Clinical trial results:
Phase II clinical trial for the evaluation of different regimens of benznidazole as a treatment for Chagas disease in chronic phase in adult patients. Berenice project.

Summary

EudraCT number	2016-003789-21
Trial protocol	ES
Global end of trial date	21 September 2020

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022

Trial information

Trial identification

Sponsor protocol code	MULTBENZ

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Fundació Hospital Universitari Vall d´Hebron - Institut de Recerca (VHIR)
Sponsor organisation address	Passeig Vall Hebron 119-129, Barcelona, Spain, 08035
Public contact	Israel Molina Romero, Fundación Hospital Universitari Vall d'Hebron - Institut de Recerca, 34 932746080, aro@vhir.org
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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	13 July 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 September 2020
Global end of trial reached?	Yes
Global end of trial date	21 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of different benznidazole regimens using the proportion of patients with sustained load suppression parasitic measured with PCR in peripheral blood during the first 12 months follow-up after the start treatment, in patients equal to or older than 18 years with Chagas disease in chronic phase both in its form indeterminate as in organic (digestive o cardiac)

Protection of trial subjects:

There is no need to have special measurements to protect patients in this assay, since no pain or stress is expected

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 January 2017
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	Brazil: 60
Country: Number of subjects enrolled	Argentina: 60
Country: Number of subjects enrolled	Colombia: 58
Country: Number of subjects enrolled	Spain: 60
Worldwide total number of subjects	238
EEA total number of subjects	60

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)	200

From 65 to 84 years	38
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	238
Number of subjects completed	238

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	Rama B300/60

Arm description:

Benznidazole 150 mg is administered every 12 hours for 60 days.

Arm type	Placebo
Investigational medicinal product name	Benznidazole 150mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Benznidazole 150 mg is administered every 12 hours for 60 days.

Arm title	B150/60

Arm description:

Benznidazole 150mg is administered every 24 hours for 60 days.

Arm type	Experimental
Investigational medicinal product name	Benznidazole 150mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Benznidazole 150mg is administered every 24 hours for 60 days.

Arm title	B400/15

Arm description:

Benznidazole 200 mg is administered every 12 hours for 15 days.

Arm type	Experimental

Investigational medicinal product name	Benznidazole 200mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Benznidazole 200 mg is administered every 12 hours for 15 days.

Number of subjects in period 1	Rama B300/60	B150/60	B400/15
Started	79	80	79
Completed	54	62	62
Not completed	25	18	17
Physician decision	-	9	7
Lost to follow-up	12	9	10
Lack of efficacy	13	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Rama B300/60
Reporting group description: Benznidazole 150 mg is administered every 12 hours for 60 days.	
Reporting group title	B150/60
Reporting group description: Benznidazole 150mg is administered every 24 hours for 60 days.	
Reporting group title	B400/15
Reporting group description: Benznidazole 200 mg is administered every 12 hours for 15 days.	

Reporting group values	Rama B300/60	B150/60	B400/15
Number of subjects	79	80	79
Age categorical Units: Subjects			
Adults (18-64 years)	66	67	67
From 65-84 years	13	13	12
Age continuous Units: years			
arithmetic mean	44.6	47.6	46.9
standard deviation	± 16.2	± 11.2	± 13
Gender categorical Units: Subjects			
Female	53	48	45
Male	26	32	34

Reporting group values	Total		
Number of subjects	238		
Age categorical Units: Subjects			
Adults (18-64 years)	200		
From 65-84 years	38		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	146		
Male	92		

End points

End points reporting groups

Reporting group title	Rama B300/60
Reporting group description:	
Benznidazole 150 mg is administered every 12 hours for 60 days.	
Reporting group title	B150/60
Reporting group description:	
Benznidazole 150mg is administered every 24 hours for 60 days.	
Reporting group title	B400/15
Reporting group description:	
Benznidazole 200 mg is administered every 12 hours for 15 days.	
Subject analysis set title	Overall study
Subject analysis set type	Full analysis
Subject analysis set description:	
All the patients who started the treatment are included	

Primary: To assess the efficacy of different benznidazole regimens using the patients with sustained load suppression parasitic measured with PCR in peripheral blood during the first 12 months follow-up after the start treatment

End point title	To assess the efficacy of different benznidazole regimens using the patients with sustained load suppression parasitic measured with PCR in peripheral blood during the first 12 months follow-up after the start treatment
End point description:	
End point type	Primary
End point timeframe:	
R300/60 and R150/60 at 60 days after introduction of IMP R400/15 at 15 days after introduction of IMP	

End point values	Rama B300/60	B150/60	B400/15	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	79	80	79	
Units: Percentage				
number (not applicable)	54	62	67	

Statistical analyses

Statistical analysis title	Treatment
Comparison groups	Rama B300/60 v B150/60 v B400/15

Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3631
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	25
Reporting groups	
Reporting group title	All groups

Reporting group description: -

Serious adverse events	All groups		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 228 (3.51%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Cardiac disorders			
Heart failure			
subjects affected / exposed	2 / 228 (0.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Supraventricular tachyarrhythmia			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 228 (0.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			

Rash	Additional description: Rash and fever		
subjects affected / exposed	2 / 228 (0.88%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	All groups		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	177 / 228 (77.63%)		
Nervous system disorders			
Headache			
subjects affected / exposed	52 / 228 (22.81%)		
occurrences (all)	52		
Dysgeusia			
subjects affected / exposed	13 / 228 (5.70%)		
occurrences (all)	13		
Paresthesia			
subjects affected / exposed	10 / 228 (4.39%)		
occurrences (all)	10		
Dizziness			
subjects affected / exposed	8 / 228 (3.51%)		
occurrences (all)	8		
Blood and lymphatic system disorders			
leucopenia			
subjects affected / exposed	12 / 228 (5.26%)		
occurrences (all)	12		
Social circumstances			
Anxiety			
subjects affected / exposed	5 / 228 (2.19%)		
occurrences (all)	5		
Insomnia			
subjects affected / exposed	36 / 228 (15.79%)		
occurrences (all)	36		
Gastrointestinal disorders			

Nausea subjects affected / exposed occurrences (all)	59 / 228 (25.88%) 59		
Epigastric discomfort subjects affected / exposed occurrences (all)	55 / 228 (24.12%) 55		
Diffuse abdominal pain subjects affected / exposed occurrences (all)	31 / 228 (13.60%) 31		
Diarrhoea subjects affected / exposed occurrences (all)	15 / 228 (6.58%) 15		
Transaminases increased subjects affected / exposed occurrences (all)	100 / 228 (43.86%) 100		
Skin and subcutaneous tissue disorders			
Pruritus subjects affected / exposed occurrences (all)	61 / 228 (26.75%) 61		
Rash subjects affected / exposed occurrences (all)	81 / 228 (35.53%) 81		
Urticaria subjects affected / exposed occurrences (all)	14 / 228 (6.14%) 14		
Facial oedema subjects affected / exposed occurrences (all)	5 / 228 (2.19%) 5		
Musculoskeletal and connective tissue disorders			
Musculoskeletal disorder subjects affected / exposed occurrences (all)	59 / 228 (25.88%) 59		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 August 2016	Due to the fact that recruitment is lower than expected, it was decided to include a new center in Spain (Ramon y Cajal Hospital).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported