Clinical trial results:
A Phase 2a open label, non-comparative, single dose escalation study to evaluate the dynamics of viral clearance, pharmacokinetics and tolerability of ensovibep in patients with symptomatic COVID-19 disease

Summary

EudraCT number	2021-000365-33
Trial protocol	NL
Global end of trial date	20 August 2021

Results information

Result version number	v1
This version publication date	13 October 2022
First version publication date	13 October 2022

Trial information

Trial identification

Sponsor protocol code	MP0420-CP204

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04834856
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Molecular Partners AG
Sponsor organisation address	Wagistrasse 14, Schlieren, Switzerland, 8952
Public contact	Medical Director, Molecular Partners AG, info@molecularpartners.com
Scientific contact	Medical Director, Molecular Partners AG, info@molecularpartners.com

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	20 August 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 August 2021
Global end of trial reached?	Yes
Global end of trial date	20 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

(1))To characterize the dynamics of viral clearance (incl. viral cultures, qPCR) following ensovibep administration. (2) To evaluate the serum pharmacokinetics of single, i.v. doses of ensovibep in patients with symptomatic COVID-19 disease.

Protection of trial subjects:

This study was conducted in accordance with the Note for Guidance on Good Clinical Practice (GCP) International Council for Harmonisation (ICH) Harmonised Tripartite Guideline E6 (R1)/Integrated Addendum E6 (R2); US Food and Drug Administration (FDA) Code of Federal Regulations (CFR) (Title 21 Parts 50, 56, 312), requirements for the conduct of clinical studies as provided in the EU Directive 2001/20/EC, the general guidelines indicated in the Declaration of Helsinki; and all applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 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	Netherlands: 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:

Participants were enrolled at 1 research center in the Netherlands from 01Apr2021 to 21May2021. The first 6 participants who were enrolled were assigned to Arm 1. After assessment by the data review committee, the next 6 participants who were enrolled were assigned to Arm 2.

Pre-assignment

Screening details:

14 patients were screened. There were 2 screen failures (Reasons: negative rapid antigen test at day of dosing and prior anti-SARS-COV-2 vaccination).

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	Ensovibep 225 mg

Arm description:

Single flat dose of 225 mg ensovibep i.v.

Arm type	Experimental
Investigational medicinal product name	Ensovibep
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

225 mg single flat dose administered as i.v. infusion.

Arm title	Ensovibep 600 mg

Arm description:

Single flat dose of 600 mg ensovibep i.v.

Arm type	Experimental
Investigational medicinal product name	Ensovibep
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

600 mg single flat dose administered as i.v. infusion.

Number of subjects in period 1	Ensovibep 225 mg	Ensovibep 600 mg
Started	6	6
Completed	6	6

Baseline characteristics

Reporting groups	
Reporting group title	Ensovibep 225 mg
Reporting group description:	
Single flat dose of 225 mg ensovibep i.v.	
Reporting group title	Ensovibep 600 mg
Reporting group description:	
Single flat dose of 600 mg ensovibep i.v.	

Reporting group values	Ensovibep 225 mg	Ensovibep 600 mg	Total
Number of subjects	6	6	12
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	23.0	26.8	
standard deviation	± 2.1	± 8.5	-
Gender categorical			
Units: Subjects			
Female	2	2	4
Male	4	4	8
Race			
Units: Subjects			
Multiple	0	1	1
White	6	5	11

End points

End points reporting groups

Reporting group title	Ensovibep 225 mg
Reporting group description: Single flat dose of 225 mg ensovibep i.v.	
Reporting group title	Ensovibep 600 mg
Reporting group description: Single flat dose of 600 mg ensovibep i.v.	
Subject analysis set title	ensovibep 225 mg
Subject analysis set type	Full analysis
Subject analysis set description: one time administration of ensovibep at day 1 -	
Subject analysis set title	ensovibep 600mg
Subject analysis set type	Full analysis
Subject analysis set description: one time administration of ensovibep 600mg at Day 1	

Primary: Changes from baseline to each time point of measurement in viral load (quantitative PCR) as per assessment schedule

End point title	Changes from baseline to each time point of measurement in viral load (quantitative PCR) as per assessment schedule[1]
End point description:	
End point type	Primary
End point timeframe: change from baseline (mean) at day 8	

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: Descriptive statistics, no statistical hypothesis verified.

End point values	Ensovibep 225 mg	Ensovibep 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: log10 copies/mL				
arithmetic mean (standard deviation)	-3.602 (± 0.9418)	-3.420 (± 1.8205)		

Attachments (see zip file)	420_204_CFB viral load.pdf

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients with negative PCR

End point title	Number of patients with negative PCR[2]

End point description:

End point type	Primary

End point timeframe:

at day 8

Notes:

[2] - 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: Descriptive statistics, no statistical hypothesis verified.

End point values	Ensovibep 225 mg	Ensovibep 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: number of patients	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: AUCinf

End point title	AUCinf[3]

End point description:

End point type	Primary

End point timeframe:

28 days

Notes:

[3] - 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: Descriptive statistics, no statistical hypothesis verified.

End point values	Ensovibep 225 mg	Ensovibep 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5[4]	6		
Units: h*ug/mL				
geometric mean (standard deviation)	37170 (± 18.1)	100068 (± 37.9)		

Notes:

[4] - 1 patient was not evaluable for this parameter

Attachments (see zip file)	summary PK.pdf

Statistical analyses

No statistical analyses for this end point

Primary: Clearance (CL)

End point title	Clearance (CL)[5]

End point description:

End point type	Primary

End point timeframe:

28 days

Notes:

[5] - 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: Descriptive statistics, no statistical hypothesis verified.

End point values	Ensovibep 225 mg	Ensovibep 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5[6]	6		
Units: mL/h				
arithmetic mean (standard deviation)	6.13 (± 1.02)	6.39 (± 2.81)		

Notes:

[6] - 1 patient was not evaluable for this parameter

Statistical analyses

No statistical analyses for this end point

Primary: C max

End point title	C max[7]

End point description:

End point type	Primary

End point timeframe:

28 days

Notes:

[7] - 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: Descriptive statistics, no statistical hypothesis verified.

End point values	Ensovibep 225 mg	Ensovibep 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: ug/mL				
geometric mean (geometric coefficient of variation)	88.8 (± 20.3)	233 (± 19.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Half-life T1/2

End point title	Half-life T1/2[8]

End point description:

End point type	Primary

End point timeframe:

28 days

Notes:

[8] - 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: Descriptive statistics, no statistical hypothesis verified.

End point values	Ensovibep 225 mg	Ensovibep 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5[9]	6		
Units: hours				
arithmetic mean (standard deviation)	326 (± 119)	303 (± 136)		

Notes:

[9] - 1 patient was not evaluable for this parameter

Statistical analyses

No statistical analyses for this end point

Primary: T max

End point title	T max[10]

End point description:

End point type	Primary

End point timeframe:

28 days

Notes:

[10] - 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: Descriptive statistics, no statistical hypothesis verified.

End point values	Ensovibep 225 mg	Ensovibep 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: hours				
median (full range (min-max))	1.42 (1.40 to 2.70)	2.04 (1.37 to 2.68)		

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in the Assessment of 14 Common COVID-19-Related Symptoms score per the assessment schedule

End point title	Changes in the Assessment of 14 Common COVID-19-Related Symptoms score per the assessment schedule

End point description:

Symptoms related to COVID-19 were assessed daily (pre-dose until Day 15) and on Day 22 and 29 using the 14 Common COVID-19-Related Symptom questionnaire. Symptoms were rated on either a 3- or 4-point ordinal scale and a total symptom score was calculated as the sum individual symptoms (range: 0 – 40).

End point type	Secondary

End point timeframe:

Symptoms related to COVID-19 were assessed daily (pre-dose until Day 15) and on Day 22 and 29 using the 14 Common COVID-19-Related Symptom questionnaire. Data on day 8 is presented.

End point values	Ensovibep 225 mg	Ensovibep 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Total Covid-19 Related Symptoms Scores				
number (not applicable)	-9.6	-8.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Adverse events of special interest (AESIs)

End point title	Adverse events of special interest (AESIs)

End point description:

End point type	Secondary

End point timeframe:

by day 28

End point values	Ensovibep 225 mg	Ensovibep 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: nr of AESI	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Infusion-related reactions (IRRs)

End point title	Infusion-related reactions (IRRs)

End point description:

End point type	Secondary

End point timeframe:
by day 28

End point values	Ensovibep 225 mg	Ensovibep 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: nr of IRR	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of local tolerability at injection site (Visual Infusion Phlebitis score)

End point title	Assessment of local tolerability at injection site (Visual Infusion Phlebitis score)

End point description:

End point type	Secondary

End point timeframe:
at 30 min post injection

End point values	Ensovibep 225 mg	Ensovibep 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: point				
arithmetic mean (standard deviation)	0.2 (± 0.41)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Timeframe for AE	
Adverse event reporting additional description:	
AE additional description	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	MP0420 225 mg
Reporting group description: -	
Reporting group title	MP0420 600 mg
Reporting group description: -	

Serious adverse events	MP0420 225 mg	MP0420 600 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (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: 0 %

Non-serious adverse events	MP0420 225 mg	MP0420 600 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	3 / 6 (50.00%)	
Investigations			
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Aspartate aminotransferase increased	Additional description: Aspartate aminotransferase increased		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	

Bilirubin increased	Additional description: Bilirubin increased		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache	Additional description: Headache		
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	3 / 6 (50.00%)	
occurrences (all)	0	4	
General disorders and administration site conditions			
Alcoholic hangover	Additional description: Alcoholic hangover		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Ear pain	Additional description: Ear pain		
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Diarrhoea	Additional description: Diarrhoea		
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 6 (50.00%)	0 / 6 (0.00%)	
occurrences (all)	3	0	
Respiratory, thoracic and mediastinal disorders			
Cough	Additional description: Cough		
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain	Additional description: Back pain		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Muscle burning sensation	Additional description: Muscle burning sensation		

alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Hypophosphatemia	Additional description: Hypophosphatemia		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	

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.

Small sample size

Notes: