Clinical trial results:
A multicentric controlled phase I / IIb study evaluating the safety and the efficacy of in vitro expanded peripheral blood CD34+ stem cells output by the StemXpand® Automated Process, and injected in patients with an acute myocardial infarction and a LVEF remaining below 50% versus standard of care.

Summary

EudraCT number	2014-001476-63
Trial protocol	SI
Global end of trial date	15 March 2024

Results information

Result version number	v1 (current)
This version publication date	25 February 2026
First version publication date	25 February 2026

Trial information

Trial identification

Sponsor protocol code	2014-001476-63

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02669810
WHO universal trial number (UTN)	-
Other trial identifiers	VHP process: VHP590 (VHP2014137), VHP process: VHP677 (VHP2015065)

Notes:

Sponsors

Sponsor organisation name	CellProthera
Sponsor organisation address	12 rue du Parc , Mulhouse, France, 68100
Public contact	CellProthera SAS, CELLPROTHERA S.A.S, +33 369719771, medical@cellprothera.com
Scientific contact	CellProthera SAS, CELLPROTHERA S.A.S, +33 369719771, medical@cellprothera.com

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	19 June 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 March 2024
Global end of trial reached?	Yes
Global end of trial date	15 March 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the incidence of blindly adjudicated major adverse cardiac events (MACE)

Protection of trial subjects:

The investigator affirms and upholds the principle of the patient's right to privacy. The investigators shall comply with applicable privacy laws. The investigator must assure that the patient’s anonymity will be maintained and that the identities are protected from unauthorized parties. The investigator should maintain documents in strict confidence. On eCRFs and other documents, patients should not be identified by their names. All clinical and scientific data are collected under an identification code plus investigational centre number, and stored in the main clinical trial database. Individual-related data (the patient’s name and address) are linked to the code in a separate patient identification list field in the investigator site file, which is used only for identifying the patient and matching to the ProtheraCytes® batch and for sending Quality of Life questionnaires during the follow up period.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 February 2016
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: 17
Country: Number of subjects enrolled	France: 60
Worldwide total number of subjects	77
EEA total number of subjects	60

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)	46
From 65 to 84 years	31
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening echography and cMRI scheduled at D8 (±3) post AMI. A mini mental state examination (MMSE) must be performed for patients aged 75-85 years old. Persistent LVEF <50%, identification of LV Segments both non-viable, and akinetic/dyskinetic. Biological analyses and serology for the purpose of inclusion/non-inclusion criteri

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	ProtheraCytes

Arm description:

The interventional investigators will perform the ProtheraCytes® cardiac injections using a catheter introduced via the femoral route up to the left ventricle cavity for intraventricular injections (Helix/Biocardia).

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

Dosage and administration details:

Dosage : CD34+ Cells Count : ≥ 0.76 x 107
Administration : The intraventricular injection will be performed using the Helical™ catheter introduced via the femoral route up to the left ventricle cavity. The administration of the 15 (fifteen) injections – of 1 mL each – will be performed under loco-regional anaesthesia.

Arm title	Standard Of Care

Arm description:

Patients will be treated as standard treatment for Chronic Heart Failure post - AMI.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	ProtheraCytes	Standard Of Care
Started	61	16
Completed	33	16
Not completed	28	0
Consent withdrawn by subject	4	-
Adverse event, non-fatal	5	-
Manufacturing failure	13	-

Lost to follow-up	1	-
Serious Adverse Event	2	-
Serology	1	-
Wall thickness	2	-

Baseline characteristics

Reporting groups	
Reporting group title	ProtheraCytes
Reporting group description:	
The interventional investigators will perform the ProtheraCytes® cardiac injections using a catheter introduced via the femoral route up to the left ventricle cavity for intraventricular injections (Helix/Biocardia).	
Reporting group title	Standard Of Care
Reporting group description:	
Patients will be treated as standard treatment for Chronic Heart Failure post - AMI.	

Reporting group values	ProtheraCytes	Standard Of Care	Total
Number of subjects	61	16	77
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)	38	8	46
From 65-84 years	23	8	31
85 years and over	0	0	0
Adults	0	0	0
Gender categorical Units: Subjects			
Female	8	3	11
Male	53	13	66

Subject analysis sets	
Subject analysis set title	Per Protocol Safety Set (PPSS)
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients who were randomized AND for patients randomized to the ProtheraCytes® arm – who received transendocardial injection of ProtheraCytes	

Reporting group values	Per Protocol Safety Set (PPSS)		
Number of subjects	49		
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)	33		
From 65-84 years	16		
85 years and over	0		
Adults	0		
Gender categorical Units: Subjects			
Female	13		
Male	42		

End points

End points reporting groups

Reporting group title	ProtheraCytes

Reporting group description:

The interventional investigators will perform the ProtheraCytes® cardiac injections using a catheter introduced via the femoral route up to the left ventricle cavity for intraventricular injections (Helix/Biocardia).

Reporting group title	Standard Of Care

Reporting group description:

Patients will be treated as standard treatment for Chronic Heart Failure post - AMI.

Subject analysis set title	Per Protocol Safety Set (PPSS)
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients who were randomized AND for patients randomized to the ProtheraCytes® arm – who received transendocardial injection of ProtheraCytes

Primary: Incidence of Majors Cardiacs Events

End point title	Incidence of Majors Cardiacs Events[1]

End point description:

Incidence of MACE which have been adjudicated and confirmed to be MACE by an independent and blinded CEC from randomization up to 6 months in both treatments arms.

End point type	Primary

End point timeframe:

Randomization up to 6 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No-comparative study :

This proportion will be given with its associated exact confidence interval, based on the binomial distribution. The proportion of adverse event will also be given in the controlgroup. It must be stressed that no formal comparison (i.e. implying a statistical test), will be used to compare the two groups. Indeed, since the study is a phase I/II trial, it is not meant to provide a formal superiority or non-inferiority test and then is not powered for such a comparison

End point values	ProtheraCytes	Standard Of Care	Per Protocol Safety Set (PPSS)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	33	16	49	
Units: %	10	3	13	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Any important adverse events occurring from the time of signing of the informed consent, throughout the screening period and clinical trial, up to and including the last visit at M6.

Adverse event reporting additional description:

AE and SAE are reported as : Treatment Emergent Adverse Event
For the SoC arm, a TEAE is any AE that occurred after randomization to the SoC arm.
For the ProtheraCytes® arm, a TEAE is any AE that occurred during or after the first administration of ProtheraCytes

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25

Reporting groups

Reporting group title	PPSS Population

Reporting group description: -

Serious adverse events	PPSS Population		
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 49 (48.98%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
All Vascular disorders			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
All Cardiac Disorders			
subjects affected / exposed	16 / 49 (32.65%)		
occurrences causally related to treatment / all	1 / 22		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
All Surgical and medical procedures			
subjects affected / exposed	7 / 49 (14.29%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

All Nervous Systeme disorders			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
All General disorders and administration site conditions			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
All Gastrointestinal disorders			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
All Respiratory, thoracic and mediastinal disorders			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
All Psychiatric disorders			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
All Renal and urinary disorders			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
All Musculoskeletal and connective tissue disorders			

subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
All Infections and infestations			
subjects affected / exposed	1 / 49 (2.04%)		
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	PPSS Population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 49 (67.35%)		
Vascular disorders			
All Vascular Disorders			
subjects affected / exposed	7 / 49 (14.29%)		
occurrences (all)	7		
General disorders and administration site conditions			
All General disorders and administration site conditions			
subjects affected / exposed	3 / 49 (6.12%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders			
All Respiratory, thoracic and mediastinal disorders			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	5		
Psychiatric disorders			
All Psychiatric disorders			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences (all)	1		
Cardiac disorders			
All Cardiac Disorders			
subjects affected / exposed	3 / 49 (6.12%)		
occurrences (all)	6		
Nervous system disorders			

All Nervous system disorders subjects affected / exposed occurrences (all)	3 / 49 (6.12%) 3		
Blood and lymphatic system disorders All Blood and lymphatic system disorders subjects affected / exposed occurrences (all)	2 / 49 (4.08%) 2		
Eye disorders All Eye disorders subjects affected / exposed occurrences (all)	1 / 49 (2.04%) 1		
Gastrointestinal disorders All Gastrointestinal disorders subjects affected / exposed occurrences (all)	1 / 49 (2.04%) 1		
Renal and urinary disorders All Renal and urinary disorders subjects affected / exposed occurrences (all)	1 / 49 (2.04%) 2		
Musculoskeletal and connective tissue disorders All Musculoskeletal and connective tissue disorders subjects affected / exposed occurrences (all)	3 / 49 (6.12%) 3		
Infections and infestations All infections and infestations subjects affected / exposed occurrences (all)	8 / 49 (16.33%) 9		
Metabolism and nutrition disorders All Metabolism and nutrition disorders subjects affected / exposed occurrences (all)	2 / 49 (4.08%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 March 2017	Feasibility Relaxing calendar constraints for the limit date for the screening phase Concomitant treatments Request, if possible, for ICD implantation location on the right side of the body in order to limit CMR artifact Inclusion criteria Patient's upper limit age increased from 75 to 80
05 November 2019	Trial management Subcontracting vigilance, data management, statistics and monitoring activities to CROs Assessment 99mTc-SPECT became optional Patient profile The assessment of non-viable segments is performed by CMR instead of SPECT Data analysis Addition of the two intermediate analyses at about 1/3 and 2/3 of the recruitment
17 September 2020	Trial Management Constitution of the study steering committee Patient profile AMI not limited to anterior location any more Stenting not mandatory any more Addition of Troponin peak >70x ULN inclusion criteria in order to limit the rate of screen failures FEVG threshold increased from 45% to 50% Patient's upper limit age increased from 80 to 85 Feasibility Relaxing calendar constraints up to two months post AMI for the limit date of ProtheraCytes® injection Switch from split G-CSF half doses of 5 µg/kg to a single dose of 10 µg/kg/day
02 August 2021	Safety Urgent safety measure adding mandatory Echography for monitoring pericardial effusion after the transendocardial injection procedure

21 October 2021	Safety Safety Leukocytosis threshold for G-CSF dose cancellation increased form 50G/L to 60 G/L Inclusion criteria Clarification of the definition of non-viable segment combining transmurality >50% and akinesia/dyskinesia Possibility to enroll non reperfused patients and patients who healed from Hepatitis B Initial investigational product specifications CD34+ cell count change from "≥ 10x106" to "≥ 8x106" Purity change from "≥ 85%" to "≥ 80%" Monocytes changes from "≤ 10%" to "≤ 15%"
12 April 2022	Study design Change of the randomization ratio from 3:1 to 7:1 after the completion of the Standard of Care arm Assessment Constitution of the CEC for the adjudication of MACE Feasibility Relaxing calendar constraint for randomization from 14 days to 28 days
27 March 2023	Study procedure Adding the possibility to treat via the intracoronary delivery pathway the patients diagnosed pre-injection with LV thrombus without impacting the power of the study, the required number of patients injected transendocardially remaining the same. Patients intracoronarly injected will not be analyzed per protocol. Feasibility Relaxing calendar constraints for the pre-injection CMR pathway to R15 (±2) for facilitating the pre-injection detection of LV thrombus Product specification update: CD34+ Cell Count changes from "≥ 8x106" to "≥ 7.6x106" Purity changes from "≥ 85%" to "≥ 76%" Viability changes from ">95%" to "≥ 90%"

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
02 July 2018	Interruption following an inspection by the competent authorities	05 November 2019

Notes:

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/39676512

http://www.ncbi.nlm.nih.gov/pubmed/40929748