



Clinical trial results:

A Single Center, Double-Blind, Placebo-Controlled, Randomized, Crossover, Phase II Study to Assess the Effect of Alogliptazar on Cardiac Energetics and Function in Patients With Uncomplicated Type 2 Diabetes Mellitus (T2D) and no History of Coronary Artery Disease (CAD) who are Drug-Naïve or Treated With Stable Metformin Monotherapy

Summary

EudraCT number	2012-001639-29
Trial protocol	GB
Global end of trial date	03 September 2013

Results information

Result version number	v1 (current)
This version publication date	16 March 2016
First version publication date	16 March 2016

Trial information

Trial identification

Sponsor protocol code	BC25445
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01680978
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche Ltd
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	17 October 2013
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	03 September 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate if aleglitazar improves cardiac energetics, by means of magnetic resonance spectroscopy (MRS), in uncomplicated type 2 diabetes mellitus (T2D) participants with no history of coronary artery disease (CAD), after 6 weeks of treatment

Protection of trial subjects:

The study was conducted in accordance with the principles of the Declaration of Helsinki or with the laws and regulations of the country in which the research was conducted, whichever afforded the greater protection to the individual. Written informed consent was obtained from each participant before they participated in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 October 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 18
Worldwide total number of subjects	18
EEA total number of subjects	18

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)	13
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

18 participants were recruited from 1 center in UK.

Pre-assignment

Screening details:

A total of 18 participants were enrolled, of which 13 participants (uncomplicated T2DM and no CAD who were drug-naïve or treated with stable metformin monotherapy) were randomized to receive either aloglitazar or placebo and 5 participants were non-diabetic control.

Period 1

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

Blinding implementation details:

Eligible T2D participants were randomized in a 1:1 ratio to the order of receiving 150 µg aloglitazar and matching placebo, in a blinded fashion. No stratification was applied. The Randomization List was not be available at the study center, to the monitors, project statisticians, or to the project team at Roche.

Arms

Are arms mutually exclusive?	Yes
Arm title	T2DM Participants

Arm description:

Eligible T2DM participants were randomized in a 1:1 ratio to one of the two possible sequences: 150 microgram (µg) aloglitazar followed by matching placebo or placebo followed by 150 µg aloglitazar. Each treatment (aloglitazar and placebo) was received for 6 consecutive weeks, in a randomized order, separated by a 6-week treatment-free wash-out period.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo tablets orally once-a-day for 6 weeks.

Investigational medicinal product name	Aloglitazar
Investigational medicinal product code	RO0728804
Other name	dual PPAR alpha/gamma agonist
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received 150 µg aloglitazar once daily for 6 weeks followed by a 6-week washout period.

Arm title	Non-diabetic Control
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Arm description:

Non-diabetic controls (referred to as the calibration group) underwent only the assessments at screening and baseline and did not receive any study drug.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	T2DM Participants	Non-diabetic Control
Started	13	5
Completed	8	5
Not completed	5	0
Non compliance	1	-
STUDY TERMINATED BY SPONSOR	4	-

Baseline characteristics

Reporting groups

Reporting group title	T2DM Participants
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Reporting group description:

Eligible T2DM participants were randomized in a 1:1 ratio to one of the two possible sequences: 150 microgram (µg) aleglitazar followed by matching placebo or placebo followed by 150 µg aleglitazar. Each treatment (aleglitazar and placebo) was received for 6 consecutive weeks, in a randomized order, separated by a 6-week treatment-free wash-out period.

Reporting group title	Non-diabetic Control
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Reporting group description:

Non-diabetic controls (referred to as the calibration group) underwent only the assessments at screening and baseline and did not receive any study drug.

Reporting group values	T2DM Participants	Non-diabetic Control	Total
Number of subjects	13	5	18
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	54.1 ± 9.6	54.6 ± 7.8	-
Gender categorical Units: Subjects			
Female	6	2	8
Male	7	3	10
Cardiac PCr/ATP ratio			
Cardiac phosphocreatine/adenosine triphosphate (PCr/ATP)			
Units: ratio arithmetic mean standard deviation	1.45 ± 0.35	1.89 ± 0.32	-
Cardiac Fat/Water ratio Units: ratio arithmetic mean standard deviation	1.06 ± 0.62	0.47 ± 0.31	-
Hepatic Fat/Water ratio Units: ratio arithmetic mean standard deviation	14.99 ± 10.77	1.6 ± 1.48	-

End points

End points reporting groups

Reporting group title	T2DM Participants
Reporting group description: Eligible T2DM participants were randomized in a 1:1 ratio to one of the two possible sequences: 150 microgram (µg) aleglitazar followed by matching placebo or placebo followed by 150 µg aleglitazar. Each treatment (aleglitazar and placebo) was received for 6 consecutive weeks, in a randomized order, separated by a 6-week treatment-free wash-out period.	
Reporting group title	Non-diabetic Control
Reporting group description: Non-diabetic controls (referred to as the calibration group) underwent only the assessments at screening and baseline and did not receive any study drug.	

Primary: Change From Baseline to 6 Weeks After Treatment in Phosphocreatine/Adenosine Triphosphate (PCr/ATP) Ratio

End point title	Change From Baseline to 6 Weeks After Treatment in Phosphocreatine/Adenosine Triphosphate (PCr/ATP) Ratio ^[1]
End point description: Participants underwent a cardiovascular magnetic resonance (CMR) scan performed on a 3 Tesla magnetic resonance (MR) system to assess cardiac mass, volumes (global function and dilatation), strain and torsion, cardiac and liver lipid content and cardiac energy metabolism. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Due to the early termination of the study by the sponsor, insufficient data were available to perform all planned analyses. Only available baseline values are reported in the baseline characteristics.	
End point type	Primary
End point timeframe: Baseline, 6 Weeks after treatment	
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 the early termination of the study by the sponsor, insufficient data were available to perform all planned statistical analyses.	

End point values	T2DM Participants	Non-diabetic Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[2]	0 ^[3]		
Units: ratio				
arithmetic mean (standard deviation)	()	()		

Notes:

[2] - Due to early termination of study, insufficient data were available to perform all planned analyses.

[3] - Due to early termination of study, insufficient data were available to perform all planned analyses.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to 6 Weeks in Left Ventricular Diastolic Function

End point title	Change From Baseline to 6 Weeks in Left Ventricular Diastolic Function
End point description: Transthoracic echocardiography (Phillips iE33) was used to assess diastolic function. For determination	

of E/A, E deceleration times, and E/E', participants were scanned in a left lateral position with pulse wave velocities obtained at the mitral valve tips and tissue Doppler as an average of the basal septum and lateral walls.

Due to the early termination of the study by the sponsor, insufficient data were available to perform all planned analyses.

End point type	Secondary
End point timeframe:	
Baseline, 6 Weeks after treatment	

End point values	T2DM Participants	Non-diabetic Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[4]	0 ^[5]		
Units: ratio				
arithmetic mean (standard deviation)	()	()		

Notes:

[4] - Due to early termination of study, insufficient data were available to perform all planned analyses.

[5] - Due to early termination of study, insufficient data were available to perform all planned analyses.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline to 6 Weeks in Cardiac and Hepatic Triglyceride Content

End point title	Change From Baseline to 6 Weeks in Cardiac and Hepatic Triglyceride Content
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End point description:

Measurement of myocardial triglycerides were performed using spin echo imaging for localization of the voxels in the septum followed by 31P and 1H MR to obtain spectra. To obtain hepatic proton MR spectra, a voxel will was positioned in the liver, avoiding gross vascular structures and adipose tissue deposits. Spectra with and without water suppression was obtained to calculate hepatic triglyceride content as a percentage of water.

Due to the early termination of the study by the sponsor, insufficient data were available to perform all planned analyses. Only available baseline values are reported in the baseline characteristics.

End point type	Secondary
End point timeframe:	
Baseline, 6 Weeks after treatment	

End point values	T2DM Participants	Non-diabetic Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[6]	0 ^[7]		
Units: ratio				
arithmetic mean (standard deviation)	()	()		

Notes:

[6] - Due to early termination of study, insufficient data were available to perform all planned analyses.

[7] - Due to early termination of study, insufficient data were available to perform all planned analyses.

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to follow-up (6 weeks after the last dose of study medication)

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.0
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Reporting groups

Reporting group title	T2DM Participants
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Reporting group description:

Eligible T2DM participants were randomized in a 1:1 ratio to one of two possible sequences: 150 microgram (µg) aleglitazar followed by matching placebo or placebo followed by 150 µg aleglitazar. Each treatment (aleglitazar and placebo) was received for 6 consecutive weeks, in a randomized order, separated by a 6-week treatment-free wash-out period. All adverse events which were observed across both the treatment group (placebo/aleglitazar) and during wash-out/follow-up after treatment completion reported.

Serious adverse events	T2DM Participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	T2DM Participants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 13 (38.46%)		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Joint Injury			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
General disorders and administration site conditions			

Influenza Like Illness subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Skin and subcutaneous tissue disorders Dry Skin subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Psoriasis subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Viral Infection subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Urinary Tract Infection subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 June 2012	Modified liver disease characteristic and specified the use of metformin as background therapy. The reasons for participant's discontinuation have been clarified and 2 withdrawal rules were implemented.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to the early termination of the study by the sponsor, insufficient data were available to perform all planned analyses.

Notes: