



Clinical trial results:

A Phase 3b Study to Evaluate the Potential of Alogliptazar to Reduce Cardiovascular Risk in Patients with Stable Cardiovascular Disease and Glucose Abnormalities

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2012-000671-16
Trial protocol	GB SE CZ HU LT AT EE LV IT ES FI PL
Global end of trial date	13 November 2013

Results information

Result version number	v2 (current)
This version publication date	09 June 2016
First version publication date	06 August 2015
Version creation reason	Correction of full data set QC of the full data set after the system downtime

Trial information

Trial identification

Sponsor protocol code	BC28027
-----------------------	---------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01715818
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F.Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, F.Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F.Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 December 2013
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	13 November 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine whether the addition of aleglitazar versus placebo will reduce a composite outcome of cardiovascular (CV) death, non-fatal myocardial infarction (MI) or non-fatal stroke in patients with stable cardiovascular disease (CVD) and glucose abnormalities.

Protection of trial subjects:

This study was conducted in full conformance with the ICH E6 guideline for Good Clinical Practice and the principles of the declaration of Helsinki, or the laws and regulations of the country in which the research was conducted, whichever afforded the greater protection to the individual.

Background therapy:

All participants were to be managed according to the best judgment of their treating physicians as informed by current local clinical practice guidelines and the best clinical evidence for participants with stable CVD, CV risk factors and abnormalities.

Evidence for comparator: -

Actual start date of recruitment	13 December 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 205
Country: Number of subjects enrolled	Spain: 190
Country: Number of subjects enrolled	Sweden: 81
Country: Number of subjects enrolled	United Kingdom: 178
Country: Number of subjects enrolled	Austria: 8
Country: Number of subjects enrolled	Czech Republic: 99
Country: Number of subjects enrolled	Estonia: 4
Country: Number of subjects enrolled	Germany: 92
Country: Number of subjects enrolled	Hungary: 161
Country: Number of subjects enrolled	Italy: 23
Country: Number of subjects enrolled	Lithuania: 15
Country: Number of subjects enrolled	Australia: 29
Country: Number of subjects enrolled	Thailand: 5
Country: Number of subjects enrolled	Malaysia: 23
Country: Number of subjects enrolled	Korea, Republic of: 71
Country: Number of subjects enrolled	Colombia: 9
Country: Number of subjects enrolled	Mexico: 23

Country: Number of subjects enrolled	Romania: 32
Country: Number of subjects enrolled	Canada: 214
Country: Number of subjects enrolled	United States: 537
Worldwide total number of subjects	1999
EEA total number of subjects	1088

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	846
From 65 to 84 years	1148
85 years and over	5

Subject disposition

Recruitment

Recruitment details:

The target population comprised male and female participants with established evidence of stable CVD, and with glucose abnormalities [either established Type 2 Diabetes Mellitus (T2D), or no evidence of T2D with glycosylated hemoglobin A1c (HbA1c) $\geq$ 5.7%] as markers of CV risk.

Pre-assignment

Screening details:

Screening period was up to 4 weeks duration

Period 1

Period 1 title	Double-blind period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Aleglitazar

Arm description:

Participants randomized to this arm received aleglitazar 150 micrograms (μ g) tablet orally once daily

Arm type	Experimental
Investigational medicinal product name	Aleglitazar
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants in this arm received 150 μ g aleglitazar tablet orally once daily, preferably at the same time of the day.

