



Clinical trial results: Expanded Access Treatment Protocol: Remdesivir (RDV; GS-5734) for the Treatment of SARS-CoV2 (CoV) Infection

Summary

EudraCT number	2020-001453-49
Trial protocol	ES
Global end of trial date	23 September 2020

Results information

Result version number	v1 (current)
This version publication date	02 October 2021
First version publication date	02 October 2021

Trial information

Trial identification

Sponsor protocol code	GS-US-540-5821
-----------------------	----------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04323761
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.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	23 September 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 September 2020
Global end of trial reached?	Yes
Global end of trial date	23 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to provide expanded access of remdesivir for the treatment of serious acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 March 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 36
Country: Number of subjects enrolled	United States: 1719
Country: Number of subjects enrolled	Italy: 109
Country: Number of subjects enrolled	Poland: 80
Country: Number of subjects enrolled	Switzerland: 34
Country: Number of subjects enrolled	Netherlands: 29
Country: Number of subjects enrolled	France: 25
Country: Number of subjects enrolled	Denmark: 23
Country: Number of subjects enrolled	United Kingdom: 21
Country: Number of subjects enrolled	Portugal: 19
Country: Number of subjects enrolled	Austria: 17
Country: Number of subjects enrolled	Australia: 16
Country: Number of subjects enrolled	Israel: 14
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Romania: 9
Country: Number of subjects enrolled	Belgium: 8

Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Slovenia: 5
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Czechia: 3
Country: Number of subjects enrolled	Slovakia: 3
Country: Number of subjects enrolled	Estonia: 1
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Ireland: 1
Worldwide total number of subjects	2191
EEA total number of subjects	383

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)	1332
From 65 to 84 years	803
85 years and over	56

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Australia, Canada, Europe, Israel, and United States. The first participant was screened on 27 March 2020. The last study visit occurred on 23 September 2020.

Pre-assignment

Screening details:

2191 participants were screened and enrolled. There were 3 participants whose age was not known. These 3 participants are added to the "Adults (18-64)" category in the Trial Information section because there is no separate age category for "missing".

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
------------------------------	-----

Arm title	Remdesivir 10 Days
------------------	--------------------

Arm description:

Participants who required mechanical ventilation at baseline received intravenous (IV) infusion of remdesivir 200 mg on Day 1 followed by IV infusion of remdesivir 100 mg on Days 2, 3, 4, 5, 6, 7, 8, 9, and 10.

Arm type	Experimental
Investigational medicinal product name	Remdesivir
Investigational medicinal product code	
Other name	GS-5734™, Veklury®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

200 mg administered on Day 1 followed by 100 mg up to Day 10.

Arm title	Remdesivir 5 Days
------------------	-------------------

Arm description:

Participants who were not on mechanical ventilation at baseline received IV infusion of remdesivir 200 mg on Day 1 followed by IV infusion of remdesivir 100 mg on Days 2, 3, 4, and 5. Participants originally not requiring mechanical ventilation at baseline who subsequently required mechanical ventilation prior to the Day 5 dose continued to receive remdesivir for up to 10 days.

Arm type	Experimental
Investigational medicinal product name	Remdesivir
Investigational medicinal product code	
Other name	GS-5734™, Veklury®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

200 mg administered on Day 1 followed by 100 mg up to Day 10.

Number of subjects in period 1 ^[1]	Remdesivir 10 Days	Remdesivir 5 Days
	Started	1786
Completed	1786	293

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 109 participants who were enrolled but not treated and 3 participants who had missing mechanical ventilation status at baseline were not included in the Safety Analysis Set for Period 1 table reported above.

Baseline characteristics

Reporting groups

Reporting group title	Remdesivir 10 Days
-----------------------	--------------------

Reporting group description:

Participants who required mechanical ventilation at baseline received intravenous (IV) infusion of remdesivir 200 mg on Day 1 followed by IV infusion of remdesivir 100 mg on Days 2, 3, 4, 5, 6, 7, 8, 9, and 10.

Reporting group title	Remdesivir 5 Days
-----------------------	-------------------

Reporting group description:

Participants who were not on mechanical ventilation at baseline received IV infusion of remdesivir 200 mg on Day 1 followed by IV infusion of remdesivir 100 mg on Days 2, 3, 4, and 5. Participants originally not requiring mechanical ventilation at baseline who subsequently required mechanical ventilation prior to the Day 5 dose continued to receive remdesivir for up to 10 days.

Reporting group values	Remdesivir 10 Days	Remdesivir 5 Days	Total
Number of subjects	1786	293	2079
Age categorical			
Units: Subjects			
< 50	379	66	445
≥ 50 - < 65	726	97	823
≥ 65 - < 75	485	70	555
≥ 75	195	60	255
Missing	1	0	1
Gender categorical			
Units: Subjects			
Female	614	107	721
Male	1172	186	1358
Race			
Not Permitted = local regulators did not allow collection of race or ethnicity information			
Units: Subjects			
American Indian or Alaska Native	13	0	13
Asian	143	20	163
Black	270	27	297
Native Hawaiian or Pacific Islander	9	0	9
White	920	217	1137
Not Permitted	123	9	132
Other	279	18	297
Missing	29	2	31
Ethnicity			
Not Permitted = local regulators did not allow collection of race or ethnicity information			
Units: Subjects			
Hispanic or Latino	611	38	649
Not Hispanic or Latino	1076	241	1317
Not Permitted	60	13	73
Missing	39	1	40

End points

End points reporting groups

Reporting group title	Remdesivir 10 Days
-----------------------	--------------------

Reporting group description:

Participants who required mechanical ventilation at baseline received intravenous (IV) infusion of remdesivir 200 mg on Day 1 followed by IV infusion of remdesivir 100 mg on Days 2, 3, 4, 5, 6, 7, 8, 9, and 10.

Reporting group title	Remdesivir 5 Days
-----------------------	-------------------

Reporting group description:

Participants who were not on mechanical ventilation at baseline received IV infusion of remdesivir 200 mg on Day 1 followed by IV infusion of remdesivir 100 mg on Days 2, 3, 4, and 5. Participants originally not requiring mechanical ventilation at baseline who subsequently required mechanical ventilation prior to the Day 5 dose continued to receive remdesivir for up to 10 days.

Primary: Percentage of Participants Experiencing Treatment-Emergent Adverse Events (AEs)

End point title	Percentage of Participants Experiencing Treatment-Emergent Adverse Events (AEs) ^[1]
-----------------	--

End point description:

An AE was any untoward medical occurrence in a participant administered study drug, which did not necessarily have a causal relationship with the treatment. An AE can therefore be any unfavorable and/or unintended sign, symptom, or disease temporally associated with the use of study drug, whether or not considered related to the study drug. A treatment-emergent AE was defined as any AE that began on or after the date of first dose of study drug up to the date of last dose of study drug plus 30 days. The Safety Analysis Set included all participants who received at least 1 dose of study drug.

End point type	Primary
----------------	---------

End point timeframe:

First dose date up to last dose (Day 10) plus 30 days

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: No statistical comparison was planned or performed.

End point values	Remdesivir 10 Days	Remdesivir 5 Days		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1786	293		
Units: percentage of participants				
number (not applicable)	67.1	36.2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: First dose date up to last dose (Day 10) plus 30 days; All-Cause Mortality: Enrollment up to the end of study (maximum: up to 49 days)

Adverse event reporting additional description:

The Safety Analysis Set included all participants who received at least 1 dose of study drug.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	22
--------------------	----

Reporting groups

Reporting group title	Remdesivir 10 Days
-----------------------	--------------------

Reporting group description:

Participants who required mechanical ventilation at Baseline received IV infusion of remdesivir 200 mg on Day 1 followed by IV infusion of remdesivir 100 mg on Days 2, 3, 4, 5, 6, 7, 8, 9, and 10.

Reporting group title	Remdesivir 5 Days
-----------------------	-------------------

Reporting group description:

Participants who were not on mechanical ventilation at Baseline received IV infusion of remdesivir 200 mg on Day 1 followed by IV infusion of remdesivir 100 mg on Days 2, 3, 4, and 5. Participants originally not requiring mechanical ventilation at baseline who subsequently required mechanical ventilation prior to the Day 5 dose continued to receive remdesivir for up to 10 days.

Serious adverse events	Remdesivir 10 Days	Remdesivir 5 Days	
Total subjects affected by serious adverse events			
subjects affected / exposed	865 / 1786 (48.43%)	58 / 293 (19.80%)	
number of deaths (all causes)	761	48	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pancreatic carcinoma			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	0 / 1786 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
Hypotension			

subjects affected / exposed	34 / 1786 (1.90%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 34	0 / 1
deaths causally related to treatment / all	0 / 11	0 / 0
Shock		
subjects affected / exposed	17 / 1786 (0.95%)	3 / 293 (1.02%)
occurrences causally related to treatment / all	0 / 17	0 / 3
deaths causally related to treatment / all	0 / 10	0 / 1
Haemodynamic instability		
subjects affected / exposed	9 / 1786 (0.50%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 9	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0
Shock haemorrhagic		
subjects affected / exposed	8 / 1786 (0.45%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	1 / 8	0 / 0
deaths causally related to treatment / all	1 / 6	0 / 0
Hypertension		
subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hypovolaemic shock		
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Peripheral ischaemia		
subjects affected / exposed	1 / 1786 (0.06%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Bloody discharge		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Circulatory collapse		

subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cyanosis			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive urgency			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotensive crisis			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Extubation			
subjects affected / exposed	4 / 1786 (0.22%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Hospice care			

subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	79 / 1786 (4.42%)	10 / 293 (3.41%)	
occurrences causally related to treatment / all	1 / 79	0 / 10	
deaths causally related to treatment / all	1 / 72	0 / 10	
Cardiac death			
subjects affected / exposed	6 / 1786 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 5	0 / 0	
Death			
subjects affected / exposed	4 / 1786 (0.22%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 4	0 / 0	
Pyrexia			
subjects affected / exposed	2 / 1786 (0.11%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain death			
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Multi-organ disorder			
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Complication associated with device			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Condition aggravated			

subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug interaction			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthermia			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Cytokine storm			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (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			
Respiratory failure			
subjects affected / exposed	141 / 1786 (7.89%)	19 / 293 (6.48%)	
occurrences causally related to treatment / all	1 / 141	0 / 19	
deaths causally related to treatment / all	1 / 112	0 / 15	
Acute respiratory failure			
subjects affected / exposed	77 / 1786 (4.31%)	3 / 293 (1.02%)	
occurrences causally related to treatment / all	0 / 77	0 / 3	
deaths causally related to treatment / all	0 / 71	0 / 1	
Pneumothorax			
subjects affected / exposed	54 / 1786 (3.02%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 54	0 / 1	
deaths causally related to treatment / all	0 / 17	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	40 / 1786 (2.24%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 40	0 / 1	
deaths causally related to treatment / all	0 / 35	0 / 1	

Hypoxia			
subjects affected / exposed	30 / 1786 (1.68%)	2 / 293 (0.68%)	
occurrences causally related to treatment / all	0 / 30	0 / 2	
deaths causally related to treatment / all	0 / 20	0 / 0	
Pulmonary embolism			
subjects affected / exposed	17 / 1786 (0.95%)	2 / 293 (0.68%)	
occurrences causally related to treatment / all	0 / 17	0 / 2	
deaths causally related to treatment / all	0 / 13	0 / 1	
Respiratory distress			
subjects affected / exposed	18 / 1786 (1.01%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 19	0 / 1	
deaths causally related to treatment / all	0 / 10	0 / 0	
Respiratory disorder			
subjects affected / exposed	11 / 1786 (0.62%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 11	0 / 1	
deaths causally related to treatment / all	0 / 7	0 / 0	
Pneumomediastinum			
subjects affected / exposed	6 / 1786 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory acidosis			
subjects affected / exposed	5 / 1786 (0.28%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 3	0 / 0	
Pleural effusion			
subjects affected / exposed	4 / 1786 (0.22%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory arrest			
subjects affected / exposed	3 / 1786 (0.17%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 3	0 / 1	
Dyspnoea			

subjects affected / exposed	2 / 1786 (0.11%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0
Haemothorax		
subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0
Lung consolidation		
subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Pneumothorax spontaneous		
subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Pulmonary haemorrhage		
subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 3	0 / 0
Chronic obstructive pulmonary disease		
subjects affected / exposed	1 / 1786 (0.06%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1
Dependence on respirator		
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Epistaxis		
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Hypercapnia		

subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0
Pneumonitis		
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0
Bronchial secretion retention		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Cystic lung disease		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Dyspnoea exertional		
subjects affected / exposed	0 / 1786 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Interstitial lung disease		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Lung opacity		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Mediastinal haemorrhage		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Pneumonia aspiration		

subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory gas exchange disorder			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stridor			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachypnoea			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intensive care unit delirium			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			

Device connection issue			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device dislocation			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device leakage			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis in device			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	19 / 1786 (1.06%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	8 / 19	0 / 1	
deaths causally related to treatment / all	0 / 6	0 / 0	
Blood creatinine increased			
subjects affected / exposed	16 / 1786 (0.90%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	2 / 16	0 / 0	
deaths causally related to treatment / all	0 / 5	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	13 / 1786 (0.73%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	6 / 13	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Liver function test increased			
subjects affected / exposed	13 / 1786 (0.73%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	4 / 13	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Transaminases increased			
subjects affected / exposed	8 / 1786 (0.45%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	8 / 8	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Creatinine renal clearance abnormal			
subjects affected / exposed	8 / 1786 (0.45%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 8	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Creatinine renal clearance decreased			
subjects affected / exposed	7 / 1786 (0.39%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 7	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Glomerular filtration rate abnormal			
subjects affected / exposed	6 / 1786 (0.34%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	2 / 6	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 1	
Blood bilirubin increased			
subjects affected / exposed	4 / 1786 (0.22%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	3 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerular filtration rate decreased			
subjects affected / exposed	3 / 1786 (0.17%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemoglobin decreased			
subjects affected / exposed	4 / 1786 (0.22%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oxygen saturation decreased			
subjects affected / exposed	3 / 1786 (0.17%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatic enzyme increased			

subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Staphylococcus test positive		
subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Aspergillus test positive		
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Blood creatine phosphokinase increased		
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Blood creatinine abnormal		
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Klebsiella test positive		
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Alanine aminotransferase abnormal		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Aspartate aminotransferase abnormal		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Blood alkaline phosphatase increased		

subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Blood bilirubin abnormal		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Blood potassium abnormal		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Blood pressure abnormal		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Blood sodium decreased		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Blood urea increased		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
C-reactive protein increased		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Carbon dioxide abnormal		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Chest X-ray abnormal		

subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Computerised tomogram abdomen abnormal			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Creatinine renal clearance increased			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Electrocardiogram QRS complex prolonged			
subjects affected / exposed	0 / 1786 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 1786 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Fibrin D dimer increased			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal test positive			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gram stain positive			

subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammatory marker increased			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Low density lipoprotein increased			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mean arterial pressure decreased			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oxygen saturation abnormal			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Serum ferritin increased			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin increased			
subjects affected / exposed	0 / 1786 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urine output decreased			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Injury, poisoning and procedural complications			
Brain herniation			

subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Barotrauma			
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Endotracheal intubation complication			
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal procedural complication			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infusion related reaction			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mechanical ventilation complication			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Post procedural oedema			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product dose omission issue			

subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheal injury			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Tracheostomy malfunction			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	163 / 1786 (9.13%)	8 / 293 (2.73%)	
occurrences causally related to treatment / all	3 / 165	0 / 8	
deaths causally related to treatment / all	3 / 137	0 / 7	
Cardio-respiratory arrest			
subjects affected / exposed	72 / 1786 (4.03%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	1 / 73	0 / 0	
deaths causally related to treatment / all	1 / 67	0 / 0	
Pulseless electrical activity			
subjects affected / exposed	16 / 1786 (0.90%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 16	0 / 0	
deaths causally related to treatment / all	0 / 9	0 / 0	
Bradycardia			
subjects affected / exposed	12 / 1786 (0.67%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	1 / 12	0 / 0	
deaths causally related to treatment / all	0 / 8	0 / 0	
Atrial fibrillation			
subjects affected / exposed	6 / 1786 (0.34%)	2 / 293 (0.68%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 0	
Cardiac failure			

subjects affected / exposed	6 / 1786 (0.34%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 4	0 / 0
Cardiogenic shock		
subjects affected / exposed	6 / 1786 (0.34%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 4	0 / 0
Supraventricular tachycardia		
subjects affected / exposed	6 / 1786 (0.34%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 7	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 0
Arrhythmia		
subjects affected / exposed	6 / 1786 (0.34%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 4	0 / 0
Tachycardia		
subjects affected / exposed	4 / 1786 (0.22%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	2 / 4	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0
Ventricular tachycardia		
subjects affected / exposed	5 / 1786 (0.28%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0
Myocarditis		
subjects affected / exposed	2 / 1786 (0.11%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Acute myocardial infarction		
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiac failure acute		

subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0
Myocardial infarction		
subjects affected / exposed	1 / 1786 (0.06%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Sinus arrest		
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Sinus tachycardia		
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Ventricular arrhythmia		
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Atrial flutter		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiac disorder		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Cardiac failure congestive		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiomyopathy		

subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiopulmonary failure		
subjects affected / exposed	0 / 1786 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Cardiovascular insufficiency		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Cor pulmonale		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Extrasystoles		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pericardial effusion		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pericarditis		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Right ventricular failure		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Sinus bradycardia		

subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	7 / 1786 (0.39%)	3 / 293 (1.02%)	
occurrences causally related to treatment / all	0 / 7	0 / 3	
deaths causally related to treatment / all	0 / 3	0 / 1	
Encephalopathy			
subjects affected / exposed	7 / 1786 (0.39%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 7	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	7 / 1786 (0.39%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 7	0 / 0	
deaths causally related to treatment / all	0 / 4	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	6 / 1786 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Haemorrhagic stroke			
subjects affected / exposed	5 / 1786 (0.28%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Metabolic encephalopathy			
subjects affected / exposed	4 / 1786 (0.22%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			

subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ischaemic stroke			
subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Seizure			
subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Toxic encephalopathy			
subjects affected / exposed	2 / 1786 (0.11%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intensive care unit acquired weakness			
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal ganglia haematoma			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain injury			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Brain oedema			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebellar infarction			

subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cerebral ischaemia		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Coma		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Generalised tonic-clonic seizure		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hypotonia		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Hypoxic-ischaemic encephalopathy		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Lethargy		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Mental impairment		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Moyamoya disease		

subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Unresponsive to stimuli			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 1786 (0.45%)	2 / 293 (0.68%)	
occurrences causally related to treatment / all	0 / 8	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Disseminated intravascular coagulation			
subjects affected / exposed	5 / 1786 (0.28%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Blood loss anaemia			
subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			

subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulopathy			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heparin-induced thrombocytopenia			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	14 / 1786 (0.78%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 14	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	12 / 1786 (0.67%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	1 / 12	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Retroperitoneal haemorrhage			
subjects affected / exposed	4 / 1786 (0.22%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	2 / 4	0 / 0	
deaths causally related to treatment / all	2 / 3	0 / 0	
Mouth haemorrhage			
subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haematochezia			
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			

subjects affected / exposed	1 / 1786 (0.06%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Intra-abdominal haemorrhage		
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0
deaths causally related to treatment / all	1 / 2	0 / 0
Lower gastrointestinal haemorrhage		
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Oedematous pancreatitis		
subjects affected / exposed	1 / 1786 (0.06%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Rectal haemorrhage		
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Colitis		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Colitis ischaemic		
subjects affected / exposed	0 / 1786 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Diverticular perforation		
subjects affected / exposed	0 / 1786 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Duodenal ulcer perforation		

subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastric ulcer		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal disorder		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Gastrointestinal necrosis		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Intestinal ischaemia		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Intestinal perforation		
subjects affected / exposed	0 / 1786 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Large intestine perforation		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Obstruction gastric		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Pancreatitis		

subjects affected / exposed	0 / 1786 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haematoma			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatic failure			
subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Liver injury			
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute hepatic failure			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			

subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis toxic			
subjects affected / exposed	0 / 1786 (0.00%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver disorder			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-alcoholic steatohepatitis			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Subcutaneous emphysema			
subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angioedema			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decubitus ulcer			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash macular			

subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	137 / 1786 (7.67%)	3 / 293 (1.02%)	
occurrences causally related to treatment / all	11 / 138	0 / 3	
deaths causally related to treatment / all	2 / 25	0 / 1	
Renal failure			
subjects affected / exposed	28 / 1786 (1.57%)	5 / 293 (1.71%)	
occurrences causally related to treatment / all	2 / 28	1 / 5	
deaths causally related to treatment / all	1 / 11	0 / 1	
Renal impairment			
subjects affected / exposed	8 / 1786 (0.45%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	1 / 8	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	5 / 1786 (0.28%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular necrosis			
subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Azotaemia			
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal injury			

subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anuria			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oliguria			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proteinuria			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Septic shock			
subjects affected / exposed	79 / 1786 (4.42%)	4 / 293 (1.37%)	
occurrences causally related to treatment / all	1 / 81	0 / 4	
deaths causally related to treatment / all	1 / 53	0 / 3	
Pneumonia			
subjects affected / exposed	30 / 1786 (1.68%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 30	0 / 1	
deaths causally related to treatment / all	0 / 22	0 / 1	

Covid-19			
subjects affected / exposed	29 / 1786 (1.62%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 29	0 / 0	
deaths causally related to treatment / all	0 / 29	0 / 0	
Sepsis			
subjects affected / exposed	21 / 1786 (1.18%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 21	0 / 1	
deaths causally related to treatment / all	0 / 10	0 / 1	
Covid-19 pneumonia			
subjects affected / exposed	18 / 1786 (1.01%)	3 / 293 (1.02%)	
occurrences causally related to treatment / all	0 / 18	0 / 3	
deaths causally related to treatment / all	0 / 16	0 / 3	
Systemic candida			
subjects affected / exposed	5 / 1786 (0.28%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 3	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	4 / 1786 (0.22%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	4 / 1786 (0.22%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Pneumonia staphylococcal			
subjects affected / exposed	3 / 1786 (0.17%)	1 / 293 (0.34%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Bacteraemia			
subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Bacterial infection			

subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumonia acinetobacter		
subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0
Staphylococcal sepsis		
subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Acinetobacter infection		
subjects affected / exposed	1 / 1786 (0.06%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1
Bacterial sepsis		
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0
Klebsiella bacteraemia		
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Pneumonia viral		
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0
Acinetobacter sepsis		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Bacterial abdominal infection		

subjects affected / exposed	0 / 1786 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Bacterial tracheitis		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Candida infection		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Empyema		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Enterococcal sepsis		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Escherichia bacteraemia		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Escherichia infection		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Escherichia sepsis		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Klebsiella sepsis		

subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Nosocomial infection		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Pneumocystis jirovecii pneumonia		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Pneumonia escherichia		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Pseudomembranous colitis		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Pseudomonal bacteraemia		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Severe acute respiratory syndrome		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Staphylococcal infection		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Streptococcal bacteraemia		

subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Metabolic acidosis			
subjects affected / exposed	6 / 1786 (0.34%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	1 / 6	0 / 0	
deaths causally related to treatment / all	1 / 2	0 / 0	
Hyperkalaemia			
subjects affected / exposed	5 / 1786 (0.28%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Acidosis			
subjects affected / exposed	4 / 1786 (0.22%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Hypernatraemia			
subjects affected / exposed	3 / 1786 (0.17%)	0 / 293 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid overload			

subjects affected / exposed	1 / 1786 (0.06%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hyperglycaemia		
subjects affected / exposed	1 / 1786 (0.06%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hypokalaemia		
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Metabolic alkalosis		
subjects affected / exposed	2 / 1786 (0.11%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Decreased appetite		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Electrolyte imbalance		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hypocalcaemia		
subjects affected / exposed	0 / 1786 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hypomagnesaemia		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Lactic acidosis		

subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Malnutrition		
subjects affected / exposed	1 / 1786 (0.06%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Remdesivir 10 Days	Remdesivir 5 Days	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	151 / 1786 (8.45%)	19 / 293 (6.48%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	56 / 1786 (3.14%)	17 / 293 (5.80%)	
occurrences (all)	56	17	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	99 / 1786 (5.54%)	2 / 293 (0.68%)	
occurrences (all)	100	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 April 2020	<ul style="list-style-type: none">- Per regulatory agency requests, study eligibility criteria have been expanded to include pregnant participants and adolescents, to exclude participants who are eligible for participation on a randomized clinical trial studying remdesivir for treatment of SARS-CoV2 at the medical facility where the participant is admitted, and to exclude participants with a known hypersensitivity to the study drug, the metabolites, or formulation excipient. Additional criteria for permanent discontinuation of study drug were included, should the participant develop alanine transaminase (ALT) levels $\geq 3 \times$ upper limit of normal (ULN) and bilirubin $\geq 2 \times$ ULN or experience acute anaphylactic reaction to remdesivir.- New protocol study procedures were added in for follow-up assessments (on-site or telephone) on Day 15 and Day 28.- Increased number of participants to up to approximately 15,000.- The study protocol has also been revised to include additional details and clarity regarding the following topics: Study drug formulation, storage and handling, and accountability; Prohibited concomitant medications; Study procedures; Serious adverse event reporting; Telephone consent; Study files and retention of records; Financial disclosures; and Case report forms.
15 May 2020	<ul style="list-style-type: none">- Updated eligibility criteria: a) Removed invasive mechanical ventilation as inclusion criteria to expand the target population. The revised inclusion criteria requires participants to have oxygen saturation (SpO2) $\leq 94\%$ on room air or requiring supplemental oxygen at baseline. b) Revised liver function test (LFT) inclusion criteria, added contraception inclusion criteria, and added lactating women and nursing inclusion criteria. c) Added venous arterial (V-A) extracorporeal membrane oxygenation (ECMO) exclusion criteria.- The remdesivir treatment course duration is modified to align with the United States Food and Drug Administration (US FDA) emergency use authorization fact sheet and Committee for Medicinal Products for Human Use (CHMP) Article 83 compassionate use recommendations for participants who are not on invasive mechanical ventilation. These participants will receive a 5 day treatment course. Any participant who is not on invasive mechanical ventilation at baseline, but requires invasive mechanical ventilation prior to the Day 5 dose should continue to receive remdesivir on Days 6, 7, 8, 9, and 10.- Study procedures updates: a) Baseline procedures must be done within 2 days prior to enrollment. b) Pregnancy testing is noted as a baseline assessment. c) Laboratory testing procedures are modified to specify those which should be done daily to ensure participant safety. All other laboratory testing is to be done as per local standard of care. d) Follow-up assessment visit windows were expanded. e) Added guidance regarding study drug restart after an interruption. f) Study Procedures Table was added to present the procedures to be done for participants who do not require mechanical ventilation at baseline.- Serious adverse reporting will now be done primarily through electronic submission in the electronic case report form (eCRF) system.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported