Clinical trial results:
A randomized, prospective, double-blind study with placebo to evaluate the efficacy of treatment of patients with angina resistant to pharmacological treatment and induced myocardial ischemia without possibility of effective revascularization, using isolated from bone marrow, autological CD133+ cells administered directly into the muscle of left ventricle. REGENT-VSEL Study.

Summary

EudraCT number	2011-005435-98
Trial protocol	PL
Global end of trial date	05 September 2016

Results information

Result version number	v1 (current)
This version publication date	25 April 2022
First version publication date	25 April 2022
Summary attachment (see zip file)	Circ Res Publication (CIRCRESAHA.116.309009.pdf) secondary publication (58991-161719-3-PB (1).pdf)

Trial information

Trial identification

Sponsor protocol code	version_2.0_dated_19.04.2011

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01660581
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Śląski Uniwersytet Medyczny W Katowicach
Sponsor organisation address	Poniatowskiego 15, Katowice, Poland,
Public contact	Katarzyna Bigosińska , Śląski Uniwersytet Medyczny W Katowicach, 48 322088804, kbigosinska@sum.edu.pl
Scientific contact	Wojciech Wojakowski, III Division of Cardiology, 48 322523930, wwojakowski@sum.edu.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	01 November 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 September 2015
Global end of trial reached?	Yes
Global end of trial date	05 September 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

1. Assessment of influence of direct administration of isolated from bone marrow, autological CD133+ cells on improvement of myocardial perfusion and function and decrease of occurrence of symptomatic angina of patients with angina resistant to pharmacological treatment without possibility of effective revascularization
2. Assessment of therapy safety

Protection of trial subjects:

personal data protection, during each invasive procedure appropriate local or general anesthesia was used, patients had access to 27/4 emergency consulting

Background therapy:

Maximum tolerated doses of angina pharmacotherapy for at least 2 weeks
Seconadary prevention of CAD (statins), beta blockers or CCB, Antihypertensive therapy when appropriate
Revascularization

Evidence for comparator: -

Actual start date of recruitment	15 April 2012
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: 31
Worldwide total number of subjects	31
EEA total number of subjects	31

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)	12
From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The screening was based on angina symptoms according to the CCS classification and validated by stress test when applicable.

Pre-assignment

Screening details:

90 pateints with refractory angina screened, 52 did not meet inclusion criteria, 7 declined

Period 1

Period 1 title	period 1 (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	active

Arm description:

CD133+ cells

Arm type	Experimental
Investigational medicinal product name	CD133+ cells
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Injection

Dosage and administration details:

The dosing ranges were 2.8×106 and 5.3×106 cells

Arm title	control

Arm description:

placebo

Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Injection

Dosage and administration details:

placebo - equal volume to active arm

Number of subjects in period 1	active	control
Started	16	15
Completed	16	15

Baseline characteristics

Reporting groups	
Reporting group title	period 1

Reporting group description: -

Reporting group values	period 1	Total	
Number of subjects	31	31	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	12	12	
From 65-84 years	19	19	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	8	8	
Male	23	23	

End points

End points reporting groups

Reporting group title	active
Reporting group description: CD133+ cells	
Reporting group title	control
Reporting group description: placebo	

Primary: change of myocardial perfusion by 99mTc-MIBI SPECT at 4 months after cell/placebo injection

End point title	change of myocardial perfusion by 99mTc-MIBI SPECT at 4 months after cell/placebo injection
End point description:	
End point type	Primary
End point timeframe: 4 months after treatment	

End point values	active	control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	15		
Units: numner of ischemic segments	16	15		

Statistical analyses

Statistical analysis title	statistical analysis

Statistical analysis description:

All analyses were performed according to the intention-to-treat scheme. Categorical variables were presented as numbers and percentages. Continuous variables were expressed as mean±standard deviation (SD) or median and interquartile range. Differences between groups were compared using the Student’s or the Welch’s t test depending on the equality of variances for normally distributed variables. The MannWhitney U test was used for non-normally distributed continuous variables. Normality was asses

Comparison groups	active v control
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
12 months	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10

Reporting groups	
Reporting group title	placebo
Reporting group description: -	
Reporting group title	active
Reporting group description: -	

Serious adverse events	placebo	active	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 15 (13.33%)	3 / 16 (18.75%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Femoral artery aneurysm			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	2 / 15 (13.33%)	3 / 16 (18.75%)	
occurrences causally related to treatment / all	2 / 2	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
unstable angina			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
acute back pain			

subjects affected / exposed	0 / 15 (0.00%)	1 / 16 (6.25%)	
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: 5 %

Non-serious adverse events	placebo	active	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	
Ear and labyrinth disorders			
transient vertigo month after procedure			
subjects affected / exposed	1 / 15 (6.67%)	0 / 16 (0.00%)	
occurrences (all)	1	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

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

none

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27903568

http://www.ncbi.nlm.nih.gov/pubmed/30211929