Clinical trial results:
Albumin infusion effects in patients with cirrhosis hepatic encephalopathy

Summary

EudraCT number	2014-004809-33
Trial protocol	ES
Global end of trial date	08 June 2020

Results information

Result version number	v1 (current)
This version publication date	06 November 2021
First version publication date	06 November 2021

Trial information

Trial identification

Sponsor protocol code	BETA

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02401490
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	VHIR
Sponsor organisation address	Passeig Vall Hebron 119-129, Barcelona, Spain, 08035
Public contact	Joaquin Lopez-Soriano, VHIR, joaquin.lopez.soriano@vhir.org
Scientific contact	Inmaculada Fuentes, VHIR-Unitat de Suport a la Investigació Clínica (USIC), usic@vhir.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	Interim
Date of interim/final analysis	08 June 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 June 2020
Global end of trial reached?	Yes
Global end of trial date	08 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess whether albumin administration after an episode of hepatic encephalopathy improves survival at 90 days (mortality endpoint treated as a composite endpoint death and/ or liver transplantation).

Protection of trial subjects:

The underlying HE cause was properly addressed according to guidelines. Moreover, laxative treatment was administered

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 March 2015
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: 82
Worldwide total number of subjects	82
EEA total number of subjects	82

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)	40
From 65 to 84 years	42
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	82
Number of subjects completed	82

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Albumin

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Albumin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

The first dose was administered within the first 48 hours of admission with an HE grade ≥2 (1.5g/kg of albumin or the equivalent milliliter of saline solution). The second dose (1g/kg of albumin or the equivalent milliliters of saline solution) was administered 48 to 72 hours after the first administration. Both doses where adjusted according to ideal weight and infused at 5ml/hour.

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

The first dose was administered within the first 48 hours of admission with an HE grade ≥2 (the equivalent milliliter of saline solution to 1.5g/kg of albumin). The second dose (the equivalent milliliters of saline solution to 1g/kg of albumin) was administered 48 to 72 hours after the first administration. Both doses where adjusted according to ideal weight and infused at 5ml/hour.

Number of subjects in period 1	Albumin	Placebo
Started	41	41
Completed	41	40
Not completed	0	1
Consent withdrawn by subject	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	82	82	
Age categorical Units: Subjects			
Adults (18-64 years)	40	40	
From 65-84 years	42	42	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	27	27	
Male	55	55	

End points

End points reporting groups	
Reporting group title	Albumin
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Survival at 180 days	
End point title	Survival at 180 days
End point description:	
End point type	Primary
End point timeframe:	
180 days	

End point values	Albumin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: percent				
number (not applicable)	78.7	67.8		

Statistical analyses

Statistical analysis title	Survival 180 days
Comparison groups	Placebo v Albumin
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.2413
Method	Chi-squared

Secondary: Survival at 90 days	
End point title	Survival at 90 days
End point description:	
End point type	Secondary
End point timeframe:	
90 days	

End point values	Albumin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	40		
Units: percent				
number (not applicable)	87.36	80.49		

Statistical analyses

Statistical analysis title	Survival 90 days
Comparison groups	Albumin v Placebo
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.38
Method	Chi-squared

Adverse events

Adverse events information

Timeframe for reporting adverse events:

End of study

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Albumin
Reporting group description: -	
Reporting group title	Placebo

Reporting group description: -

Serious adverse events	Albumin	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 40 (22.50%)	26 / 40 (65.00%)	
number of deaths (all causes)	14	19	
number of deaths resulting from adverse events	0	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 40 (7.50%)	2 / 40 (5.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 40 (2.50%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic encephalopathy			
subjects affected / exposed	9 / 40 (22.50%)	11 / 40 (27.50%)	
occurrences causally related to treatment / all	0 / 9	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatorenal syndrome			

subjects affected / exposed	4 / 40 (10.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	3 / 40 (7.50%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular carcinoma			
subjects affected / exposed	3 / 40 (7.50%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 40 (2.50%)	3 / 40 (7.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 40 (0.00%)	2 / 40 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Peritonitis bacterial			
subjects affected / exposed	1 / 40 (2.50%)	2 / 40 (5.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 40 (0.00%)	3 / 40 (7.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Albumin	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 40 (85.00%)	11 / 40 (27.50%)	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 40 (10.00%)	5 / 40 (12.50%)	
occurrences (all)	4	5	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 40 (10.00%)	1 / 40 (2.50%)	
occurrences (all)	4	1	
Hepatobiliary disorders			
Hepatic encephalopathy			
subjects affected / exposed	9 / 40 (22.50%)	9 / 40 (22.50%)	
occurrences (all)	12	12	
Ascites			
subjects affected / exposed	13 / 40 (32.50%)	4 / 40 (10.00%)	
occurrences (all)	13	4	
Hepatocellular carcinoma			
subjects affected / exposed	4 / 40 (10.00%)	2 / 40 (5.00%)	
occurrences (all)	4	2	
Hepatorenal syndrome			
subjects affected / exposed	3 / 40 (7.50%)	2 / 40 (5.00%)	
occurrences (all)	3	2	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	6 / 40 (15.00%)	2 / 40 (5.00%)	
occurrences (all)	6	2	
Acute kidney injury			
subjects affected / exposed	1 / 40 (2.50%)	5 / 40 (12.50%)	
occurrences (all)	1	5	
Urinary tract infection			
subjects affected / exposed	3 / 40 (7.50%)	3 / 40 (7.50%)	
occurrences (all)	3	3	
Metabolism and nutrition disorders			
Hyponatraemia			

subjects affected / exposed occurrences (all)	4 / 40 (10.00%) 4	2 / 40 (5.00%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 April 2015	Changes in the MELD score range from 15-25 to 14-30 was approved in order to increase recruitment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported