Clinical trial results:
A randomized, double-blind, placebo-controlled, multicenter study of ensovibep (MP0420) in ambulatory adult patients with symptomatic COVID-19

Summary

EudraCT number	2021-000890-10
Trial protocol	HU NL
Global end of trial date	27 January 2022

Results information

Result version number	v2 (current)
This version publication date	18 January 2023
First version publication date	18 December 2022
Version creation reason	• Correction of full data set Timeframe correction for PK endpoints.

Trial information

Trial identification

Sponsor protocol code	MP0420-CP302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04828161
WHO universal trial number (UTN)	-
Other trial identifiers	CSKO136A12201J: Novartis protocol identifier

Notes:

Sponsors

Sponsor organisation name	Molecular Partners AG
Sponsor organisation address	Wagistrasse 14, Schlieren, Switzerland, 8952
Public contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111, Novartis.email@Novartis.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	27 January 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 January 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Part A: To assess the effect of ensovibep, compared to placebo, in reducing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral load from Baseline through Day 8.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 May 2021
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	Hungary: 3
Country: Number of subjects enrolled	India: 49
Country: Number of subjects enrolled	Netherlands: 19
Country: Number of subjects enrolled	South Africa: 87
Country: Number of subjects enrolled	United States: 242
Worldwide total number of subjects	400
EEA total number of subjects	22

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)	388
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study consisted of 2 parts, Part A and Part B. The Part A was Phase II proof of efficacy study conducted in ambulatory adult participants with symptomatic coronavirus disease 2019 (COVID-19). The Part B was to be Phase III confirmatory study. Only Part A analysis is reported as Part B of the study was not initiated.

Pre-assignment

Screening details:

Part A of the study consisted of a screening period (up to 3 days) followed by study treatment on Day 1. Participants were randomized in 1:1:1:1 ratio, stratified by risk for COVID-19 disease progression, to receive 1 of 4 study treatments (Ensovibep 600 mg or 225 mg or 75 mg or Placebo). A total of 400 participants were treated in the study.

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, Monitor, Carer

Blinding implementation details:

Two patients randomized to ensovibep 225 mg didn't receive treatment they were randomized to: 1 patient received no active drug as infusion was not prepared correctly; 1 patient received lower dose (<75 mg) as infusion was interrupted. For Safety set, these 2 were reported in placebo and ensovibep 75 mg arms, respectively.

Arms

Are arms mutually exclusive?	Yes
Arm title	Ensovibep 600 mg

Arm description:

Participants received single intravenous (IV) infusion of ensovibep 600 milligram (mg) on Day 1.

Arm type	Experimental
Investigational medicinal product name	Ensovibep
Investigational medicinal product code	MP0420, SKO136
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single IV infusion of ensovibep 600 mg was administered for over 60 minutes on Day 1.

Arm title	Ensovibep 225 mg

Arm description:

Participants received single IV infusion of ensovibep 225 mg on Day 1.

Arm type	Experimental
Investigational medicinal product name	Ensovibep
Investigational medicinal product code	MP0420, SKO136
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single IV infusion of ensovibep 225 mg was administered for over 60 minutes on Day 1.

Arm title	Ensovibep 75 mg

Arm description:	
Participants received single IV infusion of ensovibep 75 mg on Day 1.	
Arm type	Experimental
Investigational medicinal product name	Ensovibep
Investigational medicinal product code	MP0420, SKO136
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Single IV infusion of ensovibep 75 mg was administered for over 60 minutes on Day 1.	
Arm title	Placebo
Arm description:	
Participants received single IV infusion of placebo matching with ensovibep on Day 1.	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Single IV infusion of placebo matching with ensovibep was administered for over 60 minutes on Day 1.	

Number of subjects in period 1	Ensovibep 600 mg	Ensovibep 225 mg	Ensovibep 75 mg
Started	100	100	101
Completed	97	95	96
Not completed	3	5	5
Consent withdrawn by subject	-	1	2
Death	-	-	-
Unspecified	2	-	1
Lost to follow-up	1	4	2

Number of subjects in period 1	Placebo
Started	99
Completed	94
Not completed	5
Consent withdrawn by subject	1
Death	2
Unspecified	-
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	Ensovibep 600 mg
Reporting group description:	
Participants received single intravenous (IV) infusion of ensovibep 600 milligram (mg) on Day 1.	
Reporting group title	Ensovibep 225 mg
Reporting group description:	
Participants received single IV infusion of ensovibep 225 mg on Day 1.	
Reporting group title	Ensovibep 75 mg
Reporting group description:	
Participants received single IV infusion of ensovibep 75 mg on Day 1.	
Reporting group title	Placebo
Reporting group description:	
Participants received single IV infusion of placebo matching with ensovibep on Day 1.	

Reporting group values	Ensovibep 600 mg	Ensovibep 225 mg	Ensovibep 75 mg
Number of subjects	100	100	101
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	40.6	40.2	41.5
standard deviation	± 11.50	± 12.90	± 12.84
Gender categorical Units: Subjects			
Female	47	54	60
Male	53	46	41
Race and Ethnicity Units: Subjects			
White	59	63	62
Asian	14	14	13
Black or African American	16	11	14
Multiple	5	4	6
Not reported	1	4	3
Native Hawaiian or Other Pacific Islander	1	1	2
American Indian or Alaska Native	3	0	1
Unknown	1	3	0

Reporting group values	Placebo	Total	
Number of subjects	99	400	
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	42.3		
standard deviation	± 13.75	-	
Gender categorical Units: Subjects			
Female	57	218	
Male	42	182	
Race and Ethnicity Units: Subjects			
White	63	247	
Asian	16	57	
Black or African American	11	52	
Multiple	8	23	
Not reported	1	9	
Native Hawaiian or Other Pacific Islander	0	4	
American Indian or Alaska Native	0	4	
Unknown	0	4	

End points

End points reporting groups

Reporting group title	Ensovibep 600 mg
Reporting group description:	
Participants received single intravenous (IV) infusion of ensovibep 600 milligram (mg) on Day 1.	
Reporting group title	Ensovibep 225 mg
Reporting group description:	
Participants received single IV infusion of ensovibep 225 mg on Day 1.	
Reporting group title	Ensovibep 75 mg
Reporting group description:	
Participants received single IV infusion of ensovibep 75 mg on Day 1.	
Reporting group title	Placebo
Reporting group description:	
Participants received single IV infusion of placebo matching with ensovibep on Day 1.	
Subject analysis set title	Phase 3/Part B: Ensovibep 75 mg
Subject analysis set type	Full analysis
Subject analysis set description:	
Phase 3/Part B: ensovibep active treatment. Part B was not initiated.	
Subject analysis set title	Phase 3/Part B: Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Phase 3/Part B: Placebo. Part B was not initiated.	

Primary: Part A: Time-Weighted Change From Baseline in Log10 SARSCoV- 2 Viral Load Through Day 8

End point title	Part A: Time-Weighted Change From Baseline in Log10 SARSCoV- 2 Viral Load Through Day 8
End point description:	
The SARS-CoV-2 viral load was measured by means of a nasopharyngeal swab, followed by quantitative reverse transcription-polymerase chain reaction assay at a central laboratory. The multiple comparison procedure-modeling methodology was used. Time-weighted change from baseline was used as viral loads were measured at multiple time points. The full analysis set (FAS) included all participants in the randomized set for whom IV infusion of study treatment was administered. Only participants included in the analysis are reported.	
End point type	Primary
End point timeframe:	
Baseline (Day 1) and Days 3, 5 and 8	

End point values	Ensovibep 600 mg	Ensovibep 225 mg	Ensovibep 75 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89	97	97	87
Units: log10 copies/milliliter (mL)				
least squares mean (standard error)	-1.99 (± 0.097)	-1.73 (± 0.093)	-1.81 (± 0.093)	-1.40 (± 0.098)

Statistical analyses

Statistical analysis title	Treatment difference in SARSCoV- 2 Viral Load - 1
Comparison groups	Ensovibep 600 mg v Placebo
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Least square (LS) mean difference
Point estimate	-0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.86
upper limit	-0.32
Variability estimate	Standard error of the mean
Dispersion value	0.138

Statistical analysis title	Treatment difference in SARSCoV- 2 Viral Load - 2
Comparison groups	Ensovibep 225 mg v Placebo
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	-0.07
Variability estimate	Standard error of the mean
Dispersion value	0.135

Statistical analysis title	Treatment difference in SARSCoV- 2 Viral Load - 3
Comparison groups	Ensovibep 75 mg v Placebo
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.42

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.68
upper limit	-0.15
Variability estimate	Standard error of the mean
Dispersion value	0.135

Primary: Part B: Percentage of Participants With Hospitalizations and/or Emergency Room (ER) Visits Related to COVID-19 or Death From Any Cause

End point title	Part B: Percentage of Participants With Hospitalizations and/or Emergency Room (ER) Visits Related to COVID-19 or Death From Any Cause[1]

End point description:

Percentage of participants experiencing hospitalizations [>= 24 hour (h) of acute care] and/or ER visits related to COVID-19 or death from any cause up to Day 29. The Part B of the study was not initiated based on regulatory feedback indicating that with evolving treatment options, a placebo controlled design was no longer considered to be appropriate.

End point type	Primary

End point timeframe:

Up to Day 29

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: The Part B of the study was not initiated based on regulatory feedback indicating that with evolving treatment options, a placebo controlled design was no longer considered to be appropriate.

End point values	Phase 3/Part B: Ensovibep 75 mg	Phase 3/Part B: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[2]	0[3]		
Units: percentage of participants				
number (not applicable)				

Notes:

[2] - Part B was not initiated.

[3] - Part B was not initiated.

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Percentage of Participants With Hospitalizations and/or ER Visits Related to COVID-19 or Death From Any Cause

End point title	Part A: Percentage of Participants With Hospitalizations and/or ER Visits Related to COVID-19 or Death From Any Cause

End point description:

Percentage of participants experiencing hospitalizations (>= 24 h of acute care) and/or ER visits related to COVID-19 or death from any cause up to Day 29 were presented along with relative risk to placebo. The FAS included all participants in the randomized set for whom IV infusion of study treatment was administered.

End point type	Secondary

End point timeframe:

Up to Day 29

End point values	Ensovibep 600 mg	Ensovibep 225 mg	Ensovibep 75 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	100	101	99
Units: percentage of participants				
number (not applicable)				
Any event	1.0	3.0	0.0	6.1
Hospitalizations (≥ 24 h of acute care)	0.0	2.0	0.0	5.1
ER visits related to COVID-19	1.0	1.0	0.0	5.1
Death from any cause	0.0	0.0	0.0	2.0

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Time to Sustained Clinical Recovery

End point title	Part A: Time to Sustained Clinical Recovery

End point description:

Sustained clinical recovery was defined as follows;
1. All symptoms from the modified Food and Drug Administration (FDA) COVID-19 questionnaire scored as moderate or severe at baseline were subsequently scored as mild or absent, and
2. All symptoms from the modified FDA COVID-19 questionnaire scored as mild or absent at baseline were subsequently scored as absent, with no subsequent worsening, up to Day 29.
The FAS included all participants in the randomized set for whom IV infusion of study treatment was administered. Only participants included in the analysis are reported.

End point type	Secondary

End point timeframe:

Up to Day 29

End point values	Ensovibep 600 mg	Ensovibep 225 mg	Ensovibep 75 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	66	74	70
Units: days				
median (confidence interval 95%)	23.0 (14.0 to 29.0)	15.0 (13.0 to 21.0)	14.0 (11.0 to 28.0)	29.0 (21.0 to 32.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Observed Maximum Serum Concentration (Cmax) of Total and Free Ensovibep

End point title	Part A: Observed Maximum Serum Concentration (Cmax) of Total and Free Ensovibep[4]

End point description:

Blood samples were collected to determine the Cmax of free ensovibep (ensovibep not bound to target) and total ensovibep (sum of ensovibep not bound to and bound to target) concentrations in serum. The Pharmacokinetic (PK) analysis set included all participants with at least 1 available valid (that is, not flagged for exclusion) PK concentration measurement, who received any study treatment and with no protocol deviations that impacted PK data. Here, 'n' is number of participants analyzed for each parameter.

End point type	Secondary

End point timeframe:

Data was summarized from pre-dose and at 15 minutes and 90 minutes after end of study drug infusion on Day 1, and at Days 3, 8, 15, 29, 61 and 91

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants who received study treatment were analyzed for this endpoint.

End point values	Ensovibep 600 mg	Ensovibep 225 mg	Ensovibep 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	94	92	95	
Units: microgram (mcg) per mL				
geometric mean (geometric coefficient of variation)				
Total Ensovibep (n=94, 90, 93)	187 (± 25.3)	70.4 (± 27.5)	25.1 (± 38.4)	
Free Ensovibep (n=94, 92, 95)	210 (± 26.3)	78.1 (± 31.5)	29.3 (± 46.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Area Under the Concentration-Time Curve From Time Zero to the Time of the Last Quantifiable Concentration (AUClast) of Total and Free Ensovibep

End point title	Part A: Area Under the Concentration-Time Curve From Time Zero to the Time of the Last Quantifiable Concentration (AUClast) of Total and Free Ensovibep[5]

End point description:

Blood samples were collected to determine the AUClast of free ensovibep (ensovibep not bound to target) and total ensovibep (sum of ensovibep not bound to and bound to target) concentrations in serum. The PK analysis set included all participants with at least 1 available valid (that is, not flagged for exclusion) PK concentration measurement, who received any study treatment and with no protocol deviations that impacted PK data. Here, 'n' is number of participants analyzed for each parameter.

End point type	Secondary

End point timeframe:

Data was summarized from pre-dose and at 15 minutes and 90 minutes after end of study drug infusion on Day 1, and at Days 3, 8, 15, 29, 61 and 91

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants who received study treatment were analyzed for this endpoint.

End point values	Ensovibep 600 mg	Ensovibep 225 mg	Ensovibep 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	94	91	95	
Units: h*mcg/mL				
geometric mean (geometric coefficient of variation)				
Total Ensovibep (n=94, 88, 95)	63300 (± 87.6)	21100 (± 122.0)	7950 (± 67.1)	
Free Ensovibep (n=94, 91, 95)	68200 (± 84.4)	22500 (± 126.9)	8380 (± 67.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Area Under the Concentration-Time Curve From Time Zero to 48 Hours (AUC 0-48h) of Total and Free Ensovibep

End point title	Part A: Area Under the Concentration-Time Curve From Time Zero to 48 Hours (AUC 0-48h) of Total and Free Ensovibep[6]

End point description:

Blood samples were collected to determine the AUC 0-48h of free ensovibep (ensovibep not bound to target) and total ensovibep (sum of ensovibep not bound to and bound to target) concentrations in serum. The PK analysis set included all participants with at least 1 available valid (that is, not flagged for exclusion) PK concentration measurement, who received any study treatment and with no protocol deviations that impacted PK data. Here, 'n' is number of participants analyzed for each parameter.

End point type	Secondary

End point timeframe:

Data was summarized from pre-dose and at 15 minutes and 90 minutes after end of study drug infusion on Day 1, and at Day 3

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants who received study treatment were analyzed for this endpoint.

End point values	Ensovibep 600 mg	Ensovibep 225 mg	Ensovibep 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	95	90	95	
Units: h*mcg/mL				
geometric mean (geometric coefficient of variation)				
Total Ensovibep (n=93, 89, 95)	7520 (± 35.3)	2830 (± 35.7)	999 (± 34.4)	
Free Ensovibep (n=95, 90, 95)	8290 (± 32.1)	2800 (± 156.2)	1120 (± 36.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Area Under the Concentration-Time Curve From Time Zero to 168 Hours (AUC 0-168h) of Total and Free Ensovibep

End point title	Part A: Area Under the Concentration-Time Curve From Time Zero to 168 Hours (AUC 0-168h) of Total and Free Ensovibep[7]

End point description:

Blood samples were collected to determine the AUC 0-168h of free ensovibep (ensovibep not bound to target) and total ensovibep (sum of ensovibep not bound to and bound to target) concentrations in serum. The PK analysis set included all participants with at least 1 available valid (that is, not flagged for exclusion) PK concentration measurement, who received any study treatment and with no protocol deviations that impacted PK data. Here, 'n' is number of participants analyzed for each parameter.

End point type	Secondary

End point timeframe:

Data was summarized from pre-dose and at 15 minutes and 90 minutes after end of study drug infusion on Day 1, and at Days 3 and 8

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants who received study treatment were analyzed for this endpoint.

End point values	Ensovibep 600 mg	Ensovibep 225 mg	Ensovibep 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	95	89	95	
Units: h*mcg/mL				
geometric mean (geometric coefficient of variation)				
Total Ensovibep (n=93, 89, 94)	23000 (± 23.7)	8570 (± 33.1)	3020 (± 31.4)	
Free Ensovibep (n= 95, 89, 95)	25200 (± 23.2)	8940 (± 73.2)	3390 (± 35.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Area Under the Concentration-Time Curve From Time Zero to 336 Hours (AUC 0-336h) of Total and Free Ensovibep

End point title	Part A: Area Under the Concentration-Time Curve From Time Zero to 336 Hours (AUC 0-336h) of Total and Free Ensovibep[8]

End point description:

Blood samples were collected to determine the AUC 0-336h of free ensovibep (ensovibep not bound to target) and total ensovibep (sum of ensovibep not bound to and bound to target) concentrations in serum. The PK analysis set included all participants with at least 1 available valid (that is, not flagged for exclusion) PK concentration measurement, who received any study treatment and with no protocol deviations that impacted PK data. Here, 'n' is number of participants analyzed for each parameter.

End point type	Secondary

End point timeframe:

Data was summarized from pre-dose and at 15 minutes and 90 minutes after end of study drug infusion on Day 1, and at Days 3, 8 and 15

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants who received study treatment were analyzed for this endpoint.

End point values	Ensovibep 600 mg	Ensovibep 225 mg	Ensovibep 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	95	88	94	
Units: h*mcg/mL				
geometric mean (geometric coefficient of variation)				
Total Ensovibep (n=93, 87, 93)	38200 (± 23.2)	13800 (± 37.6)	5040 (± 31.9)	
Free Ensovibep (n=95, 88, 94)	41800 (± 23.5)	15300 (± 41.6)	5620 (± 39.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Area Under the Concentration-Time Curve From Time Zero to Infinity (AUCinfinity) of Total and Free Ensovibep

End point title	Part A: Area Under the Concentration-Time Curve From Time Zero to Infinity (AUCinfinity) of Total and Free Ensovibep[9]

End point description:

Blood samples were collected to determine the AUCinfinity of free ensovibep (ensovibep not bound to target) and total ensovibep (sum of ensovibep not bound to and bound to target) concentrations in serum. The PK analysis set included all participants with at least 1 available valid (that is, not flagged for exclusion) PK concentration measurement, who received any study treatment and with no protocol deviations that impacted PK data. Here, 'n' is number of participants analyzed for each parameter.

End point type	Secondary

End point timeframe:

Data was summarized from pre-dose and at 15 minutes and 90 minutes after end of study drug infusion on Day 1, and at Days 3, 8, 15, 29, 61 and 91

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants who received study treatment were analyzed for this endpoint.

End point values	Ensovibep 600 mg	Ensovibep 225 mg	Ensovibep 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	87	82	82	
Units: h*mcg/mL				
geometric mean (geometric coefficient of variation)				
Total Ensovibep (n=87, 77, 82)	75400 (± 33.5)	27600 (± 36.3)	9930 (± 41.0)	
Free Ensovibep (n=87, 82, 80)	80100 (± 40.6)	29400 (± 34.8)	9540 (± 45.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Time to Reach the Maximum Concentration (Tmax) of Total and Free Ensovibep

End point title	Part A: Time to Reach the Maximum Concentration (Tmax) of Total and Free Ensovibep[10]

End point description:

Blood samples were collected to determine the Tmax of free ensovibep (ensovibep not bound to target) and total ensovibep (sum of ensovibep not bound to and bound to target) concentrations in serum. The PK analysis set included all participants with at least 1 available valid (that is, not flagged for exclusion) PK concentration measurement, who received any study treatment and with no protocol deviations that impacted PK data. Here, 'n' is number of participants analyzed for each parameter.

End point type	Secondary

End point timeframe:

Data was summarized from pre-dose and at 15 minutes and 90 minutes after end of study drug infusion on Day 1, and at Days 3, 8, 15, 29, 61 and 91

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only participants who received study treatment were analyzed for this endpoint.

End point values	Ensovibep 600 mg	Ensovibep 225 mg	Ensovibep 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	95	92	95	
Units: hour				
geometric mean (geometric coefficient of variation)				
Total Ensovibep (n=95, 90, 92)	0.935 (± 457.5)	1.30 (± 693.5)	1.05 (± 573.6)	
Free Ensovibep (n=95, 92, 95)	1.01 (± 473.8)	1.09 (± 516.6)	1.24 (± 810.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Apparent Total Body Clearance (CL) of Total and Free Ensovibep

End point title	Part A: Apparent Total Body Clearance (CL) of Total and Free Ensovibep[11]

End point description:

Blood samples were collected to determine the CL of free ensovibep (ensovibep not bound to target) and total ensovibep (sum of ensovibep not bound to and bound to target) concentrations in serum. The PK analysis set included all participants with at least 1 available valid (that is, not flagged for exclusion) PK concentration measurement, who received any study treatment and with no protocol deviations that impacted PK data. Here, 'n' is number of participants analyzed for each parameter.

End point type	Secondary

End point timeframe:

Data was summarized from pre-dose and at 15 minutes and 90 minutes after end of study drug infusion on Day 1, and at Days 3, 8, 15, 29, 61 and 91

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only participants who received study treatment were analyzed for this endpoint.

End point values	Ensovibep 600 mg	Ensovibep 225 mg	Ensovibep 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	84	80	74	
Units: mL/h				
geometric mean (geometric coefficient of variation)				
Total Ensovibep (n=77, 78, 74)	8.07 (± 35.4)	8.11 (± 36.1)	7.48 (± 42.1)	
Free Ensovibep (n=84, 80, 74)	7.55 (± 37.3)	7.64 (± 35.3)	7.78 (± 43.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Terminal Elimination Rate Constant (Lambda z) of Total and Free Ensovibep

End point title	Part A: Terminal Elimination Rate Constant (Lambda z) of Total and Free Ensovibep[12]

End point description:

Blood samples were collected to determine the lambda z of free ensovibep (ensovibep not bound to target) and total ensovibep (sum of ensovibep not bound to and bound to target) concentrations in serum. The PK analysis set included all participants with at least 1 available valid (that is, not flagged for exclusion) PK concentration measurement, who received any study treatment and with no protocol deviations that impacted PK data. Here, 'n' is number of participants analyzed for each parameter.

End point type	Secondary

End point timeframe:

Data was summarized from pre-dose and at 15 minutes and 90 minutes after end of study drug infusion on Day 1, and at Days 3, 8, 15, 29, 61 and 91

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants who received study treatment were analyzed for this endpoint.

End point values	Ensovibep 600 mg	Ensovibep 225 mg	Ensovibep 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	84	79	74	
Units: per hour				
geometric mean (geometric coefficient of variation)				
Total Ensovibep (n=83, 70, 72)	0.003 (± 52.1)	0.002 (± 50.6)	0.002 (± 39.5)	
Free Ensovibep (n=84, 79, 74)	0.003 (± 69.6)	0.003 (± 48.3)	0.003 (± 61.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Terminal Elimination Half-Life (T1/2) of Total and Free Ensovibep

End point title	Part A: Terminal Elimination Half-Life (T1/2) of Total and Free

	Ensovibep[13]

End point description:

Blood samples were collected to determine the T1/2 of free ensovibep (ensovibep not bound to target) and total ensovibep (sum of ensovibep not bound to and bound to target) concentrations in serum. The PK analysis set included all participants with at least 1 available valid (that is, not flagged for exclusion) PK concentration measurement, who received any study treatment and with no protocol deviations that impacted PK data. Here, 'n' is number of participants analyzed for each parameter.

End point type	Secondary

End point timeframe:

Data was summarized from pre-dose and at 15 minutes and 90 minutes after end of study drug infusion on Day 1, and at Days 3, 8, 15, 29, 61 and 91

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants who received study treatment were analyzed for this endpoint.

End point values	Ensovibep 600 mg	Ensovibep 225 mg	Ensovibep 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	83	83	
Units: hour				
geometric mean (geometric coefficient of variation)				
Total Ensovibep (n=89, 81, 83)	274 (± 54.0)	290 (± 53.8)	309 (± 39.8)	
Free Ensovibep (n=90, 83, 81)	262 (± 67.7)	234 (± 48.3)	215 (± 60.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part A: Apparent Volume of Distribution (Vz) of Total and Free Ensovibep

End point title	Part A: Apparent Volume of Distribution (Vz) of Total and Free Ensovibep[14]

End point description:

Blood samples were collected to determine the Vz of free ensovibep (ensovibep not bound to target) and total ensovibep (sum of ensovibep not bound to and bound to target) concentrations in serum. The PK analysis set included all participants with at least 1 available valid (that is, not flagged for exclusion) PK concentration measurement, who received any study treatment and with no protocol deviations that impacted PK data. Here, 'n' is number of participants analyzed for each parameter.

End point type	Secondary

End point timeframe:

Data was summarized from pre-dose and at 15 minutes and 90 minutes after end of study drug infusion on Day 1, and at Days 3, 8, 15, 29, 61 and 91

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants who received study treatment were analyzed for this endpoint.

End point values	Ensovibep 600 mg	Ensovibep 225 mg	Ensovibep 75 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	84	80	74	
Units: mL				
geometric mean (geometric coefficient of variation)				
Total Ensovibep (n=77, 78, 74)	3230 (± 35.0)	3310 (± 37.5)	3330 (± 38.7)	
Free Ensovibep (n=84, 80, 74)	2760 (± 46.1)	2590 (± 36.4)	2470 (± 45.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Change From Baseline in Log10 SARS-CoV-2 Viral Load Through Day 8

End point title	Part B: Change From Baseline in Log10 SARS-CoV-2 Viral Load Through Day 8

End point description:

The SARS-CoV-2 viral load was measured by means of a nasopharyngeal swab, followed by quantitative reverse transcription-polymerase chain reaction assay at a central laboratory. The multiple comparison procedure-modeling methodology was used. The Part B of the study was not initiated based on regulatory feedback indicating that with evolving treatment options, a placebo controlled design was no longer considered to be appropriate.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Days 3, 5 and 8

End point values	Phase 3/Part B: Ensovibep 75 mg	Phase 3/Part B: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[15]	0[16]		
Units: log10 values				
least squares mean (standard error)	()	()		

Notes:

[15] - Part B was not initiated.

[16] - Part B was not initiated.

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Time to Sustained Clinical Recovery

End point title	Part B: Time to Sustained Clinical Recovery

End point description:

Sustained clinical recovery was defined as follows;
1. All symptoms from the modified FDA COVID-19 questionnaire scored as moderate or severe at baseline were subsequently scored as mild or absent, and
2. All symptoms from the modified FDA COVID-19 questionnaire scored as mild or absent at baseline

were subsequently scored as absent, with no subsequent worsening, up to Day 29.
The Part B of the study was not initiated based on regulatory feedback indicating that with evolving treatment options, a placebo controlled design was no longer considered to be appropriate.

End point type	Secondary

End point timeframe:

Up to Day 29

End point values	Phase 3/Part B: Ensovibep 75 mg	Phase 3/Part B: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[17]	0[18]		
Units: days				
median (confidence interval 95%)	(to)	(to)		

Notes:

[17] - Part B was not initiated.

[18] - Part B was not initiated.

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Participants With Treatment-Emergent Anti-Drug Antibody (ADA) Response to Ensovibep

End point title	Part B: Percentage of Participants With Treatment-Emergent Anti-Drug Antibody (ADA) Response to Ensovibep

End point description:

Treatment-emergent ADA was defined as any participant with a
1. 2-fold (1 dilution) increase in titer than the minimum required dilution if no ADAs were detected at baseline (treatment-induced ADA); or,
2. 4-fold (2 dilutions) increase in titer compared with baseline if ADAs were detected at baseline (treatment-boosted ADA).
The Part B of the study was not initiated based on regulatory feedback indicating that with evolving treatment options, a placebo controlled design was no longer considered to be appropriate.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 and Days 15, 29, 61 and 91 postdose of Ensovibep

End point values	Phase 3/Part B: Ensovibep 75 mg	Phase 3/Part B: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[19]	0[20]		
Units: percentage of participants				
number (not applicable)				

Notes:

[19] - Part B was not initiated.

[20] - Part B was not initiated.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events were reported from first dose of study treatment (Day 1) until end of study treatment, up to a maximum duration of 98 days.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Ensovibep 600 mg

Reporting group description:

Participants received single IV infusion of ensovibep 600 mg on Day 1.

Reporting group title	Ensovibep 225 mg

Reporting group description:

Participants received single IV infusion of ensovibep 225 mg on Day 1.

Reporting group title	Ensovibep 75 mg

Reporting group description:

Participants received single IV infusion of ensovibep 75 mg on Day 1.

Reporting group title	Ensovibep Total

Reporting group description:

Participants received single IV infusion of ensovibep on Day 1.

Reporting group title	Placebo

Reporting group description:

Participants received single IV infusion of placebo matching with ensovibep on Day 1.

Serious adverse events	Ensovibep 600 mg	Ensovibep 225 mg	Ensovibep 75 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 100 (0.00%)	2 / 98 (2.04%)	1 / 102 (0.98%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cor pulmonale			

subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Hiatus hernia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paranasal sinus inflammation			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			

subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Ensovibep Total	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 300 (1.00%)	9 / 100 (9.00%)	
number of deaths (all causes)	0	2	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cor pulmonale			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Hiatus hernia			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pancreatitis acute			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paranasal sinus inflammation			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	1 / 300 (0.33%)	4 / 100 (4.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Sepsis			

subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 300 (0.00%)	2 / 100 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Ensovibep 600 mg	Ensovibep 225 mg	Ensovibep 75 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 100 (51.00%)	40 / 98 (40.82%)	40 / 102 (39.22%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 100 (1.00%)	2 / 98 (2.04%)	2 / 102 (1.96%)
occurrences (all)	1	2	2
Phlebitis superficial			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	2 / 100 (2.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	2	0	1
Infusion site haematoma			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Infusion site swelling			

subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 100 (0.00%)	2 / 98 (2.04%)	1 / 102 (0.98%)
occurrences (all)	0	2	1
Swelling face			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	1 / 100 (1.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	1	1	0
Vessel puncture site haematoma			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	1 / 102 (0.98%)
occurrences (all)	0	1	1
Immune system disorders			
Allergy to chemicals			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Heavy menstrual bleeding			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Chronic obstructive pulmonary			

disease			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Throat irritation			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 100 (2.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	2	0	1
Depression			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	1	0	0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	3 / 100 (3.00%)	1 / 98 (1.02%)	1 / 102 (0.98%)
occurrences (all)	3	1	1
Alanine aminotransferase increased			
subjects affected / exposed	7 / 100 (7.00%)	3 / 98 (3.06%)	1 / 102 (0.98%)
occurrences (all)	7	3	1
Aspartate aminotransferase increased			

subjects affected / exposed	6 / 100 (6.00%)	3 / 98 (3.06%)	1 / 102 (0.98%)
occurrences (all)	6	3	1
Amylase increased			
subjects affected / exposed	4 / 100 (4.00%)	1 / 98 (1.02%)	1 / 102 (0.98%)
occurrences (all)	4	1	1
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 100 (1.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	1	1	0
Blood bilirubin increased			
subjects affected / exposed	3 / 100 (3.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	3	0	1
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 100 (3.00%)	1 / 98 (1.02%)	1 / 102 (0.98%)
occurrences (all)	3	1	1
Blood creatinine increased			
subjects affected / exposed	6 / 100 (6.00%)	4 / 98 (4.08%)	3 / 102 (2.94%)
occurrences (all)	7	4	3
Blood glucose increased			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	1	0	1
Blood pressure increased			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	1 / 102 (0.98%)
occurrences (all)	0	1	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	1	0	0
Blood phosphorus decreased			
subjects affected / exposed	2 / 100 (2.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	2	0	0
Blood sodium increased			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Blood uric acid increased			

subjects affected / exposed	0 / 100 (0.00%)	3 / 98 (3.06%)	1 / 102 (0.98%)
occurrences (all)	0	3	1
Blood sodium decreased			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Fibrin D dimer increased			
subjects affected / exposed	5 / 100 (5.00%)	2 / 98 (2.04%)	4 / 102 (3.92%)
occurrences (all)	5	3	4
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 100 (3.00%)	1 / 98 (1.02%)	3 / 102 (2.94%)
occurrences (all)	3	1	3
C-reactive protein increased			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	1	0	1
Haematocrit decreased			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Hepatic enzyme increased			
subjects affected / exposed	2 / 100 (2.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	2	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Lipase increased			
subjects affected / exposed	6 / 100 (6.00%)	0 / 98 (0.00%)	3 / 102 (2.94%)
occurrences (all)	6	0	3
International normalised ratio increased			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Liver function test increased			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Monocyte count increased			

subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Pancreatic enzymes increased			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Monocyte count decreased			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Serum ferritin decreased			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Prothrombin time prolonged			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Platelet count increased			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
White blood cell count increased			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Bone contusion			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Post procedural complication			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Infusion related reaction			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Ligament sprain			

subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	2 / 100 (2.00%)	2 / 98 (2.04%)	4 / 102 (3.92%)
occurrences (all)	4	2	4
Neuropathy peripheral			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	3 / 102 (2.94%)
occurrences (all)	0	0	3
Eosinophilia			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	1	0	0
Haemorrhagic diathesis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Leukopenia			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Lymphadenopathy			

subjects affected / exposed	2 / 100 (2.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	2	0	0
Lymphocytosis			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	3 / 100 (3.00%)	1 / 98 (1.02%)	4 / 102 (3.92%)
occurrences (all)	3	1	4
Eye disorders			
Abnormal sensation in eye			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Uveitis			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Disorder of globe			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	1	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 100 (1.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	1	1	0
Aphthous ulcer			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			

subjects affected / exposed	1 / 100 (1.00%)	1 / 98 (1.02%)	1 / 102 (0.98%)
occurrences (all)	1	1	1
Haemorrhoids			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	3 / 100 (3.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	3	1	0
Pancreatitis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	3 / 100 (3.00%)	2 / 98 (2.04%)	1 / 102 (0.98%)
occurrences (all)	3	2	1
Hepatobiliary disorders			
Nonalcoholic fatty liver disease			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Eczema			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Rash papular			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Rash			

subjects affected / exposed	3 / 100 (3.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	3	1	0
Rash maculo-papular			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Hydronephrosis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Ureterolithiasis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Renal pain			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Arthritis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Myositis			

subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Infections and infestations			
COVID-19			
subjects affected / exposed	6 / 100 (6.00%)	2 / 98 (2.04%)	1 / 102 (0.98%)
occurrences (all)	6	2	1
COVID-19 pneumonia			
subjects affected / exposed	2 / 100 (2.00%)	2 / 98 (2.04%)	0 / 102 (0.00%)
occurrences (all)	2	2	0
Bronchitis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Eye infection bacterial			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	5 / 100 (5.00%)	1 / 98 (1.02%)	3 / 102 (2.94%)
occurrences (all)	5	1	4
Genital infection fungal			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Otitis media			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	1	0	0
Pancreatitis viral			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0

Pyelonephritis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Pharyngitis bacterial			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	1 / 102 (0.98%)
occurrences (all)	0	1	1
Sinusitis bacterial			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	1 / 100 (1.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	1	0	1
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Hyperamylasaemia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 100 (1.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	1	1	0
Hyperkalaemia			

subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Hyperlipidaemia			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Hypernatraemia			
subjects affected / exposed	0 / 100 (0.00%)	3 / 98 (3.06%)	0 / 102 (0.00%)
occurrences (all)	0	3	0
Hyperlipasaemia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 98 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	0 / 102 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Ensovibep Total	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	131 / 300 (43.67%)	53 / 100 (53.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 300 (1.67%)	0 / 100 (0.00%)	
occurrences (all)	5	0	
Phlebitis superficial			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Asthenia			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Fatigue			

subjects affected / exposed	3 / 300 (1.00%)	1 / 100 (1.00%)	
occurrences (all)	3	1	
Infusion site haematoma			
subjects affected / exposed	0 / 300 (0.00%)	2 / 100 (2.00%)	
occurrences (all)	0	2	
Infusion site swelling			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Non-cardiac chest pain			
subjects affected / exposed	3 / 300 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	3	0	
Swelling face			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	2 / 300 (0.67%)	0 / 100 (0.00%)	
occurrences (all)	2	0	
Vessel puncture site haematoma			
subjects affected / exposed	2 / 300 (0.67%)	0 / 100 (0.00%)	
occurrences (all)	2	0	
Immune system disorders			
Allergy to chemicals			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Heavy menstrual bleeding			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Dysmenorrhoea			

subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Haemoptysis			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Rhinitis allergic			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Throat irritation			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 300 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	3	0	
Depression			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Investigations			

Activated partial thromboplastin time prolonged			
subjects affected / exposed	5 / 300 (1.67%)	1 / 100 (1.00%)	
occurrences (all)	5	1	
Alanine aminotransferase increased			
subjects affected / exposed	11 / 300 (3.67%)	2 / 100 (2.00%)	
occurrences (all)	11	2	
Aspartate aminotransferase increased			
subjects affected / exposed	10 / 300 (3.33%)	2 / 100 (2.00%)	
occurrences (all)	10	2	
Amylase increased			
subjects affected / exposed	6 / 300 (2.00%)	2 / 100 (2.00%)	
occurrences (all)	6	2	
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 300 (0.67%)	0 / 100 (0.00%)	
occurrences (all)	2	0	
Blood bilirubin increased			
subjects affected / exposed	4 / 300 (1.33%)	0 / 100 (0.00%)	
occurrences (all)	4	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	5 / 300 (1.67%)	1 / 100 (1.00%)	
occurrences (all)	5	1	
Blood creatinine increased			
subjects affected / exposed	13 / 300 (4.33%)	6 / 100 (6.00%)	
occurrences (all)	14	6	
Blood glucose increased			
subjects affected / exposed	2 / 300 (0.67%)	1 / 100 (1.00%)	
occurrences (all)	2	1	
Blood pressure increased			
subjects affected / exposed	2 / 300 (0.67%)	1 / 100 (1.00%)	
occurrences (all)	2	1	
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Blood phosphorus decreased			

subjects affected / exposed	2 / 300 (0.67%)	1 / 100 (1.00%)		
occurrences (all)	2	1		
Blood sodium increased				
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)		
occurrences (all)	1	0		
Blood uric acid increased				
subjects affected / exposed	4 / 300 (1.33%)	1 / 100 (1.00%)		
occurrences (all)	4	1		
Blood sodium decreased				
subjects affected / exposed	1 / 300 (0.33%)	1 / 100 (1.00%)		
occurrences (all)	1	1		
Fibrin D dimer increased				
subjects affected / exposed	11 / 300 (3.67%)	3 / 100 (3.00%)		
occurrences (all)	12	3		
Gamma-glutamyltransferase increased				
subjects affected / exposed	7 / 300 (2.33%)	1 / 100 (1.00%)		
occurrences (all)	7	1		
C-reactive protein increased				
subjects affected / exposed	2 / 300 (0.67%)	0 / 100 (0.00%)		
occurrences (all)	2	0		
Haematocrit decreased				
subjects affected / exposed	1 / 300 (0.33%)	1 / 100 (1.00%)		
occurrences (all)	1	1		
Hepatic enzyme increased				
subjects affected / exposed	2 / 300 (0.67%)	2 / 100 (2.00%)		
occurrences (all)	2	2		
Haemoglobin decreased				
subjects affected / exposed	1 / 300 (0.33%)	1 / 100 (1.00%)		
occurrences (all)	1	1		
Lipase increased				
subjects affected / exposed	9 / 300 (3.00%)	1 / 100 (1.00%)		
occurrences (all)	9	1		
International normalised ratio increased				

subjects affected / exposed	0 / 300 (0.00%)	2 / 100 (2.00%)	
occurrences (all)	0	2	
Liver function test increased			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Monocyte count increased			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Pancreatic enzymes increased			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Monocyte count decreased			
subjects affected / exposed	1 / 300 (0.33%)	1 / 100 (1.00%)	
occurrences (all)	1	1	
Serum ferritin decreased			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Prothrombin time prolonged			
subjects affected / exposed	0 / 300 (0.00%)	3 / 100 (3.00%)	
occurrences (all)	0	3	
Platelet count increased			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
White blood cell count increased			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Bone contusion			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Post procedural complication			

subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Infusion related reaction			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Ligament sprain			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Procedural pain			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Skin abrasion			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 300 (0.33%)	1 / 100 (1.00%)	
occurrences (all)	1	1	
Headache			
subjects affected / exposed	8 / 300 (2.67%)	1 / 100 (1.00%)	
occurrences (all)	10	1	
Neuropathy peripheral			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 300 (1.00%)	0 / 100 (0.00%)	
occurrences (all)	3	0	
Eosinophilia			
subjects affected / exposed	1 / 300 (0.33%)	1 / 100 (1.00%)	
occurrences (all)	1	1	
Haemorrhagic diathesis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Iron deficiency anaemia			

subjects affected / exposed	1 / 300 (0.33%)	1 / 100 (1.00%)	
occurrences (all)	1	1	
Leukopenia			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Lymphadenopathy			
subjects affected / exposed	2 / 300 (0.67%)	0 / 100 (0.00%)	
occurrences (all)	2	0	
Lymphocytosis			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Neutropenia			
subjects affected / exposed	8 / 300 (2.67%)	1 / 100 (1.00%)	
occurrences (all)	8	1	
Eye disorders			
Abnormal sensation in eye			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Uveitis			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Disorder of globe			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Vision blurred			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 300 (0.67%)	0 / 100 (0.00%)	
occurrences (all)	2	0	
Abdominal pain upper			
subjects affected / exposed	0 / 300 (0.00%)	2 / 100 (2.00%)	
occurrences (all)	0	2	
Constipation			

subjects affected / exposed	2 / 300 (0.67%)	0 / 100 (0.00%)	
occurrences (all)	2	0	
Aphthous ulcer			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	3 / 300 (1.00%)	1 / 100 (1.00%)	
occurrences (all)	3	1	
Haemorrhoids			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	4 / 300 (1.33%)	2 / 100 (2.00%)	
occurrences (all)	4	2	
Pancreatitis			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	6 / 300 (2.00%)	1 / 100 (1.00%)	
occurrences (all)	6	1	
Hepatobiliary disorders			
Nonalcoholic fatty liver disease			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	1 / 300 (0.33%)	2 / 100 (2.00%)	
occurrences (all)	1	2	
Eczema			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Petechiae			

subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Rash papular			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	4 / 300 (1.33%)	0 / 100 (0.00%)	
occurrences (all)	4	0	
Rash maculo-papular			
subjects affected / exposed	1 / 300 (0.33%)	1 / 100 (1.00%)	
occurrences (all)	1	1	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Hydronephrosis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Ureterolithiasis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Renal pain			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	1 / 300 (0.33%)	1 / 100 (1.00%)	
occurrences (all)	1	1	
Arthritis			

subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Myositis			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
COVID-19			
subjects affected / exposed	9 / 300 (3.00%)	4 / 100 (4.00%)	
occurrences (all)	9	4	
COVID-19 pneumonia			
subjects affected / exposed	4 / 300 (1.33%)	1 / 100 (1.00%)	
occurrences (all)	4	1	
Bronchitis			
subjects affected / exposed	1 / 300 (0.33%)	1 / 100 (1.00%)	
occurrences (all)	1	1	
Cystitis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Eye infection bacterial			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	9 / 300 (3.00%)	5 / 100 (5.00%)	
occurrences (all)	10	5	
Genital infection fungal			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Otitis media			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	

Pancreatitis viral			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Oral candidiasis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Pyelonephritis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Pharyngitis bacterial			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	0 / 300 (0.00%)	2 / 100 (2.00%)	
occurrences (all)	0	2	
Upper respiratory tract infection			
subjects affected / exposed	2 / 300 (0.67%)	1 / 100 (1.00%)	
occurrences (all)	2	1	
Sinusitis bacterial			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	2 / 300 (0.67%)	1 / 100 (1.00%)	
occurrences (all)	2	1	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Diabetes mellitus			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Hyperamylasaemia			

subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Hyperglycaemia			
subjects affected / exposed	2 / 300 (0.67%)	0 / 100 (0.00%)	
occurrences (all)	2	0	
Hyperkalaemia			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Hyperlipidaemia			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Hypernatraemia			
subjects affected / exposed	3 / 300 (1.00%)	1 / 100 (1.00%)	
occurrences (all)	3	1	
Hyperlipasaemia			
subjects affected / exposed	0 / 300 (0.00%)	1 / 100 (1.00%)	
occurrences (all)	0	1	
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 300 (0.33%)	1 / 100 (1.00%)	
occurrences (all)	1	1	
Hypokalaemia			
subjects affected / exposed	1 / 300 (0.33%)	0 / 100 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 October 2021	- The key changes included clarification regarding the laboratory data available at the time of the database lock (DBL), unblinding after DBL, and statistical analysis. - For the primary analysis some of the biomarker assessments may not be fully completed. In this context, updates have been made to the unblinding process after the primary analysis for Part A. - The primary estimand wording was updated to follow recently published guidelines (FDA 2021). The COVID-19 related hospitalizations were added as intercurrent events for the primary endpoint; a composite strategy was to be used to handle these intercurrent events. - The definition of adverse event of special interest was updated and was no longer limited to adverse event onset within 24 h after dosing, it included infusion-site reactions and any type of hypersensitivity reactions (Grade >= 2). The reporting requirements and follow-up testing for renal events were adjusted. - The end of study assessments were clarified per a footnote in the assessment schedule. - The study stopping rules were clarified to follow common terminology criteria for adverse events grading and to explicitly include laboratory findings. - A clarification was added to distinguish between hospitalizations due to worsening of COVID-19 (secondary endpoint) and between hospitalizations meant for isolating patients following a positive SARS-CoV-2 test (not counted towards secondary endpoint). - The requirements for viral genotyping were updated to ensure that all reverse transcription-polymerase chain reaction positive samples at Baseline and from Day 8 onwards, or last positive sample in case of no viral load from Day 8 onwards, were sequenced. - In the statistical section, clarification on the multiple comparison procedure-modeling procedure was added and the symptom scores in Long COVID-19 questionnaire were explained. - Also, 2 local amendments for the USA and for India were incorporated into this global amendment.

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.

The Part B of the study was not initiated based on regulatory feedback indicating that with evolving treatment options, a placebo controlled design was no longer considered to be appropriate.

Notes: