Clinical trial results:
Regeneration of ischemic damages in cardiovascular system using Wharton's jelly as an unlimited source of mesenchymal stem cells for regenerative medicine.
Project of the National Centre for Research and Development (Poland) 'STRATEGMED II'.
Cardiovascular Clinical Project to Evaluate the Regenerative Capacity of CardioCell in patients with acute myocardial infarction (AMI).

Summary

EudraCT number	2016-004662-25
Trial protocol	PL
Global end of trial date	16 February 2021

Results information

Result version number	v1 (current)
This version publication date	14 October 2022
First version publication date	14 October 2022

Trial information

Trial identification

Sponsor protocol code	AMI-Study

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03404063
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Krakowski Szpital Specjalistyczny im. Jana Pawła II
Sponsor organisation address	Pradnicka 80, Krakow, Poland, 31-202
Public contact	Clinical Trial Information Desk, Ewa Gąsior, 48 126142000, e.gasior@szpitaljp2.krakow.pl
Scientific contact	Principal Investigator, Piotr Musiałek MD, PhD, 48 126142000, badaniakliniczne@szpitaljp2.krakow.pl

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	25 August 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 February 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Regeneration of ischemic damages in cardiovascular system using Wharton’s jelly as an unlimited source of mesenchymal stem cells for regenerative medicine.
Project of the National Centre for Research and Development (Poland) ‘STRATEGMED II’.
Cardiovascular Clinical Project to Evaluate the Regenerative Capacity of CardioCell in patients with acute myocardial infarction (AMI).

Protection of trial subjects:

The Principal Investigator (PI) retains overall responsibility for the informed consent of participants at their site and must ensure that any person delegated responsibility to participate in the informed consent process is duly authorized, trained and competent to participate according to the ethically approved protocol, principles of Good Clinical Practice (GCP) and Declaration of Helsinki.

In order to constitute evidence with respect to product safety, regulatory and legal compliance, the investigator agrees to retain project related documents in a location which is secure and to which access can be gained if required. The following documents must be archived: the investigators file with respect to all required GCP documents, including signed patient informed consent forms, CRFs and monitoring forms. Data reported into eCRF will be anonymized by patients code. The list with assigned code numbers will be stored in Investigation Centre and will not be shared.

The Sponsor has ethical, legal and scientific obligations to carefully follow this project in a detailed and orderly manner in accordance with established research principles and applicable regulations. The investigator, as part of his responsibilities, is expected to cooperate with the Sponsor in ensuring that the project adheres to the protocol and GCP requirements. As part of a concerted effort to fulfil these obligations, the Sponsor will authorize a Clinical research Organization (CRO) to perform monitoring tasks and visit the centers during the project. The processes reviewed can relate to participant enrolment, consent, eligibility, and allocation to trial groups; adherence to trial interventions and policies to protect participants, including reporting of harm and completeness, accuracy, and timeliness of data collection. The investigator will permit the Sponsor’ authorized CRO personnel to monitor the project as frequently as is deemed necessary and provide access to medical records.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 October 2017
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	Poland: 115
Worldwide total number of subjects	115
EEA total number of subjects	115

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)	78
From 65 to 84 years	37
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All patients who provided informed consent and met inclusion criteria without any exclusion criteria were enrolled to the study.

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, Monitor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	active group

Arm description: -

Arm type	Experimental
Investigational medicinal product name	CardioCell
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intracoronary use

Dosage and administration details:

Patients randomized to the active treatment group: Transcoronary or trans-bypass graft administration of 30 000 000 cells (suspended in 20 ml of 0.9% NaCl and 5% albumin) was performed using a dedicated cell delivery catheter.

Arm title	placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Cardio-cell placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intracoronary use

Dosage and administration details:

Patients randomized to the placebo group: 0.9% NaCl and 5% albumin injections (in the same volumes as CardioCell) via the coronary arter(ies)/bypass grafts. The CardioCell and placebo are distributed encoded, in an indistinguishable form.

Number of subjects in period 1[1]	active group	placebo
Started	70	35
Completed	67	33
Not completed	3	2
Adverse event, serious fatal	2	2
Lost to follow-up	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 10 patients were enrolled as a pilot cohort according to protocol

Baseline characteristics

End points

End points reporting groups	
Reporting group title	active group
Reporting group description: -	
Reporting group title	placebo
Reporting group description: -	

Primary: IS of the LV muscle (cMRI) change1	
End point title	IS of the LV muscle (cMRI) change1
End point description: IS (infarct size) of the LV (left ventricle) muscle (cMRI) change between baseline and 6 months FU	
End point type	Primary
End point timeframe: baseline vs 6 months FU	

End point values	active group	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	29		
Units: percent				
median (inter-quartile range (Q1-Q3))	-6.36 (-11.46 to -2.41)	-9.54 (-19.93 to -4.74)		

Statistical analyses

Statistical analysis title	IS of the LV muscle (cMRI) change
Comparison groups	placebo v active group
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0171
Method	t-test, 2-sided

Secondary: IS of the LV muscle (SPECT) change	
End point title	IS of the LV muscle (SPECT) change
End point description: IS of the LV muscle (SPECT) change	
End point type	Secondary
End point timeframe: baseline vs 6 months FU	

End point values	active group	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	33		
Units: number				
median (inter-quartile range (Q1-Q3))	-1.0 (-6.0 to 2.0)	-1.0 (-9.50 to 3.00)		

Statistical analyses

Statistical analysis title	IS of the LV muscle (SPECT) change
Comparison groups	active group v placebo
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6478
Method	Wilcoxon (Mann-Whitney)

Secondary: LVEF (cMRI) change	
End point title	LVEF (cMRI) change
End point description: LVEF- left ventricle ejection fraction (cMRI- cardiac magnetic resonance) change between baseline and 6 months FU	
End point type	Secondary
End point timeframe: baseline vs 6 months FU	

End point values	active group	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	31		
Units: number				
median (inter-quartile range (Q1-Q3))	4.00 (-1.00 to 11.00)	6.00 (3.00 to 9.00)		

Statistical analyses

Statistical analysis title	LVEF (cMRI) change
Comparison groups	active group v placebo

Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3319
Method	Wilcoxon (Mann-Whitney)

Secondary: LVEF (SPECT) change

End point title	LVEF (SPECT) change
End point description: LVEF (left ventricle ejection fraction) (SPECT) change between baseline and 6 months FU	
End point type	Secondary
End point timeframe: baseline vs 6 months FU	

End point values	active group	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	33		
Units: number				
median (inter-quartile range (Q1-Q3))	3.00 (-2.00 to 7.00)	3.00 (-0.50 to 7.00)		

Statistical analyses

Statistical analysis title	LVEF (SPECT) change
Comparison groups	active group v placebo
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3965
Method	t-test, 2-sided

Secondary: LVEF (echo) change

End point title	LVEF (echo) change
End point description: LVEF- left ventricle ejection fraction (echo) change between baseline and 6 months FU	
End point type	Secondary
End point timeframe: baseline vs 6 months FU	

End point values	active group	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	33		
Units: number				
median (inter-quartile range (Q1-Q3))	3.50 (0.25 to 8.00)	7.00 (1.50 to 10.00)		

Statistical analyses

Statistical analysis title	LVEF (echo) change
Comparison groups	active group v placebo
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2067
Method	t-test, 2-sided

Secondary: Death, MI and/or hospitalization for HF - up to 365 days after procedure	
End point title	Death, MI and/or hospitalization for HF - up to 365 days after procedure
End point description: Death, MI (myocardial infarct) and/or hospitalization for HF - up to 365 days after procedure	
End point type	Secondary
End point timeframe: baselien vs 6 months FU	

End point values	active group	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	35		
Units: number	5	5		

Statistical analyses

Statistical analysis title	Death, MI and/or hospitalization for HF during obs
Comparison groups	active group v placebo

Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2953
Method	Fisher exact

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported in patients from personal consent and study enrollment to last visit in the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	overall trial

Reporting group description: -

Serious adverse events	overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 105 (20.00%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	5		
Investigations			
Cardiac stress test abnormal			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Critical limb ischaemia			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac disorders			
Cardiac failure	Additional description: cardiac failure aggravated		
subjects affected / exposed	7 / 105 (6.67%)		
occurrences causally related to treatment / all	0 / 15		
deaths causally related to treatment / all	0 / 1		
Cardiac arrest			
subjects affected / exposed	3 / 105 (2.86%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 3		

Coronary artery disease progression	Additional description: Coronary artery disease progression		
subjects affected / exposed	2 / 105 (1.90%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
ventricular arrhythmia			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
unstable angina			
subjects affected / exposed	3 / 105 (2.86%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Ischemic stroke			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Transient ischemic attack			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrointestinal bleeding			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute prerenal failure			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bacterial sepsis			

subjects affected / exposed	1 / 105 (0.95%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	58 / 105 (55.24%)		
Cardiac disorders			
ICD implantation			
subjects affected / exposed	11 / 105 (10.48%)		
occurrences (all)	11		
planned PCI	Additional description: planned PCI performed prior to study procedure		
subjects affected / exposed	17 / 105 (16.19%)		
occurrences (all)	17		
planned carotid artery stenting			
subjects affected / exposed	3 / 105 (2.86%)		
occurrences (all)	3		
left ventricle thrombus			
subjects affected / exposed	3 / 105 (2.86%)		
occurrences (all)	3		
mil arrythmia			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	2		
chest pain			
subjects affected / exposed	3 / 105 (2.86%)		
occurrences (all)	4		
control angiography			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	2		
heart failure optimalisation			
subjects affected / exposed	4 / 105 (3.81%)		
occurrences (all)	4		
hypotonia and fainting			

subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	2		
pericardial effusion			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	2		
poor blood pressure control			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Gastrointestinal disorders			
cholelithiasis causing bilious colic			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
diarrhoea			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
pneumonia			
subjects affected / exposed	3 / 105 (2.86%)		
occurrences (all)	3		
Skin and subcutaneous tissue disorders			
rash	Additional description: rash after procedure		
subjects affected / exposed	3 / 105 (2.86%)		
occurrences (all)	3		
Epistaxis			
subjects affected / exposed	2 / 105 (1.90%)		
occurrences (all)	2		
hematoma on thigh			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		
Renal and urinary disorders			
Urinary tract infection			
subjects affected / exposed	3 / 105 (2.86%)		
occurrences (all)	3		
vaginal bleeding			
subjects affected / exposed	1 / 105 (0.95%)		
occurrences (all)	1		

urinary retention subjects affected / exposed occurrences (all) Nephropathy subjects affected / exposed occurrences (all) Renal colic subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1 1 / 105 (0.95%) 1 1 / 105 (0.95%) 1		
Endocrine disorders Diabetes mellitus inadequate control subjects affected / exposed occurrences (all)	2 / 105 (1.90%) 2		
Musculoskeletal and connective tissue disorders Chills subjects affected / exposed occurrences (all) Fracture of left fibula subjects affected / exposed occurrences (all)	Additional description: chills after study procedure 7 / 105 (6.67%) 7 1 / 105 (0.95%) 1		
Infections and infestations mild/moderate infection subjects affected / exposed occurrences (all)	4 / 105 (3.81%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 July 2017	Version 2.0 - following the decision to split CIRCULATE project into three separate clinical trials a version of the protocol was prepared in which the investigated medical condition was acute myocardial infarction (AMI).
12 February 2019	Version 3.0- data of new study sites was added, description of study catheter was clarified, information about additional blood collections was added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported