Clinical trial results:
Effects of rifaximin administration in patients with severe acute alcoholic hepatitis. Comparative pilot study.

Summary

EudraCT number	2012-000515-80
Trial protocol	ES
Global end of trial date	03 November 2016

Results information

Result version number	v1 (current)
This version publication date	19 December 2021
First version publication date	19 December 2021

Trial information

Trial identification

Sponsor protocol code	RIFA-AAH

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02116556
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, +34 934894779, joaquin.lopez.soriano@vhir.org
Scientific contact	Sponsor and coordinator, Juan Córdoba, +34 932746140, jcordoba@vhebron.net

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	03 November 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate whether the administration of rifaximin as an adjunct to corticosteroids decreases the number of bacterial infections in patients 90 days with acute alcoholic hepatitis.

Protection of trial subjects:

At all time points and during follow-up visits, physical examination, laboratory measurements, presence of bacterial infections, and any liver-related complications were surveyed, including presence or worsening of ascites, gastrointestinal bleeding (GIB), and acute-on-chronic liver failure (ACLF)

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 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	Spain: 63
Worldwide total number of subjects	63
EEA total number of subjects	63

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)	55
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study included 21 consecutive patients recruited from June 2013 to June 2015 who were admitted to four tertiary hospitals in Barcelona. Treated patients were compared with a carefully matched historical cohort of patients treated with standard therapy and paired by age and model for end-stage liver disease (MELD).

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	63
Number of subjects completed	63

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Prednisone

Arm description:

Prednisone plus standard supportive care measurements

Arm type	Active comparator
Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Prednisone PO 40mg/day for 30 days plus standard supportive care measurements

Arm title	Rifamixin

Arm description:

Rifaximin PO 1200 mg/day for 90 days added to standard treatment

Arm type	Experimental
Investigational medicinal product name	Rifamixin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Rifaximin PO 1200 mg/day for 90 days

Number of subjects in period 1	Prednisone	Rifamixin
Started	42	21
Completed	42	21

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	63	63	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	54.5		
inter-quartile range (Q1-Q3)	45 to 61	-	
Gender categorical Units: Subjects			
Female	19	19	
Male	44	44	

End points

End points reporting groups	
Reporting group title	Prednisone
Reporting group description: Prednisone plus standard supportive care measurements	
Reporting group title	Rifamixin
Reporting group description: Rifaximin PO 1200 mg/day for 90 days added to standard treatment	

Primary: Bacterial infections at 90 days	
End point title	Bacterial infections at 90 days
End point description:	
End point type	Primary
End point timeframe: 90 days	

End point values	Prednisone	Rifamixin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	21		
Units: Number				
number (not applicable)	26	6		

Statistical analyses

Statistical analysis title	Infections at 90 days
Comparison groups	Prednisone v Rifamixin
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	> 0.05
Method	Chi-squared

Secondary: De novo ACLF	
End point title	De novo ACLF
End point description:	
End point type	Secondary

End point timeframe: 90 days

End point values	Prednisone	Rifamixin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	21		
Units: Patients				
number (not applicable)	9	1		

Statistical analyses

Statistical analysis title	ACLF de novo
Comparison groups	Prednisone v Rifamixin
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.81
Method	Chi-squared

Secondary: Liver-related complication

End point title	Liver-related complication
End point description:	
End point type	Secondary
End point timeframe: 90 days	

End point values	Prednisone	Rifamixin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	21		
Units: Complications/patient				
number (not applicable)	1.26	0.43		

Statistical analyses

Statistical analysis title	Liver complications/patient
Comparison groups	Prednisone v Rifamixin

Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	t-test, 1-sided

Secondary: Infection-free survival time

End point title	Infection-free survival time

End point description:

End point type	Secondary

End point timeframe:

90 days

End point values	Prednisone	Rifamixin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	21		
Units: day				
number (not applicable)	57.1	70.6		

Statistical analyses

Statistical analysis title	Infection-free survival time
Comparison groups	Prednisone v Rifamixin
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.12
Method	t-test, 2-sided

Secondary: Total complications

End point title	Total complications

End point description:

End point type	Secondary

End point timeframe:

90 days

End point values	Prednisone	Rifamixin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	21		
Units: Number/patient				
number (not applicable)	1.26	0.43		

Statistical analyses

Statistical analysis title	Total complications
Comparison groups	Prednisone v Rifamixin
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.01
Method	t-test, 2-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

90 days

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Rifamixin treated

Reporting group description: -

Serious adverse events	Rifamixin treated		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 21 (52.38%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pancreatic carcinoma			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Laryngeal cancer			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Epilepsy			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Cerebral vasculitis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Right upper extremity paresis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Social circumstances			
Suicidal behaviour			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Gastrointestinal disorders			
Rectal ulcer			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Bronchoaspiration			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Pancreatitis acute			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Rifamixin treated		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 21 (57.14%)		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Mesogastrium pain			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Epidermoid cyst excision			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Hand burn			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Hyponatraemia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Abdominal wall haematoma			

subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all) Hyperglycaemia subjects affected / exposed occurrences (all)	 1 / 21 (4.76%) 1 1 / 21 (4.76%) 1		

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.

This was a pilot study, so it was underpowered by the sample size. Further studies with bigger populations should confirm these results.

Notes: