Clinical trial results:
Effects of long term albumin 20% administration on the cardiocirculatory and renal function, and hepatic hemodynamics in patients with advanced cirrhosis and ascites.

Summary

EudraCT number	2008-003920-40
Trial protocol	ES
Global end of trial date	02 April 2014

Results information

Result version number	v2 (current)
This version publication date	24 June 2023
First version publication date	17 October 2019
Version creation reason	• Correction of full data set No change in the data set. This version 2.0 was created by an error.

Trial information

Trial identification

Sponsor protocol code	IG0802

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00968695
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Instituto Grifols, S.A.
Sponsor organisation address	Can Guasch 2, Parets del Valles, Barcelona, Spain, 08150
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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	27 June 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Pharmacodynamics and pathophysiological study to assess the effects of prolonged administration of human albumin on cardiocirculatory and renal function and hepatic hemodynamics in subjects with advanced cirrhosis and ascites.

Protection of trial subjects:

Standards for Good Clinical Practice were adhered to for all procedures in this clinical study. The investigators ensured that the clinical study was conducted in full conformance with appropriate local laws and regulations and the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 September 2009
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: 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)	20
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Thirty-one subjects of both sexes, aged within 18 to 80 years of age with advance liver cirrhosis and ascites who gave their consent for participation, were included in this study.

Pre-assignment

Screening details:

Subjects of both sexes, aged 18 to 80 years, with advanced cirrhosis and ascites who gave their written informed consent to participate after being fully informed by the investigator were included in the trial. Subjects met all inclusion criteria and none of the exclusion criteria.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

This was an open-label study; therefore no blinding techniques were applicable.

Arms

Arm title	ITT Population

Arm description:

The Intention to Treat (ITT) Population was defined as the subset of subjects who received at least one dose of the study medication. The ITT Population was used for all efficacy and safety analyses.

Arm type	Experimental
Investigational medicinal product name	Albumin (Human Albumin Grifols 20% solution for infusion)
Investigational medicinal product code	B05AA01
Other name	Albutein 20%
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pre-interim analysis:
The pattern of administration of 20% human albumin was 1g/kg every 2 weeks with a dose minimum of 60g and a maximum of 100g in subjects weighing less than 60kg and more than 100kg, respectively.
Post-interim analysis:
The pattern of administration of 20% human albumin is 1.5g/kg every week with a minimum of 90g and a maximum of 150g in patients weighing less than 60kg and more than 100kg, respectively.

Treatment duration is 12 weeks, which includes 13 administrations of albumin.

Number of subjects in period 1	ITT Population
Started	31
Completed	13
Not completed	18
Eligibility criteria	5
Incorrect number of infusions	13

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study (overall period)

Reporting group description: -

Reporting group values	Overall Study (overall period)	Total	
Number of subjects	31	31	
Age categorical Units: Subjects			
Adults (18-64 years)	20	20	
From 65-84 years	11	11	
Age continuous Units: years			
arithmetic mean	61.4		
standard deviation	± 9.4	-	
Gender categorical Units: Subjects			
Female	10	10	
Male	21	21	

End points

End points reporting groups

Reporting group title	ITT Population

Reporting group description:

The Intention to Treat (ITT) Population was defined as the subset of subjects who received at least one dose of the study medication. The ITT Population was used for all efficacy and safety analyses.

Primary: Hemodynamic Parameters

End point title	Hemodynamic Parameters[1]

End point description:

Change in hemodynamic parameters from Baseline to Week 14 are described.

End point type	Primary

End point timeframe:

Baseline to Week 14

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 statistical analyses for this end point.

End point values	ITT Population			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: change from baseline				
least squares mean (standard error)				
Systolic blood pressure (mmHg)	-6.2 (± 3.0)			
Diastolic blood pressure (mmHg)	-0.1 (± 2.3)			
Mean arterial pressure (mmHg)	0.3 (± 2.2)			
Right auricular pressure (mmHg)	-0.2 (± 0.9)			
Pulmonary arterial pressure (mmHg)	-1.2 (± 1.4)			
Pulmonary capillary pressure (mmHg)	-1.4 (± 1.0)			
Heart rate (bpm)	-0.8 (± 2.9)			
Cardiac output (L/min)	-1.1 (± 0.4)			
Cardiac index (L.min-1.m-2)	-0.6 (± 0.2)			
Systolic volume (mL)	-19.2 (± 9.9)			
Systolic volume index (mL.m-2)	-14.1 (± 7.5)			
Systemic vascular resistance (dyn.s.cm-5)	78.0 (± 61.2)			
Systemic vascular resistance index(dyn.s.cm-5.m-2)	180.9 (± 72.4)			
Left ventricular cardiac work index (g.m/m2)	267.7 (± 391.7)			
Free suprahepatic pressure (mmHg)	2.1 (± 1.2)			
Suprahepatic pressure locked (mmHg)	1.5 (± 1.4)			
Hepatic venous pressure gradient (mmHg)	-0.6 (± 0.7)			
Hepatic blood flow (L/min-1)	-164 (± 238.1)			

Statistical analyses

No statistical analyses for this end point

Primary: Echocardiography Parameters

End point title	Echocardiography Parameters[2]

End point description:

Change in echocardiography parameters from Baseline to Week 14 and Week 20 are described.

End point type	Primary

End point timeframe:

Baseline to Week 14 and Week 20

Notes:

[2] - 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 statistical analyses for this end point.

End point values	ITT Population			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: change from baseline				
least squares mean (standard error)				
LV telediastolic diameter (cm) to Week 14	0.0 (± 0.1)			
LV telediastolic diameter (cm) to Week 20	-0.1 (± 0.2)			
LV telesystolic diameter (cm) to Week 14	-0.1 (± 0.1)			
LV telesystolic diameter (cm) to Week 20	0.0 (± 0.1)			
Interventricular septum thickness (cm) to Week 14	0.0 (± 0.0)			
Interventricular septum thickness (cm) to Week 20	0.0 (± 0.0)			
LV posterior wall thickness (cm) to Week 14	0.0 (± 0.0)			
LV posterior wall thickness (cm) to Week 20	0.0 (± 0.0)			
LV telediastolic volume (mL) to Week 14	6.1 (± 8.0)			
LV telediastolic volume (mL) to Week 20	9.3 (± 10.7)			
LV telesystolic volume (mL) to Week 14	-1.8 (± 3.3)			
LV telesystolic volume (mL) to Week 20	3.7 (± 4.6)			
LV ejection fraction (%) to Week 14	2.9 (± 1.6)			
LV ejection fraction (%) to Week 20	1.1 (± 2.0)			
Wall motion score index to Week 14	11.9 (± 4.4)			
Wall motion score index to Week 20	2.0 (± 5.7)			
Left ventricular mass (g) to Week 14	-5.1 (± 13.2)			
Left ventricular mass (g) to Week 20	14.2 (± 17.8)			

Anteroposterior diameter left-atrium (cm) Week 14	-0.4 (± 0.2)			
Anteroposterior diameter left-atrium (cm) Week 20	-0.5 (± 0.3)			
Early LV filling velocity (cm/s) to Week 14	-6.8 (± 4.8)			
Early LV filling velocity (cm/s) to Week 20	-1.8 (± 6.2)			
Late LV filling velocity (cm/s) to Week 14	-3.6 (± 3.8)			
Late LV filling velocity (cm/s) to Week 20	2.1 (± 4.8)			
Early diastolic mitral annular velocity (cm/s) W14	5.2 (± 4.3)			
Early diastolic mitral annular velocity (cm/s) W20	4.6 (± 4.6)			
Late diastolic mitral annular velocity (cm/s) W14	0.7 (± 1.0)			
Late diastolic mitral annular velocity (cm/s) W20	0.9 (± 1.2)			
Propagation velocity of flow-LV cavity Week 14	0.6 (± 8.4)			
Propagation velocity of flow-LV cavity Week 20	-11.9 (± 8.7)			
Systolic pulmonary venous flow velocity (cm/s) W14	1.0 (± 4.8)			
Systolic pulmonary venous flow velocity (cm/s) W20	10.3 (± 6.5)			
Diastolic pulmonary venous flow velocity(cm/s) W14	7.2 (± 5.4)			
Diastolic pulmonary venous flow velocity(cm/s) W20	9.5 (± 6.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Hormonal Parameters

End point title	Hormonal Parameters[3]

End point description:

Change in hormonal parameters from Baseline to Week 14 and to Week 20 are described.

End point type	Primary

End point timeframe:

Baseline to Week 14 and Week 20

Notes:

[3] - 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 statistical analyses for this end point.

End point values	ITT Population			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: change from baseline				
least squares mean (standard error)				
Plasma rennin activity (ng/mL/h) to Week 14	-1.3 (± 2.0)			
Plasma rennin activity (ng/mL/h) to Week 20	-1.6 (± 2.1)			
Noradrenaline (pg/mL) to Week 14	21.7 (± 113.9)			
Noradrenaline (pg/mL) to Week 20	71.9 (± 116.1)			

Statistical analyses

No statistical analyses for this end point

Primary: Isotopic Parameters

End point title	Isotopic Parameters[4]

End point description:

Change in isotopic parameters from Baseline to Week 14 are described.

End point type	Primary

End point timeframe:

Baseline to Week 14

Notes:

[4] - 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 statistical analyses for this end point.

End point values	ITT Population			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: change from baseline				
least squares mean (standard error)				
Renal blood flow (mL/min/m2)	11.2 (± 41.2)			
Glomerular filtration rate (mL/min/m2)	-2.1 (± 3.5)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Subjects were monitored from the time of the signature of the ICF to the end of the follow-up period (Week 20) for assessment of AEs.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	ITT Population

Reporting group description:

The Intention to Treat (ITT) Population was defined as the subset of subjects who received at least one dose of the study medication. The ITT Population was used for all efficacy and safety analyses.

Serious adverse events	ITT Population		
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 31 (54.84%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	5		
Injury, poisoning and procedural complications			
Osteoporotic fracture			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial tachycardia			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Neutropenia			

subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spur cell anaemia				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
General disorders and administration site conditions				
Oedema peripheral				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Wound secretion				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Gastrointestinal haemorrhage				
subjects affected / exposed	6 / 31 (19.35%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	0 / 1			
Incarcerated umbilical hernia				
subjects affected / exposed	2 / 31 (6.45%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

Abdominal incarcerated hernia				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastric disorder				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haematemesis				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Incarcerated inguinal hernia				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Melaena				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mesenteric vein thrombosis				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophagitis				
subjects affected / exposed	1 / 31 (3.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Umbilical hernia				

subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic encephalopathy			
subjects affected / exposed	9 / 31 (29.03%)		
occurrences causally related to treatment / all	0 / 12		
deaths causally related to treatment / all	0 / 2		
Ascites			
subjects affected / exposed	4 / 31 (12.90%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Oesophageal varices haemorrhage			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Acute on chronic liver failure			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hepatic failure			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Portal hypertensive gastropathy			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Portal vein thrombosis			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			

Dyspnoea			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pleural effusion			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure	Additional description: renal failure renal impairment		
subjects affected / exposed	4 / 31 (12.90%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 2		
Acute kidney injury			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Renal impairment			

subjects affected / exposed	2 / 31 (6.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Intervertebral discitis			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Bacteraemia			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Peritonitis bacterial			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Sepsis			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Septic shock			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	ITT Population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 31 (54.84%)		
Vascular disorders			
Ecchymosis			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
General disorders and administration site conditions			
Drug intolerance			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Infusion site extravasation			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Metrorrhagia			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			

subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Lower respiratory tract infection			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	2		
Respiratory tract infection			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Psychiatric disorders			
Depressed mood			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	2		
Insomnia			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	2		
Limb injury			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Presyncope			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Vertigo			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	4 / 31 (12.90%)		
occurrences (all)	9		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Haematemesis			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Oesophageal haemorrhage			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Hepatobiliary disorders			
Hepatic encephalopathy			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	3		
Ascites			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Minimal hepatic encephalopathy			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	3		
Prurigo			

subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2		
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all)	 1 / 31 (3.23%) 1		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Humerus fracture subjects affected / exposed occurrences (all) Sciatica subjects affected / exposed occurrences (all)	 1 / 31 (3.23%) 1 1 / 31 (3.23%) 1 1 / 31 (3.23%) 1		
Infections and infestations Cellulitis staphylococcal subjects affected / exposed occurrences (all) Oesophageal candidiasis subjects affected / exposed occurrences (all) Oral herpes subjects affected / exposed occurrences (all)	 1 / 31 (3.23%) 1 1 / 31 (3.23%) 1 1 / 31 (3.23%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 July 2009	To allow the inclusion of subjects who were being treated with beta-blocking drugs. The reason was that most subjects in the study population were being treated with these drugs. Therefore, allowing the inclusion of these subjects increases the number of subjects available for the study and it was possible that the sample was more similar to the study population, which was taken into account for the eventual design of Phase III. Plan to carry out an intermediate analysis when half of the expected sample (15 subjects) was recruited. If the efficacy results were positive for the product under study, it would follow the established plan. On the other hand, if the efficacy results were not positive and no serious safety problems were detected, the dose of albumin would be increased to 1.5g/kg every 2 weeks (with a minimum of 90g and a maximum of 150g per administration).
16 March 2010	The amount of blood drawn for each determination was increased from 5 ml to 10 ml. The reason was that it was observed in subjects already included in the clinical trial that a volume of 5 ml was insufficient to accurately determine the hormonal parameters. The extraction route was modified with Medicut® of 18 or 20 F, the 22F pathways are excessively small and do not allow the extraction of blood by vacuum which could contribute to the sample hemolysis. The paragraph of "prohibited treatments" and Annex 6 "Data Collection Notebook" was modified.
27 September 2011	In the intermediate analysis carried out by the investigators on the variable "plasma renin activity" the expected decrease was not observed but a slight increase (although not statistically significant): 7.1ng/mL.h at the start compared to 11.5 ng/mL.h in week 14. Given that the original design of the study did not take into account that the pharmacokinetic parameters of albumin are altered in patients with cirrhosis due to the increase in the volume of distribution, it is proposed to increase the expected maximum frequency of administration of albumin from 1.5 g/kg every 2 weeks to 1.5 g/kg every week (with a minimum of 90g and a maximum of 150g per administration).
14 June 2012	Specify that the 30 subjects scheduled for inclusion should complete all infusions of albumin according to protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported