Clinical trial results:
Randomized Phase II Study With Dendritic Cell Immunotherapy in Patients With Resected Hepatic Metastasis of Colorectal Carcinoma

Summary

EudraCT number	2008-007795-23
Trial protocol	ES
Global end of trial date	23 November 2021

Results information

Result version number	v1 (current)
This version publication date	27 August 2022
First version publication date	27 August 2022

Trial information

Trial identification

Sponsor protocol code	CD-2009-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01348256
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Clinica Universidad de Navarra
Sponsor organisation address	AVENIDA PÍO XII, Nº 36, PAMPLONA/IRUÑA, Spain, 31008
Public contact	UCEC, Clínica Universidad de Navarra, 34 948 255 400, ucicec@unav.es
Scientific contact	UCEC, Clínica Universidad de Navarra, 34 948 255 400, ucicec@unav.es

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	30 April 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 August 2016
Global end of trial reached?	Yes
Global end of trial date	23 November 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Progression Free survival

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 November 2010
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: 15
Worldwide total number of subjects	15
EEA total number of subjects	15

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)	15
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

15 patients of 18 and older were randomized. 8 in DC vaccine group and 7 at Observation group.

Pre-assignment

Screening details:

The original number patients could not be achieved due budget restrictions that forced an early termination of recruitment, when only 19 patients had signed informed consent. Three of the patients were excluded for evaluation due to positive resection margins following neoadjuvant chemotherapy and surgery and one patient withdrew informed consent.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	No Intervention: Observation

Arm description:

Observation after standard treatment.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Experimental: Dendritic cells vaccine

Arm description:

Adjuvant treatment with dendritic cells vaccine after standard treatment.

Arm type	Experimental
Investigational medicinal product name	Dendritic cells vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intradermal use

Dosage and administration details:

Mature dendritic cells pulsed with autologous tumor lysate were administered intradermally in two or three series (depending on cell availability) of 4 injections (1 per day), spaced 21 to 44 days apart. The expected dose of dendritic cells was 5,000,000, resuspended in 1-2 ml of physiological saline.

Number of subjects in period 1	No Intervention: Observation	Experimental: Dendritic cells vaccine
Started	7	8
Completed	7	8

Baseline characteristics

Reporting groups	
Reporting group title	Treatment period.

Reporting group description: -

Reporting group values	Treatment period.	Total	
Number of subjects	15	15	
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)	11	11	
From 65-84 years	4	4	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	7	7	
Male	8	8	

End points

End points reporting groups

Reporting group title	No Intervention: Observation
Reporting group description: Observation after standard treatment.	
Reporting group title	Experimental: Dendritic cells vaccine
Reporting group description: Adjuvant treatment with dendritic cells vaccine after standard treatment.	

Primary: Disease Free Survival

End point title	Disease Free Survival[1]
End point description:	
End point type	Primary
End point timeframe: Follow-up was performed every 12 weeks (range 11– 14 weeks) ever since surgical treatment by contrast abdominal CT scans.	

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: Survival curves were compared based on the Kaplan Meier estimates. A log rank test was used in order to calculate the difference between curves.
All calculations were performed with STATA v.14 statistical package (StataCorp 2015).

* 99999=N.R. (Intervention group: Superior limit of 95% C.I . was N.R.)

End point values	No Intervention: Observation	Experimental: Dendritic cells vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	8		
Units: month				
median (confidence interval 95%)	9.53 (5.32 to 18.88)	25.26 (8.74 to 99999)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From patient recruitment to trial exit.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	No Intervention: Observation
Reporting group description: -	
Reporting group title	Experimental: Dendritic cells vaccine
Reporting group description: -	

Serious adverse events	No Intervention: Observation	Experimental: Dendritic cells vaccine	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 7 (28.57%)	2 / 8 (25.00%)	
number of deaths (all causes)	2	1	
number of deaths resulting from adverse events			
Surgical and medical procedures			
Hepatectomy			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pyrexia			

subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
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	No Intervention: Observation	Experimental: Dendritic cells vaccine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 7 (57.14%)	5 / 8 (62.50%)	
Injury, poisoning and procedural complications			
Wound complication			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Muscle strain			

subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Epistaxis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Neurotoxicity			
subjects affected / exposed	1 / 7 (14.29%)	2 / 8 (25.00%)	
occurrences (all)	1	2	
Paraesthesia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Leukopenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Neutropenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 7 (28.57%)	1 / 8 (12.50%)	
occurrences (all)	3	1	
Fatigue			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	

Oedema peripheral			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	2 / 7 (28.57%)	0 / 8 (0.00%)	
occurrences (all)	3	0	
Decreased appetite			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Induration			
subjects affected / exposed	0 / 7 (0.00%)	3 / 8 (37.50%)	
occurrences (all)	0	6	
Mucosal inflammation			
subjects affected / exposed	2 / 7 (28.57%)	1 / 8 (12.50%)	
occurrences (all)	4	1	
Injection site rash			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Xerosis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	
occurrences (all)	4	1	
Dysgeusia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Abdominal discomfort			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	2 / 7 (28.57%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
Haemorrhoidal haemorrhage			

subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Aphonia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Productive cough			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 7 (14.29%)	2 / 8 (25.00%)	
occurrences (all)	1	2	
Rash			
subjects affected / exposed	2 / 7 (28.57%)	1 / 8 (12.50%)	
occurrences (all)	3	1	
Skin ulcer			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Dry skin			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Nail disorder			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Nocturia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			

Depression			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Paronychia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 June 2010	Modifications in protocol and HIP.
15 April 2011	Reduction in the number of patients.
16 October 2012	Sponsor change.
01 January 2013	Leaving from CAIBER.
05 July 2013	Modification of IMPD.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
16 July 2018	Temporary halt in recruitment due to lack of funding while new sources of funding were sought to continue recruiting.	-

Notes:

Limitations and caveats

None reported