Arm title	Placebo
------------------	---------

Arm description:

Participants randomized to this arm received placebo tablet orally once daily

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received matching placebo orally once daily, preferably at the same time of the day

Number of subjects in period 1	Aleglitazar	Placebo
Started	1000	999
Completed	0	0
Not completed	1000	999
Adverse event, serious fatal	2	3
Consent withdrawn by subject	6	5
Discontinued due to early termination of the study	980	979
Lost to follow-up	12	12

Baseline characteristics

Reporting groups

Reporting group title	Aleglitazar
Reporting group description:	
Participants randomized to this arm received aleglitazar 150 micrograms (µg) tablet orally once daily	
Reporting group title	Placebo
Reporting group description:	
Participants randomized to this arm received placebo tablet orally once daily	

Reporting group values	Aleglitazar	Placebo	Total
Number of subjects	1000	999	1999
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	66.03 ± 8.33	65.97 ± 8.25	-
Gender categorical Units: Subjects			
Female	244	282	526
Male	756	717	1473

End points

End points reporting groups

Reporting group title	Aleglitazar
Reporting group description:	
Participants randomized to this arm received aleglitazar 150 micrograms (µg) tablet orally once daily	
Reporting group title	Placebo
Reporting group description:	
Participants randomized to this arm received placebo tablet orally once daily	

Primary: Time to First Occurrence of Any Component of the Composite Event (CV Death, Non-fatal MI, Non-fatal Stroke) as Adjudicated by the Clinical Events Committee (CEC)

End point title	Time to First Occurrence of Any Component of the Composite Event (CV Death, Non-fatal MI, Non-fatal Stroke) as Adjudicated by the Clinical Events Committee (CEC) ^[1]
End point description:	
End point type	Primary
End point timeframe:	
During double blind period and at follow-up	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Due to premature termination of the study by the Sponsor, CV endpoints were not adjudicated by the CEC and the planned statistical analysis of efficacy endpoints was not performed.

End point values	Aleglitazar	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[2]	0 ^[3]		
Units: months				
arithmetic mean (standard deviation)	()	()		

Notes:

[2] - Planned analysis was not performed due to early termination of study

[3] - Planned analysis was not performed due to early termination of study

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Occurrence of a Composite With Components as Adjudicated by the CEC: CV Death, Non-fatal MI and Non-fatal Stroke [in Each of the Subgroups With or Without Evidence of T2D at Baseline]

End point title	Time to First Occurrence of a Composite With Components as Adjudicated by the CEC: CV Death, Non-fatal MI and Non-fatal Stroke [in Each of the Subgroups With or Without Evidence of T2D at Baseline]
End point description:	
End point type	Secondary

End point timeframe:

During double blind period and at follow-up

End point values	Aleglitazar	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[4]	0 ^[5]		
Units: months				
arithmetic mean (standard deviation)	()	()		

Notes:

[4] - Planned analysis was not performed due to early termination of study

[5] - Planned analysis was not performed due to early termination of study

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Occurrence of a Composite With Components as Adjudicated by the CEC: All-cause Mortality, Non-fatal MI and Non-fatal Stroke (in each of the Subgroups With or Without Evidence of T2D at Baseline)

End point title	Time to First Occurrence of a Composite With Components as Adjudicated by the CEC: All-cause Mortality, Non-fatal MI and Non-fatal Stroke (in each of the Subgroups With or Without Evidence of T2D at Baseline)
-----------------	--

End point description:

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

End point timeframe:

During double blind period and at follow-up

End point values	Aleglitazar	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[6]	0 ^[7]		
Units: months				
arithmetic mean (standard deviation)	()	()		

Notes:

[6] - Planned analysis was not performed due to early termination of study

[7] - Planned analysis was not performed due to early termination of study

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Occurrence of a Composite With Components as Adjudicated by the CEC: CV Death, Non-fatal MI, Hospitalization for Unstable Angina, Hospitalization for Heart Failure, and Non-fatal Stroke

End point title	Time to First Occurrence of a Composite With Components as Adjudicated by the CEC: CV Death, Non-fatal MI, Hospitalization for Unstable Angina, Hospitalization for Heart
-----------------	---

End point description:

End point type Secondary

End point timeframe:

During double blind period and at follow-up

End point values	Aleglitazar	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[8]	0 ^[9]		
Units: months				
arithmetic mean (standard deviation)	()	()		

Notes:

[8] - Planned analysis was not performed due to early termination of study

[9] - Planned analysis was not performed due to early termination of study

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants With All-cause Mortality (in Each of the Subgroups With or Without Evidence of T2D at Baseline)

End point title Number of participants With All-cause Mortality (in Each of the Subgroups With or Without Evidence of T2D at Baseline)

End point description:

End point type Secondary

End point timeframe:

During double blind period and at follow-up

End point values	Aleglitazar	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[10]	0 ^[11]		
Units: participants				

Notes:

[10] - Planned analysis was not performed due to early termination of study

[11] - Planned analysis was not performed due to early termination of study

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Incidence of New Onset T2D in Participants without Evidence of T2D at Baseline

End point title Number of Participants With Incidence of New Onset T2D in Participants without Evidence of T2D at Baseline

End point description:

Participants with a physician diagnosis of diabetes plus prescription of a glucose lowering drug (other than study drug) plus at least one of the following criteria [local or central laboratory parameters: HbA1c $\geq 6.5\%$ or fasting plasma glucose ≥ 126 milligrams per deciliter (mg/dL) or 2-hour plasma glucose ≥ 200 mg/dL during an oral glucose tolerance test or random plasma glucose ≥ 200 mg/dL] or participants with two consecutive post-baseline HbA1c values of $\geq 6.5\%$

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

End point timeframe:

During the double-blind period

End point values	Alelitazar	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	999	997		
Units: participants	1	5		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of treatment to 4 weeks after the EOT visit

Assessment type	Non-systematic
-----------------	----------------

Dictionary used

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

Dictionary version	16.0
--------------------	------

Reporting groups

Reporting group title	Aleglitazar
-----------------------	-------------

Reporting group description:

Participants randomized to this arm received aleglitazar 150 µg tablet orally once daily

Reporting group title	Placebo
-----------------------	---------

Reporting group description:

Participants randomized to this arm received placebo tablet orally once daily

Serious adverse events	Aleglitazar	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	45 / 999 (4.50%)	27 / 997 (2.71%)	
number of deaths (all causes)	2	4	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Orthostatic hypotension			

subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 999 (0.10%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			

subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Confusional state			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Procedural complication			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ankle fracture			
subjects affected / exposed	2 / 999 (0.20%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Head injury			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Phimosis			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiogenic shock			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Cardiac failure			
subjects affected / exposed	3 / 999 (0.30%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	2 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	3 / 999 (0.30%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	2 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 999 (0.10%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac tamponade			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 999 (0.10%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			

Aphonia			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cognitive disorder			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiculopathy			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebrobasilar insufficiency			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	3 / 999 (0.30%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal necrosis			

subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal haemorrhage			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haemorrhage			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 999 (0.00%)	2 / 997 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Skin ulcer			

subjects affected / exposed	2 / 999 (0.20%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure acute			
subjects affected / exposed	4 / 999 (0.40%)	2 / 997 (0.20%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia			
subjects affected / exposed	2 / 999 (0.20%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cellulitis			
subjects affected / exposed	1 / 999 (0.10%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related sepsis			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis viral			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroborreliosis			
subjects affected / exposed	0 / 999 (0.00%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 999 (0.10%)	1 / 997 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			

subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	2 / 999 (0.20%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 999 (0.10%)	0 / 997 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Aleglitazar	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	76 / 999 (7.61%)	42 / 997 (4.21%)	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	76 / 999 (7.61%)	42 / 997 (4.21%)	
occurrences (all)	180	97	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 February 2013	The protocol was amended to add a study drug discontinuation criterion for participants who experienced a serious gastrointestinal hemorrhage based on recommendations from the Data Safety Monitoring Board (DSMB) and the exclusion criterion of estimated glomerular filtration rate (eGFR) of <30 mL/min/1.73m ² was modified to <45 mL/min/m ² .

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported