Clinical trial results:
Allogeneic adipose tissue-derived stromal/stem cell therapy in patients with ischemic heart disease and heart failure

Summary

EudraCT number	2015-001560-19
Trial protocol	DK
Global end of trial date	31 December 2021

Results information

Result version number	v1 (current)
This version publication date	19 May 2023
First version publication date	19 May 2023
Summary attachment (see zip file)	ASC_HF II (EHF2-10-1170.pdf)

Trial information

Trial identification

Sponsor protocol code	CSCC-ASC2

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02387723
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Rigshospitalet
Sponsor organisation address	Blegdamsvej, Copenhagen, Denmark, 2100
Public contact	Jens Kastrup, Department of Cardiology, 2014, Rigshospitalet, 0045 35452819, jens.kastrup@regionh.dk
Scientific contact	Jens Kastrup, Department of Cardiology, 2014, Rigshospitalet, 0045 35452819, jens.kastrup@regionh.dk

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 April 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2021
Global end of trial reached?	Yes
Global end of trial date	31 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To perform at clinical double-blind placebo-controlled CSCC_ASC multicentre study in heart failure patients to investigate the regenerative capacity of the CSCC_ASC treatment.

Protection of trial subjects:

Patients are hospitalized 24 hours after treatment

Background therapy:

Maximal tolerable heart failure medical therapy

Evidence for comparator:

No

Actual start date of recruitment	01 September 2015
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	Denmark: 81
Worldwide total number of subjects	81
EEA total number of subjects	81

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)	39
From 65 to 84 years	42
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The planned 81 patients were enrolled in the study. 54 patients were treated with cell product and 27 with placebo. Mean age was 67.0 ± 9.0 years and 66.6 ± 8.1 years in the ASC and placebo groups, respectively.

Pre-assignment

Screening details:

Patients had to meet the predefined in- and exclusion criteria. 139 patients were screeened. 49 did not meet the inclusion criteria. 1 had severe kidney disease, 2 had infection, 2 had severe claudicatio, 1 had mural thrombus and 3 withdrew consent

Pre-assignment period milestones

Number of subjects started	81
Number of subjects completed	81

Period 1

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

Blinding implementation details:

All image data was stored on a central server and analysed blinded by two independent observers not aware of the treatment allocation. Moreover, they did not have access to each other's analysed images. The study nurses, physicians and patients were not aware of the treatment allocation.

Arms

Are arms mutually exclusive?	Yes
Arm title	ASC treatment

Arm description:

Injections of 0.3 mL CSCC_ASC (total cell dose 100 x 106 ASCs) (n=54) performed into the viable myocardium in the border zone of infarcted tissue using the NOGA Myostar® catheter (Biological Delivery System, Cordis, Johnson & Johnson, US).

Arm type	Experimental
Investigational medicinal product name	Allogeneic adipose tissue-derived stromal cells. (CSCC_ASC)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

CSCC_ASC constituted 110 million ASCs/5 mL CryoStor CS10 (BioLife Solutions).
The CSCC_ASCs were injected into the myocardium by 12-15 injections of 0.3 mL solution except the first injection, which consisted of 0.4 mL. Point by point measurement generates an electromechanical 3D LV map. The system distinguishes between viable (unipolar voltage > 12 mV, bipolar voltage > 2.5 mV, local linear shortening-LLS > 6 %), non-viable-myocardium (unipolar voltage < 6 mV, bipolar voltage < 1.5 mV, LLS < 4%) and border zone (unipolar voltage 6-12 mV, bipolar voltage 1.5-2.5 mV, LLS 4-6 %) around myocardial scar tissue. To ensure appropriate injection into the ventricle wall, the injection catheter tip was located perpendicular to the ventricle wall and a ventricular extrasystole was elicited when extending the needle into the wall before any injection. The injections were performed into the viable myocardium judged by the 3D map in the border zone of infarcted tissue tissue with a unipo

Arm title	Placebo

Arm description:

Injections of 0.3 mL isotonic saline (n=27) were performed into the viable myocardium in the border zone of infarcted tissue using the NOGA Myostar® catheter (Biological Delivery System, Cordis, Johnson & Johnson, US).

Arm type	Placebo
Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

The placebo was injected into the myocardium by 12-15 injections of 0.3 mL solution except the first injection, which consisted of 0.4 mL. Point by point measurement generates an electromechanical 3D LV map. The system distinguishes between viable (unipolar voltage > 12 mV, bipolar voltage > 2.5 mV, local linear shortening-LLS > 6 %), non-viable-myocardium (unipolar voltage < 6 mV, bipolar voltage < 1.5 mV, LLS < 4%) and border zone (unipolar voltage 6-12 mV, bipolar voltage 1.5-2.5 mV, LLS 4-6 %) around myocardial scar tissue. To ensure appropriate injection into the ventricle wall, the injection catheter tip was located perpendicular to the ventricle wall and a ventricular extrasystole was elicited when extending the needle into the wall before any injection. The injections were performed into the viable myocardium judged by the 3D map in the border zone of infarcted tissue tissue with a unipolar voltage > 6 mV.

Number of subjects in period 1	ASC treatment	Placebo
Started	54	27
Completed	52	27
Not completed	2	0
Dead	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Randomisation

Reporting group description: -

Reporting group values	Randomisation	Total	
Number of subjects	81	81	
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			
67.0 ± 9.0 years in the ASC group and 66.6 ± 8.1 years in the placebo group			
Units: years			
arithmetic mean	66.8		
standard deviation	± 8.6	-	
Gender categorical Units: Subjects			
Female	13	13	
Male	68	68	

End points

End points reporting groups

Reporting group title	ASC treatment

Reporting group description:

Injections of 0.3 mL CSCC_ASC (total cell dose 100 x 106 ASCs) (n=54) performed into the viable myocardium in the border zone of infarcted tissue using the NOGA Myostar® catheter (Biological Delivery System, Cordis, Johnson & Johnson, US).

Reporting group title	Placebo

Reporting group description:

Injections of 0.3 mL isotonic saline (n=27) were performed into the viable myocardium in the border zone of infarcted tissue using the NOGA Myostar® catheter (Biological Delivery System, Cordis, Johnson & Johnson, US).

Primary: LVESV (left ventricular end systolic volume)

End point title	LVESV (left ventricular end systolic volume)

End point description:

Difference between the two groups

End point type	Primary

End point timeframe:

6 months after ASC/placebo injections

End point values	ASC treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	27		
Units: mL				
number (not applicable)	52	27		

Statistical analyses

Statistical analysis title	T-test

Statistical analysis description:

Paired t-test was used for normal distributed continuous data comparison within groups and unpaired t-test was used for comparison between groups

Comparison groups	ASC treatment v Placebo
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0

Confidence interval	
level	90 %
sides	2-sided
lower limit	-9.1
upper limit	9
Variability estimate	Standard deviation

Notes:

[1] - Between the two grops

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
1 years followup	
Assessment type	Systematic

Dictionary used	
Dictionary name	Adverse events
Dictionary version	1

Reporting groups	
Reporting group title	ASC and placebo group

Reporting group description: -

Serious adverse events	ASC and placebo group		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 81 (3.70%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	0		
Cardiac disorders			
1 year			
subjects affected / exposed	3 / 81 (3.70%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 3		

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

Non-serious adverse events	ASC and placebo group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 81 (39.51%)		
Cardiac disorders			
1 year			
subjects affected / exposed	32 / 81 (39.51%)		
occurrences (all)	32		

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/36638837