Clinical trial results:
Metformin and its Effects on Myocardial Dimension and Left ventricular hypertrophy in normotensive patients with Coronary Artery Disease.

Summary

EudraCT number	2014-003189-26
Trial protocol	GB
Global end of trial date	30 August 2017

Results information

Result version number	v1 (current)
This version publication date	03 July 2019
First version publication date	03 July 2019
Summary attachment (see zip file)	Manuscript (MET-REMODEL Paper.pdf)

Trial information

Trial identification

Sponsor protocol code	Version 5.4

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02226510
WHO universal trial number (UTN)	-
Other trial identifiers	Sponsor Reference: 2013CV08

Notes:

Sponsors

Sponsor organisation name	University of Dundee
Sponsor organisation address	Nethergate, Dundee, United Kingdom,
Public contact	Dr Stephen McSwiggan, University of Dundee, Tayside Clinical Trials Unit, 01382 383233, s.j.mcswiggan@dundee.ac.uk
Scientific contact	Dr Stephen McSwiggan, University of Dundee, Tayside Clinical Trials Unit, 01382 383233, s.j.mcswiggan@dundee.ac.uk

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	30 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 August 2017
Global end of trial reached?	Yes
Global end of trial date	30 August 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The principal research question is to find out if metformin can cause regression of left ventricular hypertrophy (LVH) in participants with coronary artery heart disease (CAD) who are insulin resistant/pre-diabetes and on optimal current evidence based therapy for CAD.

Protection of trial subjects:

The CI and study staff involved with this study will comply with the requirements of the Data Protection Act 1998 with regard to the collection, storage, processing and disclosure of personal information and will uphold the Act’s core principles. Access to collated participant data will be restricted to those clinicians treating the participants.
Computers used to collate the data will have limited access measures via user names and passwords. Published results will not contain any personal data that could allow identification of individual participants.

All the participants were clinically periodically monitored while in the study. Any AE's and SAE's were reported to the pharmacovigilance department of the sponsor and ensured all was resolved.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	03 March 2014
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	United Kingdom: 68
Worldwide total number of subjects	68
EEA total number of subjects	68

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)	31
From 65 to 84 years	37
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

187 subjects were screened between March 2014 and September 2016 from Tayside, Scotland and 68 patients who full filled eligibility criteria were recruited in the study

Pre-assignment

Screening details:

187 subjects were screened between March 2014 and September 2016 from Tayside, Scotland, using research databases, hospital records, and local general practices.

Period 1

Period 1 title	April 2014 -September 2016 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Metformin Arm

Arm description: -

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

Dosage and administration details:

1000 mg bid

Arm title	Placebo Arm

Arm description: -

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

Dosage and administration details:

100 mg bid

Number of subjects in period 1	Metformin Arm	Placebo Arm
Started	34	34
Completed	31	32
Not completed	3	2
Physician decision	1	-
Consent withdrawn by subject	1	-

Unable to undergo MRI due to claustrophobia	1	-
Protocol deviation	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Metformin Arm
Reporting group description: -	
Reporting group title	Placebo Arm
Reporting group description: -	

Reporting group values	Metformin Arm	Placebo Arm	Total
Number of subjects	34	34	68
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)	18	16	34
From 65-84 years	16	18	34
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	5	11	16
Male	29	23	52

End points

End points reporting groups	
Reporting group title	Metformin Arm
Reporting group description: -	
Reporting group title	Placebo Arm
Reporting group description: -	

Primary: Baseline LVMI	
End point title	Baseline LVMI
End point description: Change in Left Ventricular Mass Index	
End point type	Primary
End point timeframe: 12 months	

End point values	Metformin Arm	Placebo Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	32		
Units: 47.3				
number (not applicable)	48.7	46		

Statistical analyses

Statistical analysis title	METREMODEL SAP
Comparison groups	Metformin Arm v Placebo Arm
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	≤ 0.5
Method	ANCOVA

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Entire duration of study	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups	
Reporting group title	Metformin Arm
Reporting group description: -	
Reporting group title	Placebo Arm
Reporting group description: -	

Serious adverse events	Metformin Arm	Placebo Arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 31 (19.35%)	4 / 32 (12.50%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (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	0 / 31 (0.00%)	1 / 32 (3.13%)	
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			
Chest pain			
subjects affected / exposed	2 / 31 (6.45%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo positional			

subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Metformin Arm	Placebo Arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 31 (61.29%)	15 / 32 (46.88%)	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	15 / 31 (48.39%)	3 / 32 (9.38%)	
occurrences (all)	15	3	
Flatulence			

subjects affected / exposed	8 / 31 (25.81%)	2 / 32 (6.25%)	
occurrences (all)	8	2	
Abdominal discomfort			
subjects affected / exposed	2 / 31 (6.45%)	0 / 32 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported