399 (0%)	0/527 (0%)
Bradycardia † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Cardiac failure † A	1/1394 (0.07%)	2/1399 (0.14%)	0/527 (0%)
Cardiac failure congestive † A	0/1394 (0%)	2/1399 (0.14%)	2/527 (0.38%)
Cardio-respiratory arrest † A	1/1394 (0.07%)	2/1399 (0.14%)	0/527 (0%)
Cardiomyopathy † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Cardiopulmonary failure † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Congestive cardiomyopathy † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Coronary artery disease † A	5/1394 (0.36%)	7/1399 (0.5%)	5/527 (0.95%)
Coronary artery insufficiency † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Coronary artery stenosis † A	0/1394 (0%)	1/1399 (0.07%)	1/527 (0.19%)
Hypertensive heart disease † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Ischaemic cardiomyopathy † A	1/1394 (0.07%)	2/1399 (0.14%)	1/527 (0.19%)
Left ventricular dysfunction † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Myocardial infarction † A	5/1394 (0.36%)	6/1399 (0.43%)	4/527 (0.76%)
Myocardial ischaemia † A	7/1394 (0.5%)	3/1399 (0.21%)	0/527 (0%)
Palpitations † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Pericardial effusion † A	2/1394 (0.14%)	0/1399 (0%)	0/527 (0%)
Pericarditis † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Sick sinus syndrome † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Tachycardia † A	0/1394 (0%)	1/1399 (0.07%)	1/527 (0.19%)
Ventricular extrasystoles † A	1/1394 (0.07%)	0/1399 (0%)	1/527 (0.19%)
Congenital, familial and genetic disorders			
MELAS syndrome † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Endocrine disorders			
Goitre † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Hyperthyroidism † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Eye disorders			
Cataract † A	2/1394 (0.14%)	1/1399 (0.07%)	0/527 (0%)
Diabetic retinopathy † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Glaucoma † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Iridocyclitis † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Retinal artery occlusion † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Retinal detachment † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Retinal vein thrombosis † A	0/1394 (0%)	2/1399 (0.14%)	0/527 (0%)
Vitreous haemorrhage † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Gastrointestinal disorders			
Abdominal hernia † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Abdominal pain † A	2/1394 (0.14%)	1/1399 (0.07%)	0/527 (0%)
Abdominal pain upper † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Anal fistula † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Colitis ischaemic † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Diarrhoea † A	2/1394 (0.14%)	1/1399 (0.07%)	0/527 (0%)
Diverticulum intestinal haemorrhagic † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Duodenal ulcer † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Duodenal ulcer haemorrhage † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Dyspepsia † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Gastric ulcer † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)
Gastric ulcer haemorrhage † A	1/1394 (0.07%)	2/1399 (0.14%)	0/527 (0%)
Gastritis † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)
Gastrointestinal haemorrhage † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)
Gastrointestinal hypomotility † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Gastrointestinal necrosis † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)

Haematemesis † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Haemorrhoids † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Hernial eventration † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Inguinal hernia † A	3/1394 (0.22%)	0/1399 (0%)	1/527 (0.19%)
Intestinal obstruction † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Intra-abdominal haemorrhage † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Pancreatitis † A	1/1394 (0.07%)	4/1399 (0.29%)	1/527 (0.19%)
Pancreatitis acute † A	3/1394 (0.22%)	0/1399 (0%)	0/527 (0%)
Pancreatitis relapsing † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Peptic ulcer † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Peritonitis † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Rectal polyp † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Rectal prolapse † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Salivary duct inflammation † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Small intestinal obstruction † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Umbilical hernia † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)
General disorders			
Chest pain † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)
Death † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Influenza like illness † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Non-cardiac chest pain † A	4/1394 (0.29%)	4/1399 (0.29%)	2/527 (0.38%)
Pyrexia † A	0/1394 (0%)	0/1399 (0%)	2/527 (0.38%)
Hepatobiliary disorders			
Bile duct stone † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Biliary colic † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Cholangitis † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Cholecystitis † A	1/1394 (0.07%)	2/1399 (0.14%)	0/527 (0%)
Cholecystitis acute † A	4/1394 (0.29%)	2/1399 (0.14%)	1/527 (0.19%)
Cholelithiasis † A	3/1394 (0.22%)	4/1399 (0.29%)	2/527 (0.38%)
Hepatitis † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Perforation bile duct † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Immune system disorders			
Allergic oedema † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Allergy to arthropod sting † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Infections and infestations			
Abscess limb † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)
Acquired immunodeficiency syndrome † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Appendicitis † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)
Appendicitis perforated † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Arthritis bacterial † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Bronchitis † A	0/1394 (0%)	2/1399 (0.14%)	0/527 (0%)
Bronchopneumonia † A	0/1394 (0%)	2/1399 (0.14%)	0/527 (0%)
Cellulitis † A	4/1394 (0.29%)	3/1399 (0.21%)	4/527 (0.76%)
Cholecystitis infective † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Coccidioidomycosis † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Dengue fever † A	2/1394 (0.14%)	0/1399 (0%)	0/527 (0%)
Diabetic foot infection † A	1/1394 (0.07%)	0/1399 (0%)	1/527 (0.19%)
Diverticulitis † A	2/1394 (0.14%)	2/1399 (0.14%)	0/527 (0%)
Endophthalmitis † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Erysipelas † A	2/1394 (0.14%)	3/1399 (0.21%)	0/527 (0%)
Gangrene † A	2/1394 (0.14%)	1/1399 (0.07%)	0/527 (0%)
Gastroenteritis † A	1/1394 (0.07%)	2/1399 (0.14%)	1/527 (0.19%)
Gastroenteritis viral † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Giardiasis † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Helicobacter gastritis † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Hepatitis A † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Herpes zoster † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Infected skin ulcer † A	1/1394 (0.07%)	0/1399 (0%)	1/527 (0.19%)
Labyrinthitis † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Lobar pneumonia † A	0/1394 (0%)	0/1399 (0%)	2/527 (0.38%)

Lower respiratory tract infection † A	0/1394 (0%)	1/1399 (0.07%)	1/527 (0.19%)
Lymphangitis † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Nosocomial infection † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Osteomyelitis † A	3/1394 (0.22%)	1/1399 (0.07%)	1/527 (0.19%)
Peritonsillar abscess † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Pneumococcal sepsis † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Pneumonia † A	13/1394 (0.93%)	6/1399 (0.43%)	0/527 (0%)
Pneumonia cryptococcal † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Pneumonia pneumococcal † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Post procedural infection † A	0/1394 (0%)	1/1399 (0.07%)	1/527 (0.19%)
Postoperative wound infection † A	1/1394 (0.07%)	1/1399 (0.07%)	1/527 (0.19%)
Pulmonary tuberculosis † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Pyelonephritis † A	0/1394 (0%)	2/1399 (0.14%)	0/527 (0%)
Pyelonephritis acute † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Pyelonephritis chronic † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Pyoderma † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Rectal abscess † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Septic shock † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Sialoadenitis † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Staphylococcal infection † A	2/1394 (0.14%)	0/1399 (0%)	0/527 (0%)
Subcutaneous abscess † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Tooth abscess † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Typhoid fever † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Urinary tract infection † A	5/1394 (0.36%)	4/1399 (0.29%)	0/527 (0%)
Urosepsis † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Viral infection † A	1/1394 (0.07%)	0/1399 (0%)	1/527 (0.19%)
Wound infection † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Wound sepsis † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Injury, poisoning and procedural complications			
Anaemia postoperative † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Ankle fracture † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)
Chest injury † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Clavicle fracture † A	0/1394 (0%)	2/1399 (0.14%)	0/527 (0%)
Device occlusion † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Fall † A	3/1394 (0.22%)	1/1399 (0.07%)	1/527 (0.19%)
Femoral neck fracture † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Femur fracture † A	0/1394 (0%)	1/1399 (0.07%)	1/527 (0.19%)
Foreign body trauma † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Hand fracture † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Head injury † A	0/1394 (0%)	3/1399 (0.21%)	0/527 (0%)
Hip fracture † A	1/1394 (0.07%)	3/1399 (0.21%)	0/527 (0%)
Humerus fracture † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)
Incisional hernia † A	1/1394 (0.07%)	0/1399 (0%)	1/527 (0.19%)
Incisional hernia, obstructive † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Laceration † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Lower limb fracture † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Lumbar vertebral fracture † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Multiple fractures † A	0/1394 (0%)	2/1399 (0.14%)	0/527 (0%)
Multiple injuries † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Patella fracture † A	0/1394 (0%)	1/1399 (0.07%)	1/527 (0.19%)
Post procedural complication † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Radius fracture † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Rib fracture † A	1/1394 (0.07%)	0/1399 (0%)	1/527 (0.19%)
Road traffic accident † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Subdural haematoma † A	2/1394 (0.14%)	0/1399 (0%)	1/527 (0.19%)
Tendon injury † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)
Tendon rupture † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)
Thermal burn † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Tibia fracture † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)

Traumatic fracture † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Metabolism and nutrition disorders			
Dehydration † A	0/1394 (0%)	1/1399 (0.07%)	1/527 (0.19%)
Diabetic foot † A	1/1394 (0.07%)	3/1399 (0.21%)	0/527 (0%)
Hyperglycaemia † A	1/1394 (0.07%)	3/1399 (0.21%)	3/527 (0.57%)
Hyperkalaemia † A	1/1394 (0.07%)	0/1399 (0%)	1/527 (0.19%)
Hypertriglyceridaemia † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)
Hypoglycaemic seizure † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Hyponatraemia † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)
Obesity † A	2/1394 (0.14%)	0/1399 (0%)	0/527 (0%)
Musculoskeletal and connective tissue disorders			
Arthralgia † A	0/1394 (0%)	2/1399 (0.14%)	0/527 (0%)
Arthritis † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Back pain † A	2/1394 (0.14%)	0/1399 (0%)	0/527 (0%)
Chondromalacia † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Intervertebral disc degeneration † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Intervertebral disc disorder † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Intervertebral disc protrusion † A	3/1394 (0.22%)	3/1399 (0.21%)	0/527 (0%)
Lumbar spinal stenosis † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Muscle disorder † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Muscular weakness † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Musculoskeletal chest pain † A	2/1394 (0.14%)	3/1399 (0.21%)	0/527 (0%)
Myopathy † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Osteoarthritis † A	3/1394 (0.22%)	6/1399 (0.43%)	1/527 (0.19%)
Osteochondrosis † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Rhabdomyolysis † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Rotator cuff syndrome † A	1/1394 (0.07%)	6/1399 (0.43%)	1/527 (0.19%)
Spondylolisthesis † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Synovitis † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Tendon calcification † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Adrenal adenoma † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
B-cell lymphoma † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Basal cell carcinoma † A	2/1394 (0.14%)	1/1399 (0.07%)	0/527 (0%)
Benign neoplasm of adrenal gland † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Bladder transitional cell carcinoma † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Brain neoplasm † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)
Brain neoplasm benign † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Breast cancer † A	2/1394 (0.14%)	3/1399 (0.21%)	2/527 (0.38%)
Breast cancer female † A	2/1394 (0.14%)	1/1399 (0.07%)	0/527 (0%)
Breast cancer stage I † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Breast cancer stage III † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Carcinoid tumour of the appendix † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Central nervous system neoplasm † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Cervix carcinoma stage 0 † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Cervix neoplasm † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Choroid melanoma † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Chronic lymphocytic leukaemia † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Colon cancer † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Colon cancer stage III † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Colorectal cancer † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Focal nodular hyperplasia † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Gastrointestinal stromal tumour † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)

Haemangioma of liver † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Hepatic neoplasm malignant † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Langerhans' cell granulomatosis † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Lung adenocarcinoma † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Lung cancer metastatic † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Lung neoplasm † A	0/1394 (0%)	2/1399 (0.14%)	0/527 (0%)
Lung neoplasm malignant † A	2/1394 (0.14%)	0/1399 (0%)	0/527 (0%)
Malignant melanoma in situ † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Mantle cell lymphoma † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Meningioma † A	2/1394 (0.14%)	1/1399 (0.07%)	0/527 (0%)
Mesothelioma † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Metastases to liver † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Metastases to peritoneum † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Multiple myeloma † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Neuroendocrine tumour † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Non-Hodgkin's lymphoma † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Non-small cell lung cancer metastatic † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Oesophageal adenocarcinoma † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Oligodendroglioma † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Ovarian adenoma † A	0/1394 (0%)	2/1399 (0.14%)	0/527 (0%)
Ovarian cancer † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Ovarian germ cell teratoma benign † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Pancreatic carcinoma † A	2/1394 (0.14%)	0/1399 (0%)	0/527 (0%)
Prostate cancer † A	2/1394 (0.14%)	0/1399 (0%)	1/527 (0.19%)
Prostatic adenom † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Rectal cancer † A	1/1394 (0.07%)	2/1399 (0.14%)	0/527 (0%)
Renal cell carcinoma † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Renal neoplasm † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Squamous cell carcinoma † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Thyroid cancer † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)
Thyroid neoplasm † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Transitional cell carcinoma † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Uterine leiomyoma † A	1/1394 (0.07%)	3/1399 (0.21%)	0/527 (0%)
Nervous system disorders			
Altered state of consciousness † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Amnesia † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Brain stem syndrome † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Carotid artery stenosis † A	0/1394 (0%)	3/1399 (0.21%)	0/527 (0%)
Carpal tunnel syndrome † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Cerebral artery occlusion † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Cerebral ischaemia † A	0/1394 (0%)	1/1399 (0.07%)	1/527 (0.19%)
Cerebrovascular accident † A	6/1394 (0.43%)	1/1399 (0.07%)	4/527 (0.76%)
Convulsion † A	2/1394 (0.14%)	1/1399 (0.07%)	0/527 (0%)
Diabetic mononeuropathy † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Diabetic neuropathy † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Dizziness † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)
Dysarthria † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Embolic stroke † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Facial palsy † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Grand mal convulsion † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Haemorrhage intracranial † A	2/1394 (0.14%)	0/1399 (0%)	0/527 (0%)
Haemorrhagic stroke † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Hydrocephalus † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Ischaemic stroke † A	6/1394 (0.43%)	1/1399 (0.07%)	1/527 (0.19%)
Lacunar infarction † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Loss of consciousness † A	3/1394 (0.22%)	0/1399 (0%)	0/527 (0%)
Normal pressure hydrocephalus † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)

Presyncope † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Radial nerve palsy † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Reversible ischaemic neurological deficit † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Subarachnoid haemorrhage † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Syncope † A	4/1394 (0.29%)	1/1399 (0.07%)	0/527 (0%)
Transient ischaemic attack † A	2/1394 (0.14%)	0/1399 (0%)	1/527 (0.19%)
Vascular headache † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous incomplete † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Ectopic pregnancy † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Psychiatric disorders			
Anxiety † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Anxiety disorder † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Hypnagogic hallucination † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Major depression † A	0/1394 (0%)	2/1399 (0.14%)	0/527 (0%)
Mental disorder † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Panic attack † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Suicide attempt † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Renal and urinary disorders			
Calculus ureteric † A	3/1394 (0.22%)	1/1399 (0.07%)	1/527 (0.19%)
Calculus urethral † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Diabetic nephropathy † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Haematuria † A	1/1394 (0.07%)	0/1399 (0%)	1/527 (0.19%)
Nephrolithiasis † A	2/1394 (0.14%)	5/1399 (0.36%)	1/527 (0.19%)
Postrenal failure † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Renal colic † A	2/1394 (0.14%)	1/1399 (0.07%)	0/527 (0%)
Renal failure † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Renal failure acute † A	2/1394 (0.14%)	7/1399 (0.5%)	1/527 (0.19%)
Renal failure chronic † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Stress urinary incontinence † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Tubulointerstitial nephritis † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Urinary retention † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Reproductive system and breast disorders			
Benign prostatic hyperplasia † A	1/1394 (0.07%)	2/1399 (0.14%)	0/527 (0%)
Breast calcifications † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Colpocele † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)
Endometrial hyperplasia † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)
Epididymal cyst † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Erectile dysfunction † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Fallopian tube cyst † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Genital prolapse † A	2/1394 (0.14%)	0/1399 (0%)	0/527 (0%)
Menometrorrhagia † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Menorrhagia † A	0/1394 (0%)	3/1399 (0.21%)	1/527 (0.19%)
Metrorrhagia † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Ovarian cyst † A	1/1394 (0.07%)	3/1399 (0.21%)	0/527 (0%)
Pelvic pain † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Uterine polyp † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Uterine prolapse † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Vocal cord polyp † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema † A	2/1394 (0.14%)	1/1399 (0.07%)	0/527 (0%)
Acute respiratory failure † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Asphyxia † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Asthma † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)
Asthmatic crisis † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Chronic obstructive pulmonary disease † A	2/1394 (0.14%)	2/1399 (0.14%)	0/527 (0%)
Dyspnoea † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)

Epistaxis † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Lung disorder † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Pleural effusion † A	2/1394 (0.14%)	0/1399 (0%)	0/527 (0%)
Pleurisy † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Pneumonia aspiration † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Pulmonary embolism † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Pulmonary hypertension † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Pulmonary oedema † A	1/1394 (0.07%)	1/1399 (0.07%)	0/527 (0%)
Respiratory failure † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Sleep apnoea syndrome † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Skin and subcutaneous tissue disorders			
Angioedema † A	1/1394 (0.07%)	1/1399 (0.07%)	1/527 (0.19%)
Dermatitis allergic † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Drug eruption † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Rash † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Skin necrosis † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Skin ulcer † A	2/1394 (0.14%)	0/1399 (0%)	1/527 (0.19%)
Urticaria † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Surgical and medical procedures			
Knee arthroplasty † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Vascular disorders			
Arteriosclerosis † A	0/1394 (0%)	1/1399 (0.07%)	0/527 (0%)
Deep vein thrombosis † A	2/1394 (0.14%)	1/1399 (0.07%)	0/527 (0%)
Hypertension † A	2/1394 (0.14%)	0/1399 (0%)	0/527 (0%)
Hypertensive crisis † A	1/1394 (0.07%)	0/1399 (0%)	0/527 (0%)
Pelvic venous thrombosis † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)
Peripheral vascular disorder † A	1/1394 (0.07%)	1/1399 (0.07%)	1/527 (0.19%)
Venous thrombosis † A	0/1394 (0%)	0/1399 (0%)	1/527 (0.19%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (12.0)

Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	5%		
	Alogliptin 12.5 mg Affected / at Risk (%)	**Alogliptin 25 mg** Affected / at Risk (%)	**Rescued: Alogliptin 25 mg** Affected / at Risk (%)
Total	876/1394 (62.84%)	898/1399 (64.19%)	333/527 (63.19%)
Gastrointestinal disorders			
Diarrhoea † A	108/1394 (7.75%)	115/1399 (8.22%)	53/527 (10.06%)
General disorders			
Oedema peripheral † A	70/1394 (5.02%)	84/1399 (6%)	30/527 (5.69%)
Infections and infestations			
Bronchitis † A	94/1394 (6.74%)	111/1399 (7.93%)	26/527 (4.93%)
Influenza † A	113/1394 (8.11%)	132/1399 (9.44%)	42/527 (7.97%)
Nasopharyngitis † A	133/1394 (9.54%)	162/1399 (11.58%)	44/527 (8.35%)
Pharyngitis † A	67/1394 (4.81%)	69/1399 (4.93%)	27/527 (5.12%)
Sinusitis † A	70/1394 (5.02%)	64/1399 (4.57%)	23/527 (4.36%)
Upper respiratory tract infection † A	162/1394 (11.62%)	153/1399 (10.94%)	49/527 (9.3%)
Urinary tract infection † A	155/1394 (11.12%)	163/1399 (11.65%)	71/527 (13.47%)
Metabolism and nutrition disorders			
Dyslipidaemia † A	80/1394 (5.74%)	80/1399 (5.72%)	30/527 (5.69%)
Hypertriglyceridaemia † A	54/1394 (3.87%)	62/1399 (4.43%)	28/527 (5.31%)
Musculoskeletal and connective tissue disorders			
Arthralgia † A	118/1394 (8.46%)	108/1399 (7.72%)	37/527 (7.02%)
Back pain † A	102/1394 (7.32%)	111/1399 (7.93%)	46/527 (8.73%)
Pain in extremity † A	67/1394 (4.81%)	80/1399 (5.72%)	32/527 (6.07%)
Nervous system disorders † A			

Headache	90/1394 (6.46%)	105/1399 (7.51%)	40/527 (7.59%)
Respiratory, thoracic and mediastinal disorders			
Cough † A	84/1394 (6.03%)	72/1399 (5.15%)	27/527 (5.12%)
Vascular disorders			
Hypertension † A	207/1394 (14.85%)	203/1399 (14.51%)	85/527 (16.13%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (12.0)

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

Name/Official Title:	Sr. VP, Clinical Science
Organization:	Takeda Global Research and Development Center, Inc.
Phone:	800-778-2860
Email:	clinicaltrialregistry@tpna.com

Close