Clinical trial results:
Evaluation of the potential anti-malarial effect of ivermectin: a controlled human malaria infection trial

Summary

EudraCT number	2017-002723-16
Trial protocol	DE
Global end of trial date	12 December 2018

Results information

Result version number	v1 (current)
This version publication date	02 September 2022
First version publication date	02 September 2022
Summary attachment (see zip file)	Publication on a medical journal (Metzger_2020_Ivermectin trial_TMIH.pdf)

Trial information

Trial identification

Sponsor protocol code	PREMIVER

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Universitaetsklinikum Tuebingen
Sponsor organisation address	Geissweg 3 , Tübingen, Germany, 72076
Public contact	Institut fuer Tropenmedizin, Universitaetsklinikum Tuebingen, peter.kremsner@uni-tuebingen.de
Scientific contact	Institut fuer Tropenmedizin, Universitaetsklinikum Tuebingen, peter.kremsner@uni-tuebingen.de

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	31 July 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 December 2018
Global end of trial reached?	Yes
Global end of trial date	12 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Objective: To assess whether ivermectin can inhibit the hepatic invasion and development of Plasmodium falciparum and provide partial malarial prophylaxis.

Protection of trial subjects:

This study was conducted in compliance with the protocol and with the international and national laws and regulations in effect, and in accordance with the applicable directives in particular concerning the submission to the IEC and the protection of personal data. The subject's informed consent was obtained according to the ethical principles stated in the Declaration of Helsinki 2000 version (amended in Tokyo 2004; Ethical Principles for Medical Research Involving Human Subjects.), the applicable guidelines for the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) (CPMP/ICH/135/95), and the applicable local laws and regulations. The investigator agreed, upon signing the protocol, to adhere to the instructions and procedures described within and to the principles of GCP to which it conforms. The study was monitored in accordance with ICH E6.
Permission to perform the study was obtained in accordance with all applicable regulatory requirements. All ethical and regulatory approvals were available before any subject was exposed to any study-related procedure.
Investigations related to the study were performed by scientifically and medically qualified persons, where the benefits of the study were assessed in proportion to the risks posed by participation.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 May 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 12
Worldwide total number of subjects	12
EEA total number of subjects	12

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)	12
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

21 subject were screened, 13 were eligible, 12 were enrolled one was kept as backup.
The screenings were performed from 7th to 17th May 2018

Period 1

Period 1 title	Recruitment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Verum

Arm description:

Ivermectin 400mcg/kg one time

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

Dosage and administration details:

0.4 mg/kg weight was given with waten unter fasting conditions.

Arm title	Placebo

Arm description:

Placebo were tablets containing lactose

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

Dosage and administration details:

To secure the blinding the subjects were given the amount of tablets that they would have gotten, if they would have been in the IMP group (0.4 mg/kg, one IMP tablet contains 3 mg IMP).

Number of subjects in period 1	Verum	Placebo
Started	8	4
Completed	8	4

Baseline characteristics

Reporting groups

Reporting group title	Recruitment

Reporting group description: -

Reporting group values	Recruitment	Total	
Number of subjects	12	12	
Age categorical			
Age category of the subjects included to the clinical trial			
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)	12	12	
From 65-84 years	0	0	
85 years and over	0	0	
All	0	0	
Age continuous			
from 18-45			
Units: years			
arithmetic mean	28		
full range (min-max)	23 to 37	-	
Gender categorical			
Units: Subjects			
Female	7	7	
Male	5	5	

Subject analysis sets

Subject analysis set title	Per protocol
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects that followed the clinical trial as requested per protocol

Reporting group values	Per protocol		
Number of subjects	12		
Age categorical			
Age category of the subjects included to the clinical trial			
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)	12		
From 65-84 years	0		
85 years and over	0		
All	0		
Age continuous			
from 18-45			
Units: years			
arithmetic mean	28		
full range (min-max)	23 to 37		
Gender categorical			
Units: Subjects			
Female	7		
Male	5		

End points

End points reporting groups

Reporting group title	Verum
Reporting group description: Ivermectin 400mcg/kg one time	
Reporting group title	Placebo
Reporting group description: Placebo were tablets containing lactose	
Subject analysis set title	Per protocol
Subject analysis set type	Per protocol
Subject analysis set description: Subjects that followed the clinical trial as requested per protocol	

Primary: Time to microscopically detectable parasitaemia

End point title	Time to microscopically detectable parasitaemia
End point description:	
End point type	Primary
End point timeframe: The parasitaemia was measured from day 6 on after controlled human malaria infection until positivity or treatment on day 21 twice daily.	

End point values	Verum	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	4		
Units: hour				
number (not applicable)	263	262		

Statistical analyses

Statistical analysis title	primary endpoint
Comparison groups	Verum v Placebo
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	≤ 0.5
Method	t-test, 2-sided

Notes:

[1] - The primary endpoint of successful malarial infection was assessed for each patient and the number and percent of patients achieving this endpoint summarised for each group.

Secondary: Median parasite density at day 12

End point title	Median parasite density at day 12

End point description:

End point type	Secondary

End point timeframe:
On day 12

End point values	Verum	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	4		
Units: parasites/ml				
median (standard deviation)	464 (± 52)	361 (± 58)		

Statistical analyses

No statistical analyses for this end point

Secondary: Median parasite density at day of treatment

End point title	Median parasite density at day of treatment

End point description:

End point type	Secondary

End point timeframe:
time of treatment

End point values	Verum	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	4		
Units: parasites/ml				
median (standard deviation)	5640 (± 1349)	3139 (± 1254)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: AEs were collided from signature of the informed consent form until end of follow-up on day 90.	
Assessment type	Systematic
Dictionary used	
Dictionary name	preferred term
Dictionary version	1
Reporting groups	
Reporting group title	Verum
Reporting group description: Ivermectin 400mcg/kg one time	
Reporting group title	Placebo
Reporting group description: Placebo were tablets containing lactose	

Serious adverse events	Verum	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 8 (12.50%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Verum	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	4 / 4 (100.00%)	
Vascular disorders			
Fatigue			
subjects affected / exposed	4 / 8 (50.00%)	2 / 4 (50.00%)	
occurrences (all)	4	4	
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	5 / 8 (62.50%) 5	3 / 4 (75.00%) 4	
Blood and lymphatic system disorders Lymphopenia subjects affected / exposed occurrences (all)	8 / 8 (100.00%) 7	4 / 4 (100.00%) 8	

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

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31808594