Clinical trial results:
SOdium-glucose CO-transporter inhibition in patients with newly detected Glucose Abnormalities post Myocardial Infarction (SOCOGAMI)

Summary

EudraCT number	2015-004571-73
Trial protocol	SE
Global end of trial date	25 November 2020

Results information

Result version number	v1 (current)
This version publication date	27 April 2023
First version publication date	27 April 2023

Trial information

Trial identification

Sponsor protocol code	SOCOGAMI

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Karolinska Institutet
Sponsor organisation address	Nobels väg 6, Stockholm, Sweden, 17177
Public contact	Lars Rydén, Karolinska Institutet Department of Medicine Solna, Cardiology Unit, +46 8-517 721 71, lars.ryden@ki.se
Scientific contact	Lars Rydén, Karolinska Institutet Department of Medicine Solna, Cardiology Unit, +46 8-517 721 71, lars.ryden@ki.se

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	01 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 November 2020
Global end of trial reached?	Yes
Global end of trial date	25 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To test the hypotheses that Empagliflozin (Jardiance®) will have a beneficial effect on myocardial function and structure, glucose homeostasis and beta cell function in patients with recent myocardial infarction or unstable angina pectoris and newly detected impaired glucose tolerance or type 2 diabetes.

Protection of trial subjects:

All patients signed consent to study participation following written and oral information. The trial was carried out in compliance with principles in the Declaration of Helsinki, 1996 version, in accordance with the ICH Harmonized Tripartite Guideline for Good Clinical Practice (GCP) and in accordance with applicable regulatory requirements. The protocol was approved by the Regional Ethics committee in Stockholm (Dnr 2015:4/11).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 June 2016
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	Sweden: 42
Worldwide total number of subjects	42
EEA total number of subjects	42

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)	11
From 65 to 84 years	31

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients aged > 18 years, who during the previous six months suffered AMI or unstable angina pectoris were recruited. 55 patients were screened, 13 didn't meet the inclusion criterias, and 42 patients were included.

Pre-assignment

Screening details:

Inclusion criteria: patients aged >18 years, who during the previous six months suffered AMI or unstable angina pectoris were recruited if they, had newly detected IGT or T2DM confirmed by two screening oral glucose tolerance tests (OGTT).
Exclusion criteria: known diabetes, contraindications to CMR imaging, eGFR < 30 ml/min/1.73 m2; and more.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Patients in placebo arm were randomized to 25 mg of corresponding placebo. They received a patient diary, equipment for and instruction on self-monitoring of glucose levels and were seen at the outpatient clinic one and three months later. Seven months after randomization all investigations performed during the baseline visit were repeated. Thereafter the study drug was discharged. Ten months after randomization the patient returned for a final visit, during which all investigations were repeated once more.

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:

Patients in placebo arm were randomized to 25 mg of placebo daily. After 7 months the study drug was discharged.

Arm title	Empagliflozin

Arm description:

Patients in Empagliflozin arm were randomized to 25 mg Empagliflozin daily. They received a patient diary, equipment for and instruction on self-monitoring of glucose levels and were seen at the outpatient clinic one and three months later. Seven months after randomization all investigations performed during the baseline visit were repeated. Thereafter the study drug was discharged. Ten months after randomization the patient returned for a final visit, during which all investigations were repeated once more.

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

Dosage and administration details:

Patients in Empagliflozin arm were randomized to 25 mg of Empagliflozin daily. After 7 months the study drug was discharged.

Number of subjects in period 1	Placebo	Empagliflozin
Started	22	20
Completed	22	20

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Patients in placebo arm were randomized to 25 mg of corresponding placebo. They received a patient diary, equipment for and instruction on self-monitoring of glucose levels and were seen at the outpatient clinic one and three months later. Seven months after randomization all investigations performed during the baseline visit were repeated. Thereafter the study drug was discharged. Ten months after randomization the patient returned for a final visit, during which all investigations were repeated once more.	
Reporting group title	Empagliflozin
Reporting group description:	
Patients in Empagliflozin arm were randomized to 25 mg Empagliflozin daily. They received a patient diary, equipment for and instruction on self-monitoring of glucose levels and were seen at the outpatient clinic one and three months later. Seven months after randomization all investigations performed during the baseline visit were repeated. Thereafter the study drug was discharged. Ten months after randomization the patient returned for a final visit, during which all investigations were repeated once more.	

Reporting group values	Placebo	Empagliflozin	Total
Number of subjects	22	20	42
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	68	67	
standard deviation	± 8	± 8	-
Gender categorical Units: Subjects			
Female	4	4	8
Male	18	16	34
Smoking Units: Subjects			
Yes	19	19	38
No	3	1	4
Index event Units: Subjects			
Myocardial infarction	19	17	36
Unstable angina	3	3	6
Peripheral artery disease			

Medical history			
Units: Subjects			
Yes	0	1	1
No	22	19	41
Stroke/TIA			
Medical history. TIA = transitory ischaemic attack			
Units: Subjects			
Yes	0	2	2
No	22	18	40
Heart failure			
Medical history			
Units: Subjects			
Yes	0	1	1
No	22	19	41
ACE-inhibitors/ARBs			
Pharmacological treatment. ACE = angiotensin converting enzyme; ARB = angiotensin receptor blocker			
Units: Subjects			
Yes	18	17	35
No	4	3	7
Beta-blockers			
Pharmacological treatment			
Units: Subjects			
Yes	21	17	38
No	1	3	4
Calcium channel blockers			
Pharmacological treatment			
Units: Subjects			
Yes	4	5	9
No	18	15	33
Diuretics			
Pharmacological treatment			
Units: Subjects			
Yes	3	7	10
No	19	13	32
Statins			
Pharmacological treatment			
Units: Subjects			
Yes	21	20	41
No	1	0	1
Antiaggregants			
Pharmacological treatment			
Units: Subjects			
Yes	16	19	35
No	6	1	7
Anticoagulants			
Pharmacological treatment			
Units: Subjects			
Yes	2	0	2
No	20	20	40

Body mass index			
Units: (kg/m2)			
arithmetic mean	27	27	
standard deviation	± 4	± 4	-
Systolic blood pressure			
Units: mmHg			
arithmetic mean	131	130	
standard deviation	± 16	± 16	-
Diastolic blood pressure			
Units: mmHg			
arithmetic mean	80	79	
standard deviation	± 10	± 10	-
Heart rate			
Units: beats/minute			
arithmetic mean	68	62	
standard deviation	± 8	± 7	-
Haemoglobin			
Laboratory findings			
Units: g/L			
arithmetic mean	140	142	
standard deviation	± 10	± 19	-
LDL-cholesterol			
Laboratory findings. LDL = low-density lipoprotein			
Units: mmol/L			
arithmetic mean	1.4	1.4	
standard deviation	± 0.6	± 0.3	-
Triglycerides			
Laboratory findings			
Units: mmol/L			
arithmetic mean	3.3	1.3	
standard deviation	± 9.3	± 0.6	-
Creatinine			
Laboratory findings			
Units: µmol/L			
arithmetic mean	81	86	
standard deviation	± 18	± 16	-
eGFR			
Laboratory findings. eGFR = estimated glomerular filtration			
Units: ml/min/1.73 m2			
arithmetic mean	73	68	
standard deviation	± 14	± 13	-
Troponin			
Laboratory findings			
Units: ng/L			
arithmetic mean	16	15	
standard deviation	± 12	± 14	-
hsCRP			
Laboratory findings. hsCRP = high-sensitivity C-reactive protein			
Units: mg/L			
arithmetic mean	1.7	1.2	
standard deviation	± 2.4	± 0.8	-
NT-pro-BNP			

Laboratory findings. BNP = brain natriuretic peptide			
Units: ng/L			
arithmetic mean	249	361	
standard deviation	± 305	± 406	-
Fasting plasma glucose			
Laboratory findings			
Units: mmol/L			
arithmetic mean	6.5	6.5	
standard deviation	± 1.1	± 0.9	-
2-hour post load glucose			
Laboratory findings			
Units: mmol/L			
arithmetic mean	10.6	10.9	
standard deviation	± 2.9	± 2.9	-
HbA1c			
Laboratory findings. HbA1c = glycated haemoglobin A1c			
Units: mmol/mol			
arithmetic mean	43	42	
standard deviation	± 9	± 6	-
LV end-diastolic volume			
Units: ml			
median	141	146	
standard deviation	± 39	± 33	-

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Patients in placebo arm were randomized to 25 mg of corresponding placebo. They received a patient diary, equipment for and instruction on self-monitoring of glucose levels and were seen at the outpatient clinic one and three months later. Seven months after randomization all investigations performed during the baseline visit were repeated. Thereafter the study drug was discharged. Ten months after randomization the patient returned for a final visit, during which all investigations were repeated once more.

Reporting group title	Empagliflozin

Reporting group description:

Patients in Empagliflozin arm were randomized to 25 mg Empagliflozin daily. They received a patient diary, equipment for and instruction on self-monitoring of glucose levels and were seen at the outpatient clinic one and three months later. Seven months after randomization all investigations performed during the baseline visit were repeated. Thereafter the study drug was discharged. Ten months after randomization the patient returned for a final visit, during which all investigations were repeated once more.

Primary: LV end-diastolic volume

End point title	LV end-diastolic volume

End point description:

The LV end-diastolic volume from at seven months measured by CMR.

End point type	Primary

End point timeframe:

At seven months.

End point values	Placebo	Empagliflozin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	20		
Units: ml				
arithmetic mean (standard deviation)	143 (± 39)	145 (± 41)		

Statistical analyses

Statistical analysis title	Change in the LV end-diastolic volume

Statistical analysis description:

Change in the LV end-diastolic volume from baseline to seven months measured by CMR

Comparison groups	Placebo v Empagliflozin

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	ANOVA

Adverse events

Adverse events information

Timeframe for reporting adverse events:

At each study visit i.e. after 7 months on randomized treatment and 3 months after study drug cessation.

Assessment type	Systematic

Dictionary used

Dictionary name	n/a
Dictionary version	n/a

Reporting groups

Reporting group title	Overall group

Reporting group description: -

Serious adverse events	Overall group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 42 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Overall group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 42 (21.43%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Eye disorders			

Amaurosis fugax subjects affected / exposed occurrences (all)	1 / 42 (2.38%) 1		
Respiratory, thoracic and mediastinal disorders Chest pain subjects affected / exposed occurrences (all)	2 / 42 (4.76%) 2		
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all) Fungal infection vaginal subjects affected / exposed occurrences (all)	2 / 42 (4.76%) 2 1 / 42 (2.38%) 1		

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

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

A weakness may be the limited number of patients, but it is unlikely that the inclusion of further study participants of the same kind would have changed the results.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/36336088