Clinical trial results:
A randomized, double-blind, placebo-controlled study to assess the safety and efficacy of ivermectin in asymptomatic and mild severity COVID-19 patients

Summary

EudraCT number	2021-000166-15
Trial protocol	HU
Global end of trial date	16 January 2023

Results information

Result version number	v1 (current)
This version publication date	15 September 2023
First version publication date	15 September 2023
Summary attachment (see zip file)	IVM Clinical Study Report Synopsis (IVM Clinical Study Report_v1.0 Synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	IVM-2021-01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	MEDITOP Pharmaceutical Ltd.
Sponsor organisation address	Ady Endre utca 1., Pilisborosjenő, Hungary, 2097
Public contact	Main information contact, MEDITOP Pharmaceutical Ltd., 36 26336400, info@meditop.hu
Scientific contact	Main information contact, MEDITOP Pharmaceutical Ltd., 36 26336400, info@meditop.hu

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 June 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 January 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Primary Objective: To assess the efficacy of per os ivermectin administration in asymptomatic and mild severity SARS-CoV-2 infected patients on reduction of virus load.

Protection of trial subjects:

This clinical study was conducted in accordance with the principles laid down by the 18th World Medical Assembly (Helsinki, 1964) and all applicable amendments laid down by the World Medical Assemblies, and the Good Clinical Practice (ICH GCP E6 (R2)).
This clinical study was conducted in compliance with applicable international (EU) laws and regulations, and national laws and regulations of the country where the clinical study is performed, as well as any applicable guidelines.

Patients were informed of study related details in writing (Patient Information Leaflet – PIL) and via discussion with study investigator. Written informed consent Informed Consent Forms (ICFs) for participation in the study was obtained before performing any study-related procedures (including screening evaluations). PIL and ICFs for enrolled subjects and for subjects who are not subsequently enrolled were maintained at the study site.

Background therapy:

- No standard of care COVID-19 therapies were allowed. For symptomatic relief of e.g. fever, sore throat, e.g. antipyretics, analgesics could be used concomitantly.
- Concomitant or previous administration of any experimental, non-established COVID-19 therapy, either in off-label indication of a registered medicinal product or as a non-registered drug candidate in a clinical trial setting or compassionate use program (or equivalents thereof) was not allowed.

Evidence for comparator:

NA Placebo comparator was used

Actual start date of recruitment	26 March 2021
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	Hungary: 10
Worldwide total number of subjects	10
EEA total number of subjects	10

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)	7
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Ambulatory patients with confirmed SARS-CoV-2 infection by rapid antigen test OR polymerase chain reaction mild, and asymptomatic cases were enrolled in COVID treating hospital centers. Recruitment was later extended to general practitioners and COVID test sites.

Pre-assignment

Screening details:

Screening period could last up to 3 days (D-3 … D1). If appropriate (e.g. study entry could be warranted upon positive rapid SARS-CoV-2 antigen test), the screening visit could be considered also as Day 1, start of IMP (Investigation Medicinal Product) administration. In this case, activities applicable for both Screening and Day 1 were conducted o

Pre-assignment period milestones

Number of subjects started	11[1]
Number of subjects completed	10

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screen failure: 1

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 11 patients were screened and 10 enroled to the study.

Period 1

Period 1 title	Treatment
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

This was a double-blind study. Neither the patients, physicians nor managing CRO was aware of treatment arm. Blinding was achieved by placebo arm.
Breaking the blind - unmasking of treatment allocation was only to occur in a medical emergency, by the Investigator or its medical delegate (subinvestigator), preferably after consulting this action with the Sponsor. No code breaking was needed during the study.
Emergency code break envelopes were provided for the sites with each treatment Kit for

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo 5 x 3 mg tablets once daily

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:

5 x 3 mg tablets once daily for 4 days

Arm title	Active

Arm description:	
Ivermectin	
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:	
5 x 3 mg tablets once daily for 4 days	

Number of subjects in period 1	Placebo	Active
Started	6	4
Completed	6	4

Period 2	
Period 2 title	Follow-up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst
Blinding implementation details:	
Same as before	

Arms	
Are arms mutually exclusive?	Yes
Arm title	Placebo
Arm description:	
No treatment in this period	
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:	
5 x 3 mg tablets once daily for 4 days	
Arm title	Active
Arm description:	
Ivermectin	
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:

5 x 3 mg tablets once daily for 4 days

Number of subjects in period 2	Placebo	Active
Started	6	4
Completed	6	4

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo 5 x 3 mg tablets once daily	
Reporting group title	Active
Reporting group description:	
Ivermectin	

Reporting group values	Placebo	Active	Total
Number of subjects	6	4	10
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			
Age of the subject (years)			
Units: years			
arithmetic mean	54.8	52.3	
standard deviation	± 15.03	± 15.24	-
Gender categorical			
Units: Subjects			
Female	2	1	3
Male	4	3	7

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Placebo 5 x 3 mg tablets once daily	
Reporting group title	Active
Reporting group description: Ivermectin	
Reporting group title	Placebo
Reporting group description: No treatment in this period	
Reporting group title	Active
Reporting group description: Ivermectin	

Primary: Virus copy number

End point title	Virus copy number[1]
End point description: The percentage of virus copy number at Day7 compared to baseline (i.e. 100 * (the number of virus copies at Day 7 / number of virus copies at Screening).	
End point type	Primary
End point timeframe: Screening to Day7	

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: Due to the high number of major PDs, especially on eligibility criteria, and critical PD about data quality and the low number of patients, patients were excluded from all efficacy analyses, only safety objectives were analysed. Efficacy endpoints that can be considered as safety endpoints were analysed within safety analysis.

End point values	Placebo	Active		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: %				
number (confidence interval 95%)	(to)	(to)		

Notes:

[2] - Due to quality issues patients were excluded from all efficacy analyses

[3] - Due to quality issues all patients were excluded from all efficacy analyses.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Screening to D28 FU (EOS)	
Adverse event reporting additional description:	
Adverse events, whether believed to be IMP-related or not, were recorded in the Case Report Forms. For all adverse events concomitant medications were noted.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo 5 x 3 mg tablets once daily	
Reporting group title	Active
Reporting group description:	
Ivermectin	

Serious adverse events	Placebo	Active	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Progression of OVID-19 infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0.05 %

Non-serious adverse events	Placebo	Active	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 6 (33.33%)	1 / 4 (25.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	
occurrences (all)	1	0	

Gastrointestinal disorders Upper abdominal pain subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1	 0 / 4 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0	 1 / 4 (25.00%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 April 2021	8.8.2. Protocol v3.0 06/Apr/2021 Approved on 10/May/2021 Summary of changes from version 2.2: • Introduction of D28 phone visit to complete the post-COVID symptoms questionnaires with the patients • New exclusion criteria: Start of COVID-19 related symptoms more than 5 days before start of treatment. • New endpoints: o Oxygen saturation as a secondary endpoint o Post-COVID questionnaire as a secondary endpoint
30 March 2022	8.8.3. Protocol v4.3 02/May/2022 Approved on 27/Apr/2022 (The approval text is for protocol v4.2 30/Mar/2022, but contains a condition that was implemented in version 4.3 of the protocol). Summary of changes from version 3.0: • Study population: o Inclusion of patients at high risk for developing severe COVID-19 case can be enrolled if they are vaccinated three times and the last dose was given not more than 6 months before screening. (High risk patients were excluded from the study in previous versions) o Deleted previous exclusion criteria that excluded current strong smoker patients as defined by smoking over 10 cigarettes a day, or its equivalent o True abstinence included as an acceptable method for contraception (for both gender) • Study interventions: o Urine drug test and alcohol breath test were removed from screening procedure (had been mandatory at screening in previous versions) o Day 18 visit was removed o Physical examination and body weight no longer mandatory at Day 14 o Screening radiology examination (CT or X-ray) at the discretion of the investigator • Definition of overdose was included in the clinical trial protocol

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.

Due to the high number of major PDs, especially on eligibility criteria, and critical PD about data quality and the low number of patients, patients were excluded from all efficacy analyses, only safety objectives were analysed.

Notes: