



Clinical trial results:

An International Multicenter, Adaptive, Randomized Double-Blind, Placebo-Controlled Trial of the Safety, Tolerability and Efficacy of Anti-Coronavirus Hyperimmune Intravenous Immunoglobulin for the Treatment of Adult Hospitalized Patients at Onset of Clinical Progression of COVID-19

Summary

EudraCT number	2020-002542-16
Trial protocol	GB GR DK DE
Global end of trial date	21 May 2021

Results information

Result version number	v1 (current)
This version publication date	18 April 2022
First version publication date	18 April 2022
Summary attachment (see zip file)	ITAC Primary manuscript (ITAC-primary-results_Jan2022.pdf) ITAC supplemental materials to publication (ITAC Supplemental Materials_Resubmission_Final_For_Proofs.docx)

Trial information

Trial identification

Sponsor protocol code	INSIGHT013
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04546581
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regents of the University of Minnesota
Sponsor organisation address	Office of the Vice President for Research, 420 Johnston Hall, 101 Pleasant St SE, Minneapolis, United States, 55455
Public contact	Sarah Pett, MRC CTU at UCL, 44 02076704700, s.pett@ucl.ac.uk
Scientific contact	Sarah Pett, MRC CTU at UCL, 44 02076704700, s.pett@ucl.ac.uk

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	08 July 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 May 2021
Global end of trial reached?	Yes
Global end of trial date	21 May 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary endpoint of this trial in hospitalized patients is an ordinal outcome based on the patient's clinical status on Day 7. It includes 7 mutually exclusive categories capturing the range of organ dysfunction that may be associated with progression of COVID-19, such as respiratory dysfunction and coagulation-related complications:

7. Death
6. End-organ failure
5. Life-threatening end-organ dysfunction
4. Serious end-organ dysfunction
3. Moderate end-organ dysfunction
2. Limiting symptoms due to COVID-19
1. No limiting symptoms due to COVID-19

The rationale behind this approach is to estimate in a clinically meaningful way whether the study drug has had a favourable clinical impact on the patient.

Protection of trial subjects:

Informed consent.

Clinical assessment immediately prior to study infusion to ensure participant is still eligible to receive the study product.

Careful clinical monitoring during infusion of study agent and for at least 2 hours afterward.

Background therapy:

Remdesivir was to be administered as a 200 mg IV loading dose (100 mL volume) on the first day of its infusion followed by 100mg daily for the course described below; remdesivir may have commenced prior to randomization. For participants starting remdesivir after randomization to hIVIG/placebo, the loading dose was to be given immediately after the infusion of hIVIG/placebo, once any infusion reactions from that infusion have resolved; for those who commenced remdesivir prior to randomization, the usual maintenance dose of 100 mg was to be given after the hIVIG/placebo infusion on Day 0 in the same manner. After the first remdesivir infusion, a 100 mg once-daily IV maintenance dose (also 100 mL volume) was given each day while hospitalized for up to a 10 day total course; shorter durations of 5 days could be considered by the clinical investigator as appropriate in patients who are not ventilated. Infusions were not given to participants after discharge. The total treatment course was not to exceed 10 calendar days even if an infusion was missed.

Evidence for comparator: -

Actual start date of recruitment	01 September 2020
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	Spain: 65
Country: Number of subjects enrolled	United Kingdom: 19
Country: Number of subjects enrolled	Denmark: 77
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Greece: 70
Country: Number of subjects enrolled	Indonesia: 33
Country: Number of subjects enrolled	Argentina: 4
Country: Number of subjects enrolled	Israel: 6
Country: Number of subjects enrolled	Japan: 15
Country: Number of subjects enrolled	Nigeria: 41
Country: Number of subjects enrolled	United States: 253
Worldwide total number of subjects	593
EEA total number of subjects	222

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)	371
From 65 to 84 years	204
85 years and over	18

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from participating hospitals between 8 Oct 2020 and 10 Feb 2021.

Pre-assignment

Screening details:

Hospitalized adults with COVID-19

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, Assessor

Blinding implementation details:

Randomizer was given a treatment ID, which was sent to the pharmacy. The ID was decoded in the pharmacy. A saline placebo infusion was used. The infusion bag was covered with a colored sleeve to mask the slight difference in color between the active product and placebo.

Arms

Are arms mutually exclusive?	Yes
Arm title	hIVIG

Arm description:

SARS-CoV-2 hyperimmune intravenous immunoglobulin (hIVIG) was administered intravenously as a single dose of 400 mg/kg (or 0.4 g/kg) body weight, to a maximum dose of 40 g (or 400 mL).

SARS-CoV-2 Immunoglobulin Intravenous (human) is a human hyperimmune product of the purified gamma globulin (IgG) fraction of human plasma containing polyvalent neutralizing antibodies to SARS-CoV-2. hIVIG is prepared from pooled plasma collected from healthy, adult donors who have recovered from SARS-CoV-2 infection.

Four hIVIG products were used in this trial: CSL Behring SARS-CoV-2 Hyperimmune Immunoglobulin Intravenous (human) (hIVIG), Emergent SARS-CoV-2 Hyperimmune Immunoglobulin Intravenous (human) (hIVIG), Grifols SARS-CoV-2 Hyperimmune Immunoglobulin Intravenous (human) (hIVIG), and Takeda SARS-CoV-2 Hyperimmune Immunoglobulin Intravenous (human) (hIVIG).

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

Dosage and administration details:

The hIVIG product was administered as a single dose of 400 mg/kg (or 0.4 g/kg) body weight, to a maximum dose of (40 g or 400 mL).

Arm title	Placebo
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Arm description:

Normal saline was administered as a single dose of 400 mg/kg (or 0.4 g/kg) body weight, to a maximum dose of 40 g (or 400 mL)

Arm type	Placebo
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Investigational medicinal product name	Normal saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Normal saline was administered as a single dose of 400 mg/kg (or 0.4 g/kg) body weight, to a maximum dose of 40 g (or 400 mL)

Number of subjects in period 1	hIVIG	Placebo
Started	301	292
Completed	288	279
Not completed	13	13
Consent withdrawn by subject	3	7
Adverse event, non-fatal	9	3
Administrative withdrawal	-	1
Protocol deviation	1	2

Baseline characteristics

Reporting groups

Reporting group title	hIVIG
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Reporting group description:

SARS-CoV-2 hyperimmune intravenous immunoglobulin (hIVIG) was administered intravenously as a single dose of 400 mg/kg (or 0.4 g/kg) body weight, to a maximum dose of 40 g (or 400 mL).

SARS-CoV-2 Immunoglobulin Intravenous (human) is a human hyperimmune product of the purified gamma globulin (IgG) fraction of human plasma containing polyvalent neutralizing antibodies to SARS-CoV-2. hIVIG is prepared from pooled plasma collected from healthy, adult donors who have recovered from SARS-CoV-2 infection.

Four hIVIG products were used in this trial: CSL Behring SARS-CoV-2 Hyperimmune Immunoglobulin Intravenous (human) (hIVIG), Emergent SARS-CoV-2 Hyperimmune Immunoglobulin Intravenous (human) (hIVIG), Grifols SARS-CoV-2 Hyperimmune Immunoglobulin Intravenous (human) (hIVIG), and Takeda SARS-CoV-2 Hyperimmune Immunoglobulin Intravenous (human) (hIVIG).

Reporting group title	Placebo
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Reporting group description:

Normal saline was administered as a single dose of 400 mg/kg (or 0.4 g/kg) body weight, to a maximum dose of 40 g (or 400 mL)

Reporting group values	hIVIG	Placebo	Total
Number of subjects	301	292	593
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	58.4	59.7	
standard deviation	± 15.1	± 13.8	-
Gender categorical			
Units: Subjects			
Female	149	108	257
Male	152	184	336

Subject analysis sets

Subject analysis set title	hIVIG - mITT population
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Subject analysis set type	Modified intention-to-treat
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Subject analysis set description:

Analyses were performed on a modified intention to treat (mITT) population, which included all

randomized participants who met eligibility criteria and received all or part of the assigned study product infusion. Of the 301 participants randomized to hIVIG, 295 were included in the mITT population.

Subject analysis set title	Placebo - mITT population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Analyses were performed on a modified intention to treat (mITT) population, which included all randomized participants who met eligibility criteria and received all or part of the assigned study product infusion. Of the 292 participants randomized to placebo, 284 were included in the mITT population.

Reporting group values	hIVIG - mITT population	Placebo - mITT population	
Number of subjects	295	284	
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	58.4	59.5	
standard deviation	± 15.2	± 13.8	
Gender categorical Units: Subjects			
Female	146	104	
Male	149	180	

End points

End points reporting groups

Reporting group title	hIVIG
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Reporting group description:

SARS-CoV-2 hyperimmune intravenous immunoglobulin (hIVIG) was administered intravenously as a single dose of 400 mg/kg (or 0.4 g/kg) body weight, to a maximum dose of 40 g (or 400 mL).

SARS-CoV-2 Immunoglobulin Intravenous (human) is a human hyperimmune product of the purified gamma globulin (IgG) fraction of human plasma containing polyvalent neutralizing antibodies to SARS-CoV-2. hIVIG is prepared from pooled plasma collected from healthy, adult donors who have recovered from SARS-CoV-2 infection.

Four hIVIG products were used in this trial: CSL Behring SARS-CoV-2 Hyperimmune Immunoglobulin Intravenous (human) (hIVIG), Emergent SARS-CoV-2 Hyperimmune Immunoglobulin Intravenous (human) (hIVIG), Grifols SARS-CoV-2 Hyperimmune Immunoglobulin Intravenous (human) (hIVIG), and Takeda SARS-CoV-2 Hyperimmune Immunoglobulin Intravenous (human) (hIVIG).

Reporting group title	Placebo
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Reporting group description:

Normal saline was administered as a single dose of 400 mg/kg (or 0.4 g/kg) body weight, to a maximum dose of 40 g (or 400 mL)

Subject analysis set title	hIVIG - mITT population
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Subject analysis set type	Modified intention-to-treat
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Subject analysis set description:

Analyses were performed on a modified intention to treat (mITT) population, which included all randomized participants who met eligibility criteria and received all or part of the assigned study product infusion. Of the 301 participants randomized to hIVIG, 295 were included in the mITT population.

Subject analysis set title	Placebo - mITT population
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Subject analysis set type	Modified intention-to-treat
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Subject analysis set description:

Analyses were performed on a modified intention to treat (mITT) population, which included all randomized participants who met eligibility criteria and received all or part of the assigned study product infusion. Of the 292 participants randomized to placebo, 284 were included in the mITT population.

Primary: Day 7 Ordinal Outcome

End point title	Day 7 Ordinal Outcome
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End point description:

Ordinal outcome with 7 mutually exclusive categories. On Day 7, the worst of the 7 categories the participant was in that day will constitute the primary outcome for that patient. The 7 categories are: 7) Death, 6) End-organ failure, 5) Life-threatening end-organ dysfunction, 4) Serious end-organ dysfunction, 3) Moderate end-organ dysfunction, 2) Limiting symptoms due to COVID-19, 1) No limiting symptoms due to COVID-19

End point type	Primary
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End point timeframe:

Status on Day 7

End point values	hIVIG - mITT population	Placebo - mITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	295 ^[1]	284 ^[2]		
Units: Percent				
Death	5	5		
End-organ failure	9	13		
Life-threatening end-organ dysfunction	26	26		
Serious end-organ dysfunction	25	30		
Moderate end-organ dysfunction	32	28		
Limiting symptoms due to COVID-19	67	61		
No limiting symptoms due to COVID-19	129	116		

Notes:

[1] - 295 were analyzed for this endpoint; Multiple imputation was performed for the 2 with missing data

[2] - 284 were analyzed for this endpoint; Multiple imputation was performed for the 5 with missing data

Statistical analyses

Statistical analysis title	Main analysis
Comparison groups	hIVIG - mITT population v Placebo - mITT population
Number of subjects included in analysis	579
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.72
Method	Regression, Logistic
Parameter estimate	Proportional odds ratio
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.45

Secondary: All-cause mortality through Day 28

End point title	All-cause mortality through Day 28
End point description:	
The mortality rate was estimated as the percentage of participants who died by study day 28	
End point type	Secondary
End point timeframe:	
Entire trial (through Day 28)	

End point values	hIVIG - mITT population	Placebo - mITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	295	284		
Units: percent				
number (confidence interval 95%)	6 (4 to 10)	8 (5 to 12)		

Statistical analyses

Statistical analysis title	All-cause mortality through Day 28
Comparison groups	hIVIG - mITT population v Placebo - mITT population
Number of subjects included in analysis	579
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.49
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	1.51

Secondary: Primary Safety Outcome

End point title	Primary Safety Outcome
End point description:	
Primary safety outcome - Death, SAE or Grade 3 or 4 event through Day 7	
End point type	Secondary
End point timeframe:	
Through Day 7	

End point values	hIVIG - mITT population	Placebo - mITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	295	284		
Units: Participants	71	70		

Statistical analyses

Statistical analysis title	Odds ratio (OR) for primary safety outcome
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Statistical analysis description:

hIVIG/placebo odds ratio for primary safety outcome

Comparison groups	hIVIG - mITT population v Placebo - mITT population
Number of subjects included in analysis	579
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.91
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.46

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Grade 3 and 4 AEs were reported through Day 7, SAEs were report through all of follow-up (through Day 28)

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.1
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Reporting groups

Reporting group title	hIVIG - Infused
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Reporting group description:

hIVIG participants who received any amount of infusion

Reporting group title	Placebo - infused
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Reporting group description:

Placebo participants receiving any amount of infusion

Serious adverse events	hIVIG - Infused	Placebo - infused	
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 297 (5.39%)	20 / 284 (7.04%)	
number of deaths (all causes)	18	22	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 297 (0.34%)	0 / 284 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 297 (0.34%)	0 / 284 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 297 (0.34%)	1 / 284 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute left ventricular failure			

subjects affected / exposed	1 / 297 (0.34%)	0 / 284 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 297 (0.34%)	0 / 284 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulseless electrical activity			
subjects affected / exposed	0 / 297 (0.00%)	1 / 284 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 297 (0.00%)	1 / 284 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 297 (0.34%)	2 / 284 (0.70%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Blood loss anaemia			
subjects affected / exposed	1 / 297 (0.34%)	0 / 284 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 297 (0.34%)	0 / 284 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 297 (0.00%)	1 / 284 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 297 (0.34%)	0 / 284 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haemorrhage			
subjects affected / exposed	1 / 297 (0.34%)	0 / 284 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	1 / 297 (0.34%)	2 / 284 (0.70%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 297 (0.34%)	1 / 284 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	1 / 297 (0.34%)	0 / 284 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 297 (0.00%)	1 / 284 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 297 (0.00%)	1 / 284 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 297 (0.34%)	0 / 284 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 297 (0.00%)	1 / 284 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	0 / 297 (0.00%)	1 / 284 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	3 / 297 (1.01%)	1 / 284 (0.35%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	1 / 297 (0.34%)	2 / 284 (0.70%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Sepsis			
subjects affected / exposed	0 / 297 (0.00%)	1 / 284 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
COVID-19			
subjects affected / exposed	0 / 297 (0.00%)	1 / 284 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	0 / 297 (0.00%)	1 / 284 (0.35%)	
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 / 297 (0.00%)	1 / 284 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

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

Non-serious adverse events	hIVIG - Infused	Placebo - infused	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 297 (15.49%)	35 / 284 (12.32%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	3 / 297 (1.01%)	1 / 284 (0.35%)	
occurrences (all)	3	1	
Hypertension			
subjects affected / exposed	1 / 297 (0.34%)	1 / 284 (0.35%)	
occurrences (all)	1	1	
Haemorrhage			
subjects affected / exposed	1 / 297 (0.34%)	0 / 284 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	10 / 297 (3.37%)	5 / 284 (1.76%)	
occurrences (all)	10	6	
Chills			
subjects affected / exposed	10 / 297 (3.37%)	0 / 284 (0.00%)	
occurrences (all)	10	0	
Fatigue			
subjects affected / exposed	1 / 297 (0.34%)	3 / 284 (1.06%)	
occurrences (all)	1	3	
Asthenia			
subjects affected / exposed	1 / 297 (0.34%)	0 / 284 (0.00%)	
occurrences (all)	1	0	
Chest pain			
subjects affected / exposed	1 / 297 (0.34%)	0 / 284 (0.00%)	
occurrences (all)	1	0	
Malaise			

subjects affected / exposed occurrences (all)	0 / 297 (0.00%) 0	1 / 284 (0.35%) 1	
Non-cardiac chest pain subjects affected / exposed occurrences (all)	0 / 297 (0.00%) 0	1 / 284 (0.35%) 1	
Social circumstances Dependence on oxygen therapy subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	0 / 284 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	10 / 297 (3.37%) 13	5 / 284 (1.76%) 6	
Respiratory distress subjects affected / exposed occurrences (all)	6 / 297 (2.02%) 7	5 / 284 (1.76%) 6	
Respiratory failure subjects affected / exposed occurrences (all)	4 / 297 (1.35%) 4	3 / 284 (1.06%) 3	
Cough subjects affected / exposed occurrences (all)	2 / 297 (0.67%) 2	2 / 284 (0.70%) 2	
Hypoxia subjects affected / exposed occurrences (all)	3 / 297 (1.01%) 3	0 / 284 (0.00%) 0	
Acute respiratory failure subjects affected / exposed occurrences (all)	0 / 297 (0.00%) 0	1 / 284 (0.35%) 1	
Bronchiectasis subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	0 / 284 (0.00%) 0	
Dyspnoea exertional subjects affected / exposed occurrences (all)	0 / 297 (0.00%) 0	1 / 284 (0.35%) 1	
Haemoptysis			

subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	0 / 284 (0.00%) 0	
Interstitial lung disease subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	0 / 284 (0.00%) 0	
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 297 (0.00%) 0	1 / 284 (0.35%) 1	
Pneumothorax subjects affected / exposed occurrences (all)	0 / 297 (0.00%) 0	1 / 284 (0.35%) 1	
Pulmonary oedema subjects affected / exposed occurrences (all)	0 / 297 (0.00%) 0	1 / 284 (0.35%) 1	
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	1 / 284 (0.35%) 1	
Mental status changes subjects affected / exposed occurrences (all)	0 / 297 (0.00%) 0	1 / 284 (0.35%) 1	
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	0 / 284 (0.00%) 0	
Blood glucose increased subjects affected / exposed occurrences (all)	0 / 297 (0.00%) 0	1 / 284 (0.35%) 1	
Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	1 / 284 (0.35%) 1	
Tachycardia subjects affected / exposed occurrences (all)	0 / 297 (0.00%) 0	2 / 284 (0.70%) 2	
Bradycardia			

subjects affected / exposed occurrences (all)	0 / 297 (0.00%) 0	1 / 284 (0.35%) 1	
Left ventricular failure subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	0 / 284 (0.00%) 0	
Myocardial infarction subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	0 / 284 (0.00%) 0	
Myocarditis subjects affected / exposed occurrences (all)	0 / 297 (0.00%) 0	1 / 284 (0.35%) 1	
Supraventricular tachycardia subjects affected / exposed occurrences (all)	0 / 297 (0.00%) 0	1 / 284 (0.35%) 1	
Nervous system disorders			
Ageusia subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	2 / 284 (0.70%) 2	
Anosmia subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	2 / 284 (0.70%) 2	
Headache subjects affected / exposed occurrences (all)	0 / 297 (0.00%) 0	1 / 284 (0.35%) 1	
Lethargy subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	0 / 284 (0.00%) 0	
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	3 / 297 (1.01%) 3	0 / 284 (0.00%) 0	
Leukopenia subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	0 / 284 (0.00%) 0	
Eye disorders			

Vision blurred subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	0 / 284 (0.00%) 0	
Gastrointestinal disorders			
Constipation subjects affected / exposed occurrences (all)	0 / 297 (0.00%) 0	1 / 284 (0.35%) 1	
Diarrhoea subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	0 / 284 (0.00%) 0	
Nausea subjects affected / exposed occurrences (all)	0 / 297 (0.00%) 0	1 / 284 (0.35%) 1	
Renal and urinary disorders			
Acute kidney injury subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	1 / 284 (0.35%) 1	
Anuria subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	0 / 284 (0.00%) 0	
Oliguria subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	0 / 284 (0.00%) 0	
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	0 / 297 (0.00%) 0	1 / 284 (0.35%) 1	
Muscle rigidity subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	0 / 284 (0.00%) 0	
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	0 / 297 (0.00%) 0	1 / 284 (0.35%) 1	
Infections and infestations			
COVID-19 pneumonia			

subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	1 / 284 (0.35%) 1	
Pneumonia subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	0 / 284 (0.00%) 0	
Septic shock subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	0 / 284 (0.00%) 0	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 297 (0.34%) 1	1 / 284 (0.35%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported