Clinical trial results:
A randomized, double-blind, placebo-controlled, study evaluating the efficacy and safety of otilimab in patients with severe pulmonary COVID-19 related disease

Summary

EudraCT number	2020-001759-42
Trial protocol	GB NL ES BE DE IT
Global end of trial date	16 August 2021

Results information

Result version number	v1 (current)
This version publication date	16 March 2022
First version publication date	16 March 2022

Trial information

Trial identification

Sponsor protocol code	214094

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom, TW8 9GS
Public contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.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	24 September 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of otilimab intravenous (IV) versus placebo

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 May 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	Argentina: 102
Country: Number of subjects enrolled	Belgium: 21
Country: Number of subjects enrolled	Brazil: 31
Country: Number of subjects enrolled	Canada: 19
Country: Number of subjects enrolled	Chile: 11
Country: Number of subjects enrolled	Colombia: 1
Country: Number of subjects enrolled	France: 258
Country: Number of subjects enrolled	India: 72
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Japan: 48
Country: Number of subjects enrolled	Mexico: 48
Country: Number of subjects enrolled	Netherlands: 47
Country: Number of subjects enrolled	Peru: 12
Country: Number of subjects enrolled	Poland: 12
Country: Number of subjects enrolled	Russian Federation: 113
Country: Number of subjects enrolled	South Africa: 36
Country: Number of subjects enrolled	Spain: 94
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	United States: 214
Worldwide total number of subjects	1156
EEA total number of subjects	439

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)	499
From 65 to 84 years	643
85 years and over	14

Subject disposition

Recruitment

Recruitment details:

This was a 2-part study evaluating efficacy and safety of intravenously (IV) administered otilimab in participants with severe pulmonary Coronavirus Disease-2019 (COVID-19) related disease. Part 1 consisted of participants aged 18 to 79 years and Part 2 consisted of participants aged 70 years and older.

Pre-assignment

Screening details:

A total of 1156 (806 in Part 1 and 350 in Part 2) participants were enrolled in the study (Enrolled Population: All participants who entered the study).

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1: Placebo 1

Arm description:

Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)79 years received blinded 1-hour IV infusion of placebo (sterile 0.9 percent [%] weight by volume [w/v] sodium chloride solution) once along with standard of care.

Arm type	Placebo
Investigational medicinal product name	Placebo 1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Sterile 0.9% (w/v) sodium chloride solution administered once via IV infusion

Arm title	Part 1: Otilimab 90 mg

Arm description:

Participants between the ages of >=18 years and <=79 years received blinded otilimab 90 milligrams (mg) (solution in single-use vial diluted in sterile 0.9% w/v sodium chloride solution) once as 1-hour IV infusion along with standard of care.

Arm type	Experimental
Investigational medicinal product name	Otilimab 90 mg (diluted in sodium chloride solution)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Solution in single-use vial (150 mg/milliliters [mL]) diluted in sterile 0.9% (w/v) sodium chloride solution and administered once via IV infusion

Arm title	Part 2: Placebo 2

Arm description:

Participants aged 70 years or above received blinded 1-hour IV infusion of placebo (sterile 5% w/v dextrose solution) once along with standard of care.

Arm type	Placebo
Investigational medicinal product name	Placebo 2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Sterile 5% (w/v) dextrose solution administered once via IV infusion

Arm title	Part 2: Otilimab 90 mg

Arm description:

Participants aged 70 years or above received blinded otilimab 90 mg (solution in single-use vial diluted in sterile 5% dextrose solution) once as 1-hour IV infusion along with standard of care.

Arm type	Experimental
Investigational medicinal product name	Otilimab 90 mg (diluted in dextrose solution)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Solution in single-use vial (150 mg/mL) diluted in sterile 5% (w/v) dextrose solution and administered once via IV infusion

Number of subjects in period 1	Part 1: Placebo 1	Part 1: Otilimab 90 mg	Part 2: Placebo 2
Started	403	403	175
Completed	388	379	170
Not completed	15	24	5
Consent withdrawn by subject	7	8	1
Physician decision	2	5	1
Lost to follow-up	4	8	3
Protocol deviation	2	3	-

Number of subjects in period 1	Part 2: Otilimab 90 mg
Started	175
Completed	171
Not completed	4
Consent withdrawn by subject	1
Physician decision	1
Lost to follow-up	2
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	Part 1: Placebo 1
Reporting group description:	
Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)79 years received blinded 1-hour IV infusion of placebo (sterile 0.9 percent [%] weight by volume [w/v] sodium chloride solution) once along with standard of care.	
Reporting group title	Part 1: Otilimab 90 mg
Reporting group description:	
Participants between the ages of >=18 years and <=79 years received blinded otilimab 90 milligrams (mg) (solution in single-use vial diluted in sterile 0.9% w/v sodium chloride solution) once as 1-hour IV infusion along with standard of care.	
Reporting group title	Part 2: Placebo 2
Reporting group description:	
Participants aged 70 years or above received blinded 1-hour IV infusion of placebo (sterile 5% w/v dextrose solution) once along with standard of care.	
Reporting group title	Part 2: Otilimab 90 mg
Reporting group description:	
Participants aged 70 years or above received blinded otilimab 90 mg (solution in single-use vial diluted in sterile 5% dextrose solution) once as 1-hour IV infusion along with standard of care.	

Reporting group values	Part 1: Placebo 1	Part 1: Otilimab 90 mg	Part 2: Placebo 2
Number of subjects	403	403	175
Age Categorical			
Baseline characteristics were presented for Enrolled Population.			
Units: Participants			
<18 years	0	0	0
Between 18 to 64 years	249	250	0
>=65 to 84 years	154	153	168
>=85 years	0	0	7
Age continuous			
Baseline characteristics were presented for Enrolled Population.			
Units: years			
arithmetic mean	59.4	59.8	75.0
standard deviation	± 11.86	± 11.69	± 4.67
Sex: Female, Male			
Baseline characteristics were presented for Enrolled Population.			
Units: Participants			
Female	128	101	75
Male	275	302	100
Race/Ethnicity, Customized			
Baseline characteristics were presented for Enrolled Population.			
Units: Subjects			
American Indian or Alaska Native	24	30	3
Asian - Central/South Asian Heritage	42	31	1
Asian - East Asian Heritage	4	4	0
Asian - Japanese Heritage	15	14	13
Asian - South East Asian Heritage	12	8	1
Black or African American	25	26	6

White - Arabic/North African Heritage	27	21	14
White - White/Caucasian/European Heritage	235	251	136
Mixed Asian Race	0	1	0
Mixed White Race	1	1	1
Multiple	7	7	0
Unknown	11	9	0

Reporting group values	Part 2: Otilimab 90 mg	Total	
Number of subjects	175	1156	
Age Categorical			
Baseline characteristics were presented for Enrolled Population.			
Units: Participants			
<18 years	0	0	
Between 18 to 64 years	0	499	
>=65 to 84 years	168	643	
>=85 years	7	14	
Age continuous			
Baseline characteristics were presented for Enrolled Population.			
Units: years			
arithmetic mean	75.3		
standard deviation	± 4.70	-	
Sex: Female, Male			
Baseline characteristics were presented for Enrolled Population.			
Units: Participants			
Female	73	377	
Male	102	779	
Race/Ethnicity, Customized			
Baseline characteristics were presented for Enrolled Population.			
Units: Subjects			
American Indian or Alaska Native	8	65	
Asian - Central/South Asian Heritage	0	74	
Asian - East Asian Heritage	0	8	
Asian - Japanese Heritage	5	47	
Asian - South East Asian Heritage	0	21	
Black or African American	6	63	
White - Arabic/North African Heritage	21	83	
White - White/Caucasian/European Heritage	134	756	
Mixed Asian Race	0	1	
Mixed White Race	0	3	
Multiple	0	14	
Unknown	1	21	

End points

End points reporting groups

Reporting group title	Part 1: Placebo 1
Reporting group description:	
Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)79 years received blinded 1-hour IV infusion of placebo (sterile 0.9 percent [%] weight by volume [w/v] sodium chloride solution) once along with standard of care.	
Reporting group title	Part 1: Otilimab 90 mg
Reporting group description:	
Participants between the ages of >=18 years and <=79 years received blinded otilimab 90 milligrams (mg) (solution in single-use vial diluted in sterile 0.9% w/v sodium chloride solution) once as 1-hour IV infusion along with standard of care.	
Reporting group title	Part 2: Placebo 2
Reporting group description:	
Participants aged 70 years or above received blinded 1-hour IV infusion of placebo (sterile 5% w/v dextrose solution) once along with standard of care.	
Reporting group title	Part 2: Otilimab 90 mg
Reporting group description:	
Participants aged 70 years or above received blinded otilimab 90 mg (solution in single-use vial diluted in sterile 5% dextrose solution) once as 1-hour IV infusion along with standard of care.	

Primary: Part 1: Percentage of participants alive and free of respiratory failure at Day 28

End point title	Part 1: Percentage of participants alive and free of respiratory failure at Day 28[1]
End point description:	
Participants were considered alive and free of respiratory failure if they were in category 1,2,3 or 4 from the GSK modified version ordinal scale adapted from World Health Organization (WHO) scale 2020.The 8-point scale was as follows:1)Non-hospitalized,no limitation of activity;2) Non-hospitalized,limitation of activity;3) Hospitalized,no oxygen therapy;4)Hospitalized,low-flow oxygen by mask/nasal prongs;5) Hospitalized,highflow oxygen (>=15 liters per minute),continuous positive airway pressure(CPAP),bilevel positive airway pressure(BIPAP),non-invasive ventilation;6) Hospitalized,intubation and mechanical ventilation;7) Hospitalized,mechanical ventilation plus additional organ support;8)Death.Higher scale indicate higher intensity of respiratory failure. Percentage values are rounded off.Modified intent to treat(mITT) population consisted of all randomized participants who received study intervention.Only those participants with data available at specified timepoints were analyzed	
End point type	Primary
End point timeframe:	
At Day 28	
Notes:	
[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.	

End point values	Part 1: Placebo 1	Part 1: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	393[2]	389[3]		
Units: Percentage of participants	67	71		

Notes:

[2] - mITT Population

[3] - mITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, and both clinical status at Baseline and age group as randomized. Missing data was imputed with monotone discriminant multiple imputation assuming data is missing at random.

Comparison groups	Part 1: Placebo 1 v Part 1: Otilimab 90 mg
Number of subjects included in analysis	782
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0456 [4]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.82

Notes:

[4] - p-value is from a one-sided test.

Primary: Part 2: Percentage of participants alive and free of respiratory failure at Day 28

End point title	Part 2: Percentage of participants alive and free of respiratory failure at Day 28[5]

End point description:

Participants were alive and free of respiratory failure if they were in category 1, 2, 3 or 4 from the GlaxoSmithKline (GSK) modified version ordinal scale adapted from World Health Organization (WHO) scale 2020. The 8-point scale was as follows: 1) Non-hospitalized, no limitation of activity; 2) Non-hospitalized,limitation of activity; 3) Hospitalized, no oxygen therapy; 4) Hospitalized, low-flow oxygen by mask or nasal prongs; 5) Hospitalized, highflow oxygen (>=15L/min), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BIPAP), non-invasive ventilation; 6) Hospitalized, intubation and mechanical ventilation; 7) Hospitalized, mechanical ventilation plus additional organ support; 8) Death. Higher scale indicates higher intensity of respiratory failure. Percentage values are rounded off. Only those participants with data available at the specified time points were analyzed.

End point type	Primary

End point timeframe:

At Day 28

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 2: Placebo 2	Part 2: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	170[6]	172[7]		
Units: Percentage of participants	51	52		

Notes:

[6] - mITT Population.

[7] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, age, and both clinical status at Baseline and sex as randomized. Missing data was imputed with monotone logistic multiple imputation assuming data is missing at random.

Comparison groups	Part 2: Placebo 2 v Part 2: Otilimab 90 mg
Number of subjects included in analysis	342
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8574 [8]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.61

Notes:

[8] - p-value is generated from a two-sided test.

Secondary: Part 1: Number of participants who died due to all causes at Day 60

End point title	Part 1: Number of participants who died due to all causes at Day 60[9]

End point description:

Number of participants who died due to all causes at Day 60 are reported. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 60

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 1: Placebo 1	Part 1: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	386[10]	373[11]		
Units: Participants	93	84		

Notes:

[10] - mITT Population.

[11] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, and both clinical status at Baseline and age group as randomized. Missing data was imputed with monotone discriminant multiple imputation assuming data is missing at random.

Comparison groups	Part 1: Placebo 1 v Part 1: Otilimab 90 mg
Number of subjects included in analysis	759
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2057 [12]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.22

Notes:

[12] - p-value is from a one-sided test.

Secondary: Part 2: Number of participants who died due to all causes at Day 28

End point title	Part 2: Number of participants who died due to all causes at Day 28[13]

End point description:

Number of participants who died due to all causes at Day 28 is reported. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 28

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 2: Placebo 2	Part 2: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	170[14]	172[15]		
Units: Participants	70	63		

Notes:

[14] - mITT Population.

[15] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, age, and both clinical status at Baseline and sex as randomized. Missing data was imputed with monotone logistic multiple imputation assuming data is missing at random.

Comparison groups	Part 2: Placebo 2 v Part 2: Otilimab 90 mg
Number of subjects included in analysis	342
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3061 [16]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.24

Notes:

[16] - p-value is generated from a two-sided test.

Secondary: Part 2: Number of participants who died due to all causes at Day 60

End point title	Part 2: Number of participants who died due to all causes at Day 60[17]

End point description:

Number of participants who died due to all causes at Day 60 is reported. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 60

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 2: Placebo 2	Part 2: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	170[18]	171[19]		
Units: Participants	76	74		

Notes:

[18] - mITT Population.

[19] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, age, and both clinical status at Baseline and sex as randomized. Missing data was imputed with monotone logistic multiple imputation assuming data is missing at random.

Comparison groups	Part 2: Placebo 2 v Part 2: Otilimab 90 mg
Number of subjects included in analysis	341
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6665 [20]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.41

Notes:

[20] - p-value is generated from a two-sided test.

Secondary: Part 1: Time to death due to all causes up to Day 60

End point title	Part 1: Time to death due to all causes up to Day 60[21]

End point description:

Time to death due to all causes was defined as the time (days) from dosing to death, due to any cause, up to (and including) Day 60. Median and inter-quartile range (first quartile and third quartile) of time to death are presented. Only those participants with data available at the specified time points were analyzed. 9999 indicates that <25% of participants experienced the event within the treatment arm. Hence, median and inter-quartile range could not be derived.

End point type	Secondary

End point timeframe:

Up to Day 60

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 1: Placebo 1	Part 1: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93[22]	84[23]		
Units: Days				
median (inter-quartile range (Q1-Q3))	99999 (99999 to 99999)	99999 (99999 to 99999)		

Notes:

[22] - mITT Population.

[23] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Model adjusted analysis performed using a Cox proportional hazards model adjusted by treatment, clinical status at Baseline as randomized and age group as randomized.

Comparison groups	Part 1: Placebo 1 v Part 1: Otilimab 90 mg
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1942 [24]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.18

Notes:

[24] - p-value is from a one-sided test.

Secondary: Part 2: Time to death due to all causes up to Day 60

End point title	Part 2: Time to death due to all causes up to Day 60[25]

End point description:

Time to death due to all causes was defined as the time (days) from dosing to death, due to any cause, up to (and including) Day 60. Median and inter-quartile range (first quartile and third quartile) of time to death are presented. Only those participants with data available at the specified time points were analyzed. 9999 indicates that <50% of participants experienced the event within the treatment arm. Hence, median and third-quartile could not be derived.

End point type	Secondary

End point timeframe:

Up to Day 60

Notes:

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

Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 2: Placebo 2	Part 2: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76[26]	74[27]		
Units: Days				
median (inter-quartile range (Q1-Q3))	99999 (16 to 99999)	99999 (16 to 99999)		

Notes:

[26] - mITT Population.

[27] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Model adjusted analysis performed using a Cox proportional hazards model adjusted by treatment, clinical status at Baseline as randomized, sex as randomized and age.

Comparison groups	Part 2: Placebo 2 v Part 2: Otilimab 90 mg
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5324 [28]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.24

Notes:

[28] - p-value is generated from a two-sided test

Secondary: Part 1: Percentage of participants alive and free of respiratory failure at Day 7

End point title	Part 1: Percentage of participants alive and free of respiratory failure at Day 7[29]

End point description:

Participants were alive and free of respiratory failure if they were in category 1, 2, 3 or 4 from the GlaxoSmithKline (GSK) modified version ordinal scale adapted from World Health Organization (WHO) scale 2020. The 8-point scale was as follows: 1) Non-hospitalized, no limitation of activity; 2) Non-hospitalized,limitation of activity; 3) Hospitalized, no oxygen therapy; 4) Hospitalized, low-flow oxygen by mask or nasal prongs; 5) Hospitalized, highflow oxygen (>=15L/min), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BIPAP), non-invasive ventilation; 6) Hospitalized, intubation and mechanical ventilation; 7) Hospitalized, mechanical ventilation plus additional organ support; 8) Death. Higher scale indicates higher intensity of respiratory failure. Percentage values are rounded off. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 7

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 1: Placebo 1	Part 1: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	396[30]	393[31]		
Units: Percentage of participants	42	44		

Notes:

[30] - mITT Population.

[31] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, and both clinical status at Baseline and age group as randomized. Missing data was imputed with monotone discriminant multiple imputation assuming data is missing at random.

Comparison groups	Part 1: Placebo 1 v Part 1: Otilimab 90 mg
Number of subjects included in analysis	789
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2871 [32]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.49

Notes:

[32] - p-value is from a one-sided test.

Secondary: Part 1: Percentage of participants alive and free of respiratory failure at Day 14

End point title	Part 1: Percentage of participants alive and free of respiratory failure at Day 14[33]

End point description:

Participants were alive and free of respiratory failure if they were in category 1, 2, 3 or 4 from the GlaxoSmithKline (GSK) modified version ordinal scale adapted from World Health Organization (WHO) scale 2020. The 8-point scale was as follows: 1) Non-hospitalized, no limitation of activity; 2) Non-hospitalized,limitation of activity; 3) Hospitalized, no oxygen therapy; 4) Hospitalized, low-flow oxygen by mask or nasal prongs; 5) Hospitalized, highflow oxygen (>=15L/min), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BIPAP), non-invasive ventilation; 6) Hospitalized, intubation and mechanical ventilation; 7) Hospitalized, mechanical ventilation plus additional organ support; 8) Death. Higher scale indicates higher intensity of respiratory failure. Percentage values are rounded off. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 14

Notes:

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

Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 1: Placebo 1	Part 1: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	394[34]	391[35]		
Units: Percentage of participants	61	63		

Notes:

[34] - mITT Population.

[35] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, and both clinical status at Baseline and age group as randomized. Missing data was imputed with monotone discriminant multiple imputation assuming data is missing at random.

Comparison groups	Part 1: Placebo 1 v Part 1: Otilimab 90 mg
Number of subjects included in analysis	785
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1754 [36]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.58

Notes:

[36] - p-value is from a one-sided test.

Secondary: Part 1: Percentage of participants alive and free of respiratory failure at Day 60

End point title	Part 1: Percentage of participants alive and free of respiratory failure at Day 60[37]

End point description:

Participants were alive and free of respiratory failure if they were in category 1, 2, 3 or 4 from the GlaxoSmithKline (GSK) modified version ordinal scale adapted from World Health Organization (WHO) scale 2020. The 8-point scale was as follows: 1) Non-hospitalized, no limitation of activity; 2) Non-hospitalized,limitation of activity; 3) Hospitalized, no oxygen therapy; 4) Hospitalized, low-flow oxygen by mask or nasal prongs; 5) Hospitalized, highflow oxygen (>=15L/min), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BIPAP), non-invasive ventilation; 6) Hospitalized, intubation and mechanical ventilation; 7) Hospitalized, mechanical ventilation plus additional organ support; 8) Death. Higher scale indicates higher intensity of respiratory failure. Percentage values are rounded off. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 60

Notes:

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

Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 1: Placebo 1	Part 1: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	386[38]	373[39]		
Units: Percentage of participants	74	75		

Notes:

[38] - mITT Population.

[39] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, and both clinical status at Baseline and age group as randomized. Missing data was imputed with monotone discriminant multiple imputation assuming data is missing at random.

Comparison groups	Part 1: Placebo 1 v Part 1: Otilimab 90 mg
Number of subjects included in analysis	759
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.183 [40]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.63

Notes:

[40] - p-value is from a one-sided test.

Secondary: Part 1: Percentage of participants alive and free of respiratory failure at Day 42

End point title	Part 1: Percentage of participants alive and free of respiratory failure at Day 42[41]

End point description:

Participants were alive and free of respiratory failure if they were in category 1, 2, 3 or 4 from the GlaxoSmithKline (GSK) modified version ordinal scale adapted from World Health Organization (WHO) scale 2020. The 8-point scale was as follows: 1) Non-hospitalized, no limitation of activity; 2) Non-hospitalized,limitation of activity; 3) Hospitalized, no oxygen therapy; 4) Hospitalized, low-flow oxygen by mask or nasal prongs; 5) Hospitalized, highflow oxygen (>=15L/min), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BIPAP), non-invasive ventilation; 6) Hospitalized, intubation and mechanical ventilation; 7) Hospitalized, mechanical ventilation plus additional organ support; 8) Death. Higher scale indicates higher intensity of respiratory failure. Percentage values are rounded off. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 42

Notes:

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

Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 1: Placebo 1	Part 1: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	392[42]	385[43]		
Units: Percentage of participants	70	74		

Notes:

[42] - mITT Population.

[43] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, and both clinical status at Baseline and age group as randomized. Missing data was imputed with monotone discriminant multiple imputation assuming data is missing at random.

Comparison groups	Part 1: Placebo 1 v Part 1: Otilimab 90 mg
Number of subjects included in analysis	777
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0616 [44]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.79

Notes:

[44] - p-value is from a one-sided test.

Secondary: Part 2: Percentage of participants alive and free of respiratory failure at Day 7

End point title	Part 2: Percentage of participants alive and free of respiratory failure at Day 7[45]

End point description:

Participants were alive and free of respiratory failure if they were in category 1, 2, 3 or 4 from the GlaxoSmithKline (GSK) modified version ordinal scale adapted from World Health Organization (WHO) scale 2020. The 8-point scale was as follows: 1) Non-hospitalized, no limitation of activity; 2) Non-hospitalized,limitation of activity; 3) Hospitalized, no oxygen therapy; 4) Hospitalized, low-flow oxygen by mask or nasal prongs; 5) Hospitalized, highflow oxygen (>=15L/min), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BIPAP), non-invasive ventilation; 6) Hospitalized, intubation and mechanical ventilation; 7) Hospitalized, mechanical ventilation plus additional organ support; 8) Death. Higher scale indicates higher intensity of respiratory failure. Percentage values are rounded off. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 7

Notes:

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

Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 2: Placebo 2	Part 2: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173[46]	174[47]		
Units: Percentage of participants	28	37		

Notes:

[46] - mITT Population.

[47] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, age, and both clinical status at Baseline and sex as randomized. Missing data was imputed with monotone logistic multiple imputation assuming data is missing at random.

Comparison groups	Part 2: Placebo 2 v Part 2: Otilimab 90 mg
Number of subjects included in analysis	347
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0831 [48]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	2.39

Notes:

[48] - p-value is generated from a two-sided test.

Secondary: Part 2: Percentage of participants alive and free of respiratory failure at Day 14

End point title	Part 2: Percentage of participants alive and free of respiratory failure at Day 14[49]

End point description:

Participants were alive and free of respiratory failure if they were in category 1, 2, 3 or 4 from the GlaxoSmithKline (GSK) modified version ordinal scale adapted from World Health Organization (WHO) scale 2020. The 8-point scale was as follows: 1) Non-hospitalized, no limitation of activity; 2) Non-hospitalized,limitation of activity; 3) Hospitalized, no oxygen therapy; 4) Hospitalized, low-flow oxygen by mask or nasal prongs; 5) Hospitalized, highflow oxygen (>=15L/min), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BIPAP), non-invasive ventilation; 6) Hospitalized, intubation and mechanical ventilation; 7) Hospitalized, mechanical ventilation plus additional organ support; 8) Death. Higher scale indicates higher intensity of respiratory failure. Percentage values are rounded off. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 14

Notes:

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

Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 2: Placebo 2	Part 2: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	171[50]	174[51]		
Units: Percentage of participants	43	49		

Notes:

[50] - mITT Population.

[51] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, age, and both clinical status at Baseline and sex as randomized. Missing data was imputed with monotone logistic multiple imputation assuming data is missing at random.

Comparison groups	Part 2: Placebo 2 v Part 2: Otilimab 90 mg
Number of subjects included in analysis	345
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2557 [52]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	2

Notes:

[52] - p-value is generated from a two-sided test.

Secondary: Part 2: Percentage of participants alive and free of respiratory failure at Day 42

End point title	Part 2: Percentage of participants alive and free of respiratory failure at Day 42[53]

End point description:

Participants were alive and free of respiratory failure if they were in category 1, 2, 3 or 4 from the GlaxoSmithKline (GSK) modified version ordinal scale adapted from World Health Organization (WHO) scale 2020. The 8-point scale was as follows: 1) Non-hospitalized, no limitation of activity; 2) Non-hospitalized,limitation of activity; 3) Hospitalized, no oxygen therapy; 4) Hospitalized, low-flow oxygen by mask or nasal prongs; 5) Hospitalized, highflow oxygen (>=15L/min), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BIPAP), non-invasive ventilation; 6) Hospitalized, intubation and mechanical ventilation; 7) Hospitalized, mechanical ventilation plus additional organ support; 8) Death. Higher scale indicates higher intensity of respiratory failure. Percentage values are rounded off. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 42

Notes:

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

Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 2: Placebo 2	Part 2: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	170[54]	172[55]		
Units: Percentage of participants	54	54		

Notes:

[54] - mITT Population.

[55] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, age, and both clinical status at Baseline and sex as randomized. Missing data was imputed with monotone logistic multiple imputation assuming data is missing at random.

Comparison groups	Part 2: Placebo 2 v Part 2: Otilimab 90 mg
Number of subjects included in analysis	342
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.856 [56]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.61

Notes:

[56] - p-value is generated from a two-sided test.

Secondary: Part 2: Percentage of participants alive and free of respiratory failure at Day 60

End point title	Part 2: Percentage of participants alive and free of respiratory failure at Day 60[57]

End point description:

Participants were alive and free of respiratory failure if they were in category 1, 2, 3 or 4 from the GlaxoSmithKline (GSK) modified version ordinal scale adapted from World Health Organization (WHO) scale 2020. The 8-point scale was as follows: 1) Non-hospitalized, no limitation of activity; 2) Non-hospitalized,limitation of activity; 3) Hospitalized, no oxygen therapy; 4) Hospitalized, low-flow oxygen by mask or nasal prongs; 5) Hospitalized, highflow oxygen (>=15L/min), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BIPAP), non-invasive ventilation; 6) Hospitalized, intubation and mechanical ventilation; 7) Hospitalized, mechanical ventilation plus additional organ support; 8) Death. Higher scale indicates higher intensity of respiratory failure. Percentage values are rounded off. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 60

Notes:

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

Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 2: Placebo 2	Part 2: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	170[58]	171[59]		
Units: Percentage of participants	55	56		

Notes:

[58] - mITT Population

[59] - mITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, age, and both clinical status at Baseline and sex as randomized. Missing data was imputed with monotone logistic multiple imputation assuming data is missing at random.

Comparison groups	Part 2: Placebo 2 v Part 2: Otilimab 90 mg
Number of subjects included in analysis	341
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7533 [60]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.66

Notes:

[60] - p-value is generated from a two-sided test.

Secondary: Part 1: Time to recovery from respiratory failure up to Day 28

End point title	Part 1: Time to recovery from respiratory failure up to Day

End point description:

Time to recovery from respiratory failure was defined as time (days) from dosing to last recovery from respiratory failure upto (and including) Day 28.Participants were in respiratory failure if they were in category 5 or above from the GSK modified ordinal scale adapted from WHO scale 2020.The 8-point scale was as follows:1) Non-hospitalized, no limitation of activity;2) Non-hospitalized,limitation of activity;3) Hospitalized, no oxygen therapy;4) Hospitalized, low-flow oxygen by mask/nasal prongs;5)Hospitalized,highflow oxygen(>=15L/min),continuous positive airway pressure (CPAP),bilevel positive airway pressure(BIPAP),non-invasive ventilation;6)Hospitalized, intubation and mechanical ventilation;7)Hospitalized, mechanical ventilation plus additional organ support;8)Death.9999 indicates that <75% participants experienced event within treatment arm. Third-quartile could not be derived. Only those participants with data available at the specified time points were analyzed

End point type	Secondary

End point timeframe:

Up to Day 28

Notes:

[61] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 1: Placebo 1	Part 1: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	263[62]	281[63]		
Units: Days				
median (inter-quartile range (Q1-Q3))	10 (5 to 99999)	9 (5 to 99999)		

Notes:

[62] - mITT Population.

[63] - mITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Model adjusted analysis performed using a Cox proportional hazards model adjusted by treatment, clinical status at Baseline as randomized and age group as randomized.

Comparison groups	Part 1: Placebo 1 v Part 1: Otilimab 90 mg
Number of subjects included in analysis	544
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0959 [64]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.32

Notes:

[64] - p-value is from a one-sided test.

Secondary: Part 2: Time to recovery from respiratory failure up to Day 28

End point title	Part 2: Time to recovery from respiratory failure up to Day

End point description:

Time to recovery from respiratory failure was defined as time (days) from dosing to last recovery from respiratory failure upto (and including) Day 28.Participants were in respiratory failure if they were in category 5 or above from the GSK modified ordinal scale adapted from WHO scale 2020.The 8-point scale was as follows:1) Non-hospitalized,no limitation of activity;2)Non-hospitalized,limitation of activity;3) Hospitalized, no oxygen therapy;4) Hospitalized, low-flow oxygen by mask/nasal prongs;5)Hospitalized,highflow oxygen(>=15L/min),continuous positive airway pressure (CPAP),bilevel positive airway pressure(BIPAP),non-invasive ventilation;6)Hospitalized, intubation and mechanical ventilation;7)Hospitalized, mechanical ventilation plus additional organ support;8)Death.99999 indicates that <75% participants experienced event within treatment arm. Third-quartile could not be derived. Only those participants with data available at the specified time points were analyzed

End point type	Secondary

End point timeframe:

Up to Day 28

Notes:

[65] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 2: Placebo 2	Part 2: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90[66]	91[67]		
Units: Days				
median (inter-quartile range (Q1-Q3))	24 (7 to 99999)	22 (5 to 99999)		

Notes:

[66] - mITT Population

[67] - mITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Model adjusted analysis performed using a Cox proportional hazards model adjusted by treatment, clinical status at Baseline as randomized, sex as randomized and age.

Comparison groups	Part 2: Placebo 2 v Part 2: Otilimab 90 mg
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4421 [68]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.5

Notes:

[68] - p-value is generated from a two-sided test.

Secondary: Part 1: Percentage of participants alive and independent of supplementary oxygen at Day 7

End point title	Part 1: Percentage of participants alive and independent of supplementary oxygen at Day 7[69]

End point description:

Participants were independent of supplementary oxygen if they were in category 1, 2 or 3 from the GlaxoSmithKline (GSK) modified ordinal scale adapted from World Health Organization (WHO) scale 2020. The 8-point scale was as follows: 1) Non-hospitalized, no limitation of activity; 2) Non-hospitalized,limitation of activity; 3) Hospitalized, no oxygen therapy; 4) Hospitalized, low-flow oxygen by mask or nasal prongs; 5) Hospitalized, highflow oxygen (>=15L/min), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BIPAP), non-invasive ventilation; 6) Hospitalized, intubation and mechanical ventilation; 7) Hospitalized, mechanical ventilation plus additional organ support; 8) Death. Percentage values are rounded. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 7

Notes:

[69] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 1: Placebo 1	Part 1: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	396[70]	393[71]		
Units: Percentage of participants	11	12		

Notes:

[70] - mITT Population.

[71] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, and both clinical status at Baseline and age group as randomized. Missing data was imputed with monotone discriminant multiple imputation assuming data is missing at random.

Comparison groups	Part 1: Placebo 1 v Part 1: Otilimab 90 mg
Number of subjects included in analysis	789
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2814 [72]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.8

Notes:

[72] - p-value is from a one-sided test.

Secondary: Part 1: Percentage of participants alive and independent of supplementary oxygen at Day 14

End point title	Part 1: Percentage of participants alive and independent of supplementary oxygen at Day 14[73]

End point description:

Participants were independent of supplementary oxygen if they were in category 1, 2 or 3 from the GlaxoSmithKline (GSK) modified ordinal scale adapted from World Health Organization (WHO) scale 2020. The 8-point scale was as follows: 1) Non-hospitalized, no limitation of activity; 2) Non-hospitalized,limitation of activity; 3) Hospitalized, no oxygen therapy; 4) Hospitalized, low-flow oxygen by mask or nasal prongs; 5) Hospitalized, highflow oxygen (>=15L/min), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BIPAP), non-invasive ventilation; 6) Hospitalized, intubation and mechanical ventilation; 7) Hospitalized, mechanical ventilation plus additional organ support; 8) Death. Percentage values are rounded off. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 14

Notes:

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

Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 1: Placebo 1	Part 1: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	394[74]	391[75]		
Units: Percentage of participants	37	37		

Notes:

[74] - mITT Population.

[75] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, and both clinical status at Baseline and age group as randomized. Missing data was imputed with monotone discriminant multiple imputation assuming data is missing at random.

Comparison groups	Part 1: Placebo 1 v Part 1: Otilimab 90 mg
Number of subjects included in analysis	785
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3901 [76]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.42

Notes:

[76] - p-value is from a one-sided test.

Secondary: Part 1: Percentage of participants alive and independent of supplementary oxygen at Day 28

End point title	Part 1: Percentage of participants alive and independent of supplementary oxygen at Day 28[77]

End point description:

Participants were independent of supplementary oxygen if they were in category 1, 2 or 3 from the GlaxoSmithKline (GSK) modified ordinal scale adapted from World Health Organization (WHO) scale 2020. The 8-point scale was as follows: 1) Non-hospitalized, no limitation of activity; 2) Non-hospitalized,limitation of activity; 3) Hospitalized, no oxygen therapy; 4) Hospitalized, low-flow oxygen by mask or nasal prongs; 5) Hospitalized, highflow oxygen (>=15L/min), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BIPAP), non-invasive ventilation; 6) Hospitalized, intubation and mechanical ventilation; 7) Hospitalized, mechanical ventilation plus additional organ support; 8) Death. Percentage values are rounded off. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 28

Notes:

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

Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 1: Placebo 1	Part 1: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	393[78]	389[79]		
Units: Percentage of participants	57	57		

Notes:

[78] - mITT Population.

[79] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, and both clinical status at Baseline and age group as randomized. Missing data was imputed with monotone discriminant multiple imputation assuming data is missing at random.

Comparison groups	Part 1: Placebo 1 v Part 1: Otilimab 90 mg
Number of subjects included in analysis	782
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4763 [80]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.36

Notes:

[80] - p-value is from a one-sided test.

Secondary: Part 1: Percentage of participants alive and independent of supplementary oxygen at Day 42

End point title	Part 1: Percentage of participants alive and independent of supplementary oxygen at Day 42[81]

End point description:

Participants were independent of supplementary oxygen if they were in category 1, 2 or 3 from the GlaxoSmithKline (GSK) modified ordinal scale adapted from World Health Organization (WHO) scale 2020. The 8-point scale was as follows: 1) Non-hospitalized, no limitation of activity; 2) Non-hospitalized,limitation of activity; 3) Hospitalized, no oxygen therapy; 4) Hospitalized, low-flow oxygen by mask or nasal prongs; 5) Hospitalized, highflow oxygen (>=15L/min), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BIPAP), non-invasive ventilation; 6) Hospitalized, intubation and mechanical ventilation; 7) Hospitalized, mechanical ventilation plus additional organ support; 8) Death. Percentage values are rounded off. Only those participants with data available at the specified time points were analyzed. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 42

Notes:

[81] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 1: Placebo 1	Part 1: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	392[82]	385[83]		
Units: Percentage of participants	63	66		

Notes:

[82] - mITT population.

[83] - mITT population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, and both clinical status at Baseline and age group as randomized. Missing data was imputed with monotone discriminant multiple imputation assuming data is missing at random.

Comparison groups	Part 1: Placebo 1 v Part 1: Otilimab 90 mg
Number of subjects included in analysis	777
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1973 [84]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.56

Notes:

[84] - p-value is from a one-sided test.

Secondary: Part 1: Percentage of participants alive and independent of supplementary oxygen at Day 60

End point title	Part 1: Percentage of participants alive and independent of supplementary oxygen at Day 60[85]

End point description:

Participants were independent of supplementary oxygen if they were in category 1, 2 or 3 from the GlaxoSmithKline (GSK) modified ordinal scale adapted from World Health Organization (WHO) scale 2020. The 8-point scale was as follows: 1) Non-hospitalized, no limitation of activity; 2) Non-hospitalized,limitation of activity; 3) Hospitalized, no oxygen therapy; 4) Hospitalized, low-flow oxygen by mask or nasal prongs; 5) Hospitalized, highflow oxygen (>=15L/min), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BIPAP), non-invasive ventilation; 6) Hospitalized, intubation and mechanical ventilation; 7) Hospitalized, mechanical ventilation plus additional organ support; 8) Death. Percentage values are rounded off. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 60

Notes:

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

Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 1: Placebo 1	Part 1: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	386[86]	373[87]		
Units: Percentage of participants	67	71		

Notes:

[86] - mITT Population.

[87] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, and both clinical status at Baseline and age group as randomized. Missing data was imputed with monotone discriminant multiple imputation assuming data is missing at random.

Comparison groups	Part 1: Placebo 1 v Part 1: Otilimab 90 mg
Number of subjects included in analysis	759
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1173 [88]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.67

Notes:

[88] - p-value is from a one-sided test.

Secondary: Part 2: Percentage of participants alive and independent of supplementary oxygen at Day 7

End point title	Part 2: Percentage of participants alive and independent of supplementary oxygen at Day 7[89]

End point description:

Participants were independent of supplementary oxygen if they were in category 1, 2 or 3 from the GlaxoSmithKline (GSK) modified ordinal scale adapted from World Health Organization (WHO) scale 2020. The 8-point scale was as follows: 1) Non-hospitalized, no limitation of activity; 2) Non-hospitalized,limitation of activity; 3) Hospitalized, no oxygen therapy; 4) Hospitalized, low-flow oxygen by mask or nasal prongs; 5) Hospitalized, highflow oxygen (>=15L/min), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BIPAP), non-invasive ventilation; 6) Hospitalized, intubation and mechanical ventilation; 7) Hospitalized, mechanical ventilation plus additional organ support; 8) Death. Percentage values are rounded off. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 7

Notes:

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

Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 2: Placebo 2	Part 2: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173[90]	174[91]		
Units: Percentage of participants	3	13		

Notes:

[90] - mITT Population.

[91] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, age, and both clinical status at Baseline and sex as randomized. Missing data was imputed with monotone logistic multiple imputation assuming data is missing at random.

Comparison groups	Part 2: Placebo 2 v Part 2: Otilimab 90 mg
Number of subjects included in analysis	347
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0037 [92]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.57
upper limit	10.13

Notes:

[92] - p-value is generated from a two-sided test.

Secondary: Part 2: Percentage of participants alive and independent of supplementary oxygen at Day 14

End point title	Part 2: Percentage of participants alive and independent of supplementary oxygen at Day 14[93]

End point description:

Participants were independent of supplementary oxygen if they were in category 1, 2 or 3 from the GlaxoSmithKline (GSK) modified ordinal scale adapted from World Health Organization (WHO) scale 2020. The 8-point scale was as follows: 1) Non-hospitalized, no limitation of activity; 2) Non-hospitalized,limitation of activity; 3) Hospitalized, no oxygen therapy; 4) Hospitalized, low-flow oxygen by mask or nasal prongs; 5) Hospitalized, highflow oxygen (>=15L/min), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BIPAP), non-invasive ventilation; 6) Hospitalized, intubation and mechanical ventilation; 7) Hospitalized, mechanical ventilation plus additional organ support; 8) Death. Percentage values are rounded off. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 14

Notes:

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

Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 2: Placebo 2	Part 2: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	171[94]	174[95]		
Units: Percentage of participants	23	28		

Notes:

[94] - mITT Population.

[95] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, age, and both clinical status at Baseline and sex as randomized. Missing data was imputed with monotone logistic multiple imputation assuming data is missing at random.

Comparison groups	Part 2: Placebo 2 v Part 2: Otilimab 90 mg
Number of subjects included in analysis	345
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3581 [96]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	2.06

Notes:

[96] - p-value is generated from a two-sided test.

Secondary: Part 2: Percentage of participants alive and independent of supplementary oxygen at Day 28

End point title	Part 2: Percentage of participants alive and independent of supplementary oxygen at Day 28[97]

End point description:

Participants were independent of supplementary oxygen if they were in category 1, 2 or 3 from the GlaxoSmithKline (GSK) modified ordinal scale adapted from World Health Organization (WHO) scale 2020. The 8-point scale was as follows: 1) Non-hospitalized, no limitation of activity; 2) Non-hospitalized,limitation of activity; 3) Hospitalized, no oxygen therapy; 4) Hospitalized, low-flow oxygen by mask or nasal prongs; 5) Hospitalized, highflow oxygen (>=15L/min), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BIPAP), non-invasive ventilation; 6) Hospitalized, intubation and mechanical ventilation; 7) Hospitalized, mechanical ventilation plus additional organ support; 8) Death. Percentage values are rounded off. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 28

Notes:

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

Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 2: Placebo 2	Part 2: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	170[98]	172[99]		
Units: Percentage of participants	39	38		

Notes:

[98] - mITT Population.

[99] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, age, and both clinical status at Baseline and sex as randomized. Missing data was imputed with monotone logistic multiple imputation assuming data is missing at random.

Comparison groups	Part 2: Placebo 2 v Part 2: Otilimab 90 mg
Number of subjects included in analysis	342
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9621 [100]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.54

Notes:

[100] - p-value is generated from a two-sided test.

Secondary: Part 2: Percentage of participants alive and independent of supplementary oxygen at Day 42

End point title	Part 2: Percentage of participants alive and independent of supplementary oxygen at Day 42[101]

End point description:

Participants were independent of supplementary oxygen if they were in category 1, 2 or 3 from the GlaxoSmithKline (GSK) modified ordinal scale adapted from World Health Organization (WHO) scale 2020. The 8-point scale was as follows: 1) Non-hospitalized, no limitation of activity; 2) Non-hospitalized,limitation of activity; 3) Hospitalized, no oxygen therapy; 4) Hospitalized, low-flow oxygen by mask or nasal prongs; 5) Hospitalized, highflow oxygen (>=15L/min), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BIPAP), non-invasive ventilation; 6) Hospitalized, intubation and mechanical ventilation; 7) Hospitalized, mechanical ventilation plus additional organ support; 8) Death. Percentage values are rounded off. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 42

Notes:

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

Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 2: Placebo 2	Part 2: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	170[102]	172[103]		
Units: Percentage of participants	46	41		

Notes:

[102] - mITT Population.

[103] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, age, and both clinical status at Baseline and sex as randomized. Missing data was imputed with monotone logistic multiple imputation assuming data is missing at random.

Comparison groups	Part 2: Placebo 2 v Part 2: Otilimab 90 mg
Number of subjects included in analysis	342
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4167 [104]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.29

Notes:

[104] - p-value is generated from a two-sided test.

Secondary: Part 2: Percentage of participants alive and independent of supplementary oxygen at Day 60

End point title	Part 2: Percentage of participants alive and independent of supplementary oxygen at Day 60[105]

End point description:

Participants were independent of supplementary oxygen if they were in category 1, 2 or 3 from the GlaxoSmithKline (GSK) modified ordinal scale adapted from World Health Organization (WHO) scale 2020. The 8-point scale was as follows: 1) Non-hospitalized, no limitation of activity; 2) Non-hospitalized,limitation of activity; 3) Hospitalized, no oxygen therapy; 4) Hospitalized, low-flow oxygen by mask or nasal prongs; 5) Hospitalized, highflow oxygen (>=15L/min), continuous positive airway pressure (CPAP), bilevel positive airway pressure (BIPAP), non-invasive ventilation; 6) Hospitalized, intubation and mechanical ventilation; 7) Hospitalized, mechanical ventilation plus additional organ support; 8) Death. Percentage values are rounded off. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

At Day 60

Notes:

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

Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 2: Placebo 2	Part 2: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	170[106]	171[107]		
Units: Percentage of participants	51	46		

Notes:

[106] - mITT Population.

[107] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, age, and both clinical status at Baseline and sex as randomized. Missing data was imputed with monotone logistic multiple imputation assuming data is missing at random.

Comparison groups	Part 2: Placebo 2 v Part 2: Otilimab 90 mg
Number of subjects included in analysis	341
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3408 [108]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.25

Notes:

[108] - p-value is generated from a two-sided test.

Secondary: Part 1: Time to last dependence on supplementary oxygen

End point title	Part 1: Time to last dependence on supplementary oxygen[109]

End point description:

Time to last dependence on supplementary oxygen was defined as the time (days) from dosing to last dependence on supplementary oxygen up to (and including) Day 28. Median and inter-quartile range (first quartile and third quartile) of time to last dependence on supplementary oxygen are presented. Only those participants with data available at the specified time points were analyzed. 99999 indicates that <75% of participants experienced the event within the treatment arm. Hence, third-quartile could not be derived.

End point type	Secondary

End point timeframe:

Up to Day 28

Notes:

[109] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 1: Placebo 1	Part 1: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	223[110]	221[111]		
Units: Days				
median (inter-quartile range (Q1-Q3))	22 (11 to 99999)	21 (10 to 99999)		

Notes:

[110] - mITT Population.

[111] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Model adjusted analysis performed using a Cox proportional hazards model adjusted by treatment, clinical status at Baseline as randomized and age group as randomized.

Comparison groups	Part 1: Placebo 1 v Part 1: Otilimab 90 mg
Number of subjects included in analysis	444
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.425 [112]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.23

Notes:

[112] - p-value is from a one-sided test.

Secondary: Part 2: Time to last dependence on supplementary oxygen

End point title	Part 2: Time to last dependence on supplementary oxygen[113]

End point description:

Time to last dependence on supplementary oxygen was defined as the time (days) from dosing to last dependence on supplementary oxygen up to (and including) Day 28. Median and inter-quartile range (first quartile and third quartile) of time to last dependence on supplementary oxygen are presented. Only those participants with data available at the specified time points were analyzed. 99999 indicates that <50% of participants experienced the event within the treatment arm. Hence, median and third-quartile could not be derived.

End point type	Secondary

End point timeframe:

Up to Day 28

Notes:

[113] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 2: Placebo 2	Part 2: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66[114]	68[115]		
Units: Days				
median (inter-quartile range (Q1-Q3))	99999 (15 to 99999)	99999 (13 to 99999)		

Notes:

[114] - mITT Population.

[115] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Model adjusted analysis performed using a Cox proportional hazards model adjusted by treatment, clinical status at Baseline as randomized, sex as randomized and age.

Comparison groups	Part 2: Placebo 2 v Part 2: Otilimab 90 mg
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4774 [116]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.59

Notes:

[116] - p-value is generated from a two-sided test.

Secondary: Part 1: Percentage of participants admitted to Intensive Care Unit (ICU) up to Day 28

End point title	Part 1: Percentage of participants admitted to Intensive Care Unit (ICU) up to Day 28[117]

End point description:

Participants who were admitted to the ICU up to (and including) Day 28 were evaluated. Percentage values are rounded off. mITT Population (not in ICU at Baseline) comprised of participants in the mITT population who were not in the ICU at Baseline. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Up to Day 28

Notes:

[117] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 1: Placebo 1	Part 1: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98[118]	95[119]		
Units: Percentage of participants	24	13		

Notes:

[118] - mITT Population (not in ICU at Baseline)

[119] - mITT Population (not in ICU at Baseline)

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis performed using logistic regression adjusted for treatment, and both clinical status at Baseline and age group as randomized. Missing data was imputed with monotone discriminant multiple imputation assuming data is missing at random.

Comparison groups	Part 1: Placebo 1 v Part 1: Otilimab 90 mg
Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0119 [120]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.18
upper limit	0.89

Notes:

[120] - p-value is from a one-sided test.

Secondary: Part 1: Time to final ICU discharge

End point title	Part 1: Time to final ICU discharge[121]

End point description:

Time to final ICU discharge was defined as the time from dosing to when the participant is discharged from the ICU for the last time up to (and including) Day 28. mITT Population admitted to ICU at Baseline comprised of those participants in mITT who were admitted to ICU at Baseline. Median and inter-quartile range (first quartile and third quartile) of time to final ICU discharge is presented. Only those participants with data available at the specified time points were analyzed. 99999 indicates that <75% of participants experienced the event within the treatment arm. Hence, third-quartile could not be derived.

End point type	Secondary

End point timeframe:

Up to Day 28

Notes:

[121] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 1: Placebo 1	Part 1: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	300[122]	300[123]		
Units: Days				
median (inter-quartile range (Q1-Q3))	13 (7 to 99999)	15 (7 to 99999)		

Notes:

[122] - mITT population admitted to ICU at Baseline.

[123] - mITT population admitted to ICU at Baseline.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Model adjusted analysis performed using a Cox proportional hazards model adjusted by treatment, clinical status at Baseline as randomized and age group as randomized.

Comparison groups	Part 1: Placebo 1 v Part 1: Otilimab 90 mg
Number of subjects included in analysis	600
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4404 [124]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.24

Notes:

[124] - p-value is from a one-sided test.

Secondary: Part 2: Time to final ICU discharge

End point title	Part 2: Time to final ICU discharge[125]

End point description:

Time to final ICU discharge was defined as the time from dosing to when the participant was discharged from the ICU for the last time up to (and including) Day 28. Median and inter-quartile range (first quartile and third quartile) of time to final ICU discharge is presented. Only those participants with data available at the specified time points were analyzed. 99999 indicates that <50% of participants experienced the event within the treatment arm. Hence, median and third-quartile could not be derived.

End point type	Secondary

End point timeframe:

Up to Day 28

Notes:

[125] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 2: Placebo 2	Part 2: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38[126]	44[127]		
Units: Days				
median (inter-quartile range (Q1-Q3))	99999 (12 to 99999)	99999 (7 to 99999)		

Notes:

[126] - mITT population admitted to ICU at Baseline.

[127] - mITT population admitted to ICU at Baseline.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Model adjusted analysis performed using a Cox proportional hazards model adjusted by treatment, clinical status at Baseline as randomized, sex as randomized and age.

Comparison groups	Part 2: Placebo 2 v Part 2: Otilimