Clinical trial results:
Pilot study to evaluate the potential of ivermectin to reduce COVID-19 transmission

Summary

EudraCT number	2020-001474-29
Trial protocol	ES
Global end of trial date	10 December 2020

Results information

Result version number	v1 (current)
This version publication date	04 December 2021
First version publication date	04 December 2021
Summary attachment (see zip file)	Saint_Paper (SAINT_Publicación (1).pdf)

Trial information

Trial identification

Sponsor protocol code	SAINT

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04390022
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Clinica Universidad de Navarra
Sponsor organisation address	Pio XII, Pamplona, Spain,
Public contact	UCEC, Clinica Universidad de Navarra, +34 948255400, ucicec@unav.es
Scientific contact	UCEC, Clinica Universidad de Navarra, +34 948255400, ucicec@unav.es

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	05 November 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 October 2020
Global end of trial reached?	Yes
Global end of trial date	10 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy of a single dose of ivermectin, administered to low risk, non-severe COVID-19 patients in the first 48 hours after symptoms onset to reduce the proportion of patients with detectable SARS-CoV-2 RNA by PCR from nasopharyngeal swab at day seven post-treatment.

Protection of trial subjects:

As a COVID clinical trial, besides all the protecction measures, it also took relevance the possibility of giving the patient the option of doing their follow-up at home, instead of coming to the Clinic due to privacy issues.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 July 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	24
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The recruitment took place only in Spain.
First patient recruited is dated the 24/07/2020 and last patient 11/09/2020.

Pre-assignment

Screening details:

Patients diagnosed with COVID-19 in the emergency room of the Clínica Universidad de Navarra with a positive SARS-CoV-2 PCR. Residents of the Pamplona basin ("Cuenca de Pamplona"). The patient should be between the ages of 18 and 60 years of age. Negative pregnancy test for women of child bearing age.

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

Blinding implementation details:

Before the trial begins, the sponsor will assign named independent individuals to code break activity to avoid introducing any bias for the designated safety physician, clinical team, sponsor and statistician teams.

Arms

Are arms mutually exclusive?	Yes
Arm title	ivermectina

Arm description:

The study will enroll 24 participants, 12 per arm, receiving ivermectin and placebo.

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

Dosage and administration details:

The dose will be administered using scales at the site for tailored administration. Given that dosing is limited by the size of the tablet (3mg) the participants will receive a discrete number of tablets according to their weight band. The individual dose will range from 400 mcg/kg to a maximum of 457 mcg/kg. See annex 2 for a full color-coded table.

Arm title	Placebo

Arm description:

The study will enroll 24 participants, 12 per arm, receiving ivermectin and placebo.

Arm type	placebo

No investigational medicinal product assigned in this arm

Number of subjects in period 1	ivermectina	Placebo
Started	12	12
Completed	12	12

Baseline characteristics

Reporting groups

Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	24	24	
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			
median	26		
full range (min-max)	19 to 36	-	
Gender categorical Units: Subjects			
Female	12	12	
Male	12	12	
BMI Units: kg/m2			
median	23.5		
full range (min-max)	19.6 to 27.8	-	

Subject analysis sets

Subject analysis set title	Covid patients
Subject analysis set type	Per protocol

Subject analysis set description:

Paitents with positive PCR for SARS-CoV-2 RNA, obtained from a nasopharyngeal swab in the first 72 hours after symptoms onset.

Reporting group values	Covid patients		
Number of subjects	24		
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			

Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years median full range (min-max)			
Gender categorical Units: Subjects			
Female	5		
Male	7		
BMI Units: kg/m2 median full range (min-max)			

End points

End points reporting groups

Reporting group title	ivermectina
Reporting group description:	
The study will enroll 24 participants, 12 per arm, receiving ivermectin and placebo.	
Reporting group title	Placebo
Reporting group description:	
The study will enroll 24 participants, 12 per arm, receiving ivermectin and placebo.	
Subject analysis set title	Covid patients
Subject analysis set type	Per protocol
Subject analysis set description:	
Paitents with positive PCR for SARS-CoV-2 RNA, obtained from a nasopharyngeal swab in the first 72 hours after symptoms onset.	

Primary: Primary Endpoint

End point title	Primary Endpoint
End point description:	
End point type	Primary
End point timeframe:	
Proportion of patients with a positive SARS-CoV-2 PCR from a nasopharyngeal swab at day 7 post-treatment	

End point values	ivermectina	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: positives	12	12		

Statistical analyses

Statistical analysis title	Fisher exact test
Comparison groups	Placebo v ivermectina
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.05
Method	Fisher exact

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
After treatment	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	Ivermectin
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Ivermectin	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Ivermectin	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 12 (41.67%)	5 / 12 (41.67%)	
Vascular disorders			
Dizziness			
subjects affected / exposed	5 / 12 (41.67%)	5 / 12 (41.67%)	
occurrences (all)	7	1	
Nervous system disorders			
Confusional state			
subjects affected / exposed	5 / 12 (41.67%)	5 / 12 (41.67%)	
occurrences (all)	1	0	
Somnolence			
subjects affected / exposed	5 / 12 (41.67%)	5 / 12 (41.67%)	
occurrences (all)	0	0	
Vision blurred			

subjects affected / exposed occurrences (all)	5 / 12 (41.67%) 24	5 / 12 (41.67%) 1	
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	5 / 12 (41.67%) 7	5 / 12 (41.67%) 8	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 August 2020	An exclusion criteria is modified, the time of fever or cough present for more than 48hrs, is changed to 72hrs. Other changes are related to the possibility of giving patients the option of home follow-up or, for privacy reasons.
04 November 2020	In this relevant modification, an annex I to the patient information and informed consent sheet is included to inform the patient of the possibility of participating in a final trial visit, where blood will be collected to measure the antibody titre against SARS-CoV-2. The reason for these measures is due to the fact that one of the trial patients was tested positive for serology on the 21st visit, as per protocol. This patient underwent a serology on his own and his result changed to negative. For this reason, we have added a relevant modification that requires a serology test to be performed within 8-10 weeks.

Notes:

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 trial was designed to preliminarily explore the potential benefit of ivermectin use in patients with COVID-19, but not to provide definitive evidence, which explains its small sample size.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33495752