Clinical trial results:
CD133 + CELL INFUSION IN PATIENTS WITH COLORECTAL LIVER ORIGIN METASTASES GOING TO BE SUBMITTED TO A MAJOR LIVER RESECTION

Summary

EudraCT number	2014-001402-18
Trial protocol	ES
Global end of trial date	31 December 2020

Results information

Result version number	v1 (current)
This version publication date	16 March 2022
First version publication date	16 March 2022

Trial information

Trial identification

Sponsor protocol code	CIR-MSC-2014-01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Alejandra García Botella
Sponsor organisation address	Profesor Martín Lagos s/n, Madrid, Spain, 28040
Public contact	UICEC, Fundación para la investigación biomédica del Hospital Clínico San Carlos, 0034 9133030003793, fibucicec.hcsc@salud.madrid.org
Scientific contact	UICEC, Fundación para la investigación biomédica del Hospital Clínico San Carlos, 0034 9133030003793, fibucicec.hcsc@salud.madrid.org

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	21 September 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the effectiveness of preoperative portal embolization with administration of single liver CD133 + cells mobilized with G-CSF compared to portal embolization

Protection of trial subjects:

Follow up for 24 months after the surgery and cell infusion

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2014
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	Spain: 4
Worldwide total number of subjects	4
EEA total number of subjects	4

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)	1
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment
Recruitment details:
Recruitment started on September 2014 and finished on December 2020

Pre-assignment
Screening details: -

Pre-assignment period milestones	
Number of subjects started	4
Number of subjects completed	4

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

Arms	
Are arms mutually exclusive?	Yes
Arm title	CD133+ stem cells
Arm description:	
CD133+ cells administration prior to portal vein embolization (PVE)	
Arm type	Experimental
Investigational medicinal product name	STEM CELLS PERIPHERAL BLOOD ENDOTHELIAL AUTOLOGOUS NOT EXPANDED
Investigational medicinal product code	CD133+
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intraportal use
Dosage and administration details:	
A dose in beteween 4 and 140x10^6 organisms administrated directly into intraportal vein	
Arm title	Portal Vein embolization
Arm description:	
Just portal vein embolization without cells administration	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	CD133+ stem cells	Portal Vein embolization
Started	3	1
Completed	3	1

Baseline characteristics

Reporting groups	
Reporting group title	Treatment

Reporting group description: -

Reporting group values	Treatment	Total	
Number of subjects	4	4	
Age categorical Units: Subjects			
Adults (18-64 years)	1	1	
From 65-80 years	3	3	
Gender categorical Units: Subjects			
Female	3	3	
Male	1	1	

End points

End points reporting groups

Reporting group title	CD133+ stem cells
Reporting group description:	
CD133+ cells administration prior to portal vein embolization (PVE)	
Reporting group title	Portal Vein embolization
Reporting group description:	
Just portal vein embolization without cells administration	
Subject analysis set title	Intention to treat
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
There were few patients included and no one in the PVE arm, so it was no possible to perform the comparison of groups	

Primary: Evaluate the effectiveness of preoperative portal embolization with administration of single liver CD133 + cells mobilized with G-CSF compared to portal embolization

End point title	Evaluate the effectiveness of preoperative portal embolization with administration of single liver CD133 + cells mobilized with G-CSF compared to portal embolization
End point description:	
End point type	Primary
End point timeframe:	
Before embolization, after embolization site after surgery. The first control after PVE was performed at 2 weeks and repeated every 2 weeks until surgery. After surgery monthly until month 24 (1,3,6,12,18,24).	

End point values	CD133+ stem cells	Portal Vein embolization		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	1[1]		
Units: Liver volumes (in cubic centimeters, cc)				
number (not applicable)	3	1		

Notes:

[1] - The patient assignes to this arm, was not treated dut to an adverse event

Statistical analyses

Statistical analysis title	Comparation of hepatic volumes
Statistical analysis description:	
The differences between the volume means of both groups were compared with the Student-Fisher t-test after verifying the normality of the samples (using the Shapiro-Wilk normality test), or using the Mann-Whitney U-test otherwise.	
Comparison groups	CD133+ stem cells v Portal Vein embolization

Number of subjects included in analysis	4
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	≤ 0.05 [3]
Method	Chi-squared
Parameter estimate	Mean difference (final values)
Point estimate	60
Confidence interval	
level	90 %
sides	1-sided
lower limit	40

Notes:

[2] - There were no patients in the PVE arm, so it was no possible to perform the comparison of groups

[3] - There were no patients in the PVE arm, so it was no possible to perform the comparison of groups

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Since the signing of the ICF until last sudy visit of the patient.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Experimental Arm

Reporting group description: -

Serious adverse events	Experimental Arm		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Extradural haematoma			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Gastrointestinal disorders			
Abdominal abscess			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastric ischaemia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	Experimental Arm		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)		
Vascular disorders			
Post procedural haemorrhage			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Infected skin ulcer			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 July 2015	Clarification about dose of cells Changes in inclusion ans exclusion criterias
31 August 2015	Identification of the entity in charged of the monitorization Clarification of the primary outcome
26 April 2017	Specification about period of window of the study visits and procedures Changes in the administrated dose

Notes:

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.

There were few patients included in the study, just 4, and the one patient assigned to PVE was not treated due to adverse event. So it was not possible to compare the results in between both arms nor to achieve valid conclusions.

Notes: