Clinical trial results:
The impact of free fatty acid (FFA-) suppression on myocardial lipids and function in patients with type 2 diabetes

Summary

EudraCT number	2013-002656-32
Trial protocol	AT
Global end of trial date	04 May 2016

Results information

Result version number	v1 (current)
This version publication date	21 August 2020
First version publication date	21 August 2020
Summary attachment (see zip file)	Healthy (ajpendo.00371.2014.pdf) Diabetes (Wolf Abstract.pdf)

Trial information

Trial identification

Sponsor protocol code	HYPOTESIS

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medizinische Universität Wien
Sponsor organisation address	Spitalgasse 23, Vienna, Austria, 1090
Public contact	Yvonne Winhofer, MUW, Univ.Klinik für Innere Medizin III, Abt.f.Endokrinologie und Stoffwechsel, 0043 1404004311, yvonne.winhofer@meduniwien.ac.at
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Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 May 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 May 2016
Global end of trial reached?	Yes
Global end of trial date	04 May 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Changes in myocardial lipids and function related to suppression of free fatty acids

Protection of trial subjects:

constant supervision by physician

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 July 2013
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	Austria: 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)	16
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was performed by local advertisement in the diabetes outpatient department

Pre-assignment

Screening details:

Patients were recruited from the diabetes outpatient's service at the Medical University of Vienna

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Myocardial Lipid Content Acipimox-Diabetes

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Acipimox
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

2x250 mg (0 minutes and 180 minutes)

Arm title	Hypoglycemia with Acipimox-Healthy

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Acipimox
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

2x250 mg (0 minutes and 180 minutes)

Number of subjects in period 1	Myocardial Lipid Content Acipimox-Diabetes	Hypoglycemia with Acipimox-Healthy
Started	8	10
Completed	8	9
Not completed	0	1
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Myocardial Lipid Content Acipimox-Diabetes
Reporting group description: -	
Reporting group title	Hypoglycemia with Acipimox-Healthy
Reporting group description: -	

Reporting group values	Myocardial Lipid Content Acipimox-Diabetes	Hypoglycemia with Acipimox-Healthy	Total
Number of subjects	8	10	18
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	10	16
From 65-84 years	2	0	2
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	2	0	2
Male	6	10	16

Subject analysis sets	
Subject analysis set title	Normoglycemia with Acipimox-Healthy
Subject analysis set type	Per protocol
Subject analysis set description: Normoglycemia with Acipimox-Healthy	
Subject analysis set title	Myocardial Lipid Content Acipimax-Diabetes
Subject analysis set type	Per protocol
Subject analysis set description: Myocardial Lipid Content-Diabetes	
Subject analysis set title	Normoglycemia with Placebo-Healthy
Subject analysis set type	Per protocol
Subject analysis set description: Normoglycemia with Placebo-Healthy	
Subject analysis set title	Hypoglycemia with Acipimox-Healthy
Subject analysis set type	Per protocol
Subject analysis set description: Hypoglycemia with Acipimox-Healthy	
Subject analysis set title	Hypoglycemia with Placebo-Healthy
Subject analysis set type	Per protocol

Subject analysis set description:

Hypoglycemia with Placebo-Healthy

Subject analysis set title	Myocardial Lipid Content Placebo-Diabetes
Subject analysis set type	Per protocol

Subject analysis set description:

Myocardial Lipid Content Placebo-Diabetes

Reporting group values	Normoglycemia with Acipimox-Healthy	Myocardial Lipid Content Acipimax-Diabetes	Normoglycemia with Placebo-Healthy
Number of subjects	10	8	10
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	10	6	10
From 65-84 years		2	
85 years and over			
Gender categorical Units: Subjects			
Female		2	
Male	10	6	

Reporting group values	Hypoglycemia with Acipimox-Healthy	Hypoglycemia with Placebo-Healthy	Myocardial Lipid Content Placebo-Diabetes
Number of subjects	10	10	8
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	10	10	6
From 65-84 years			2
85 years and over			
Gender categorical Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	Myocardial Lipid Content Acipimox-Diabetes
Reporting group description: -	
Reporting group title	Hypoglycemia with Acipimox-Healthy
Reporting group description: -	
Subject analysis set title	Normoglycemia with Acipimox-Healthy
Subject analysis set type	Per protocol
Subject analysis set description: Normoglycemia with Acipimox-Healthy	
Subject analysis set title	Myocardial Lipid Content Acipimax-Diabetes
Subject analysis set type	Per protocol
Subject analysis set description: Myocardial Lipid Content-Diabetes	
Subject analysis set title	Normoglycemia with Placebo-Healthy
Subject analysis set type	Per protocol
Subject analysis set description: Normoglycemia with Placebo-Healthy	
Subject analysis set title	Hypoglycemia with Acipimox-Healthy
Subject analysis set type	Per protocol
Subject analysis set description: Hypoglycemia with Acipimox-Healthy	
Subject analysis set title	Hypoglycemia with Placebo-Healthy
Subject analysis set type	Per protocol
Subject analysis set description: Hypoglycemia with Placebo-Healthy	
Subject analysis set title	Myocardial Lipid Content Placebo-Diabetes
Subject analysis set type	Per protocol
Subject analysis set description: Myocardial Lipid Content Placebo-Diabetes	

Primary: myocardial lipid content - Acipimox-Diabetes

End point title	myocardial lipid content - Acipimox-Diabetes
End point description:	
End point type	Primary
End point timeframe: 480 minutes after Acipimox or placebo	

End point values	Myocardial Lipid Content Acipimax-Diabetes	Myocardial Lipid Content Placebo-Diabetes		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	8		
Units: % of water signal				
arithmetic mean (standard deviation)	0.32 (± 0.1)	0.48 (± 0.2)		

Statistical analyses

Statistical analysis title	Anova
Comparison groups	Myocardial Lipid Content Acipimax-Diabetes v Myocardial Lipid Content Placebo-Diabetes
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other
P-value	= 5
Method	ANOVA

Primary: hypoglycemia with placebo – healthy

End point title	hypoglycemia with placebo – healthy
End point description:	
End point type	Primary
End point timeframe: 0 - 405 min	

End point values	Normoglycemia with Acipimox-Healthy	Normoglycemia with Placebo-Healthy	Hypoglycemia with Acipimox-Healthy	Hypoglycemia with Placebo-Healthy
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	10	10	10
Units: change in myocardial lipids %				
median (confidence interval 95%)	48.5 (28.5 to 62.9)	15.2 (1.8 to 28.3)	40.5 (13.7 to 58.9)	6.1 (3.7 to 15.7)

Statistical analyses

Statistical analysis title	Anova
Comparison groups	Normoglycemia with Acipimox-Healthy v Normoglycemia with Placebo-Healthy v Hypoglycemia with Acipimox-Healthy v Hypoglycemia with Placebo-Healthy

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
P-value	= 5
Method	ANOVA

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: Study day, 0- 480 min	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23

Reporting groups	
Reporting group title	healthy subjects
Reporting group description: healthy subjects	
Reporting group title	Typ-2 diabetes
Reporting group description: Typ-2 diabetes	

Serious adverse events	healthy subjects	Typ-2 diabetes	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	0 / 8 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	healthy subjects	Typ-2 diabetes	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	0 / 8 (0.00%)	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: During to the short exposure/observation time (7h) no non-serious or serious adverse events occurred.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 April 2013	According to our preliminary analyses there is evidence that inhibition of FFA-release by acipimox is associated with a significant decrease in myocardial lipid content (MYCL) as well as the ejection fraction (as a marker of systolic left ventricular function) in healthy subjects, indicating, that the heart is dependent on a constant supply of free fatty acids in order to guarantee normal cardiac function, and it further indicates, that the heart is not able to cover its energy demand by switching to glucose oxidation. Since that phenomenon, better known as "metabolic inflexibility" has been mainly described in patients with diabetes, the aim of the current study extension/amendment is to investigate the impact of FFA-inhibition on MYCL and cardiac function in patients with diabetes. Therefore, up to 14 patients with type 2 diabetes will be asked to participate in this study, which includes 2 study days. On each study day patients will start at 7 a.m. in the morning with the first MR-examination, which will be repeated after 180 and 420 minutes as well as after 24 hours. They will receive acipimox (orally) at 0 and 180 minutes. Blood samples for the measurement of glucose, free fatty acids, insulin, C-peptide and proBNP will be taken every 30 minutes. At fasting, additional blood samples will be taken for the measurement of HbA1C, cholesterol, HDL and LDL. Blood glucose excursions (hyperglycemia, hypoglycemia) will be corrected by a short acting insulin (according to routine care) or oral glucose administration.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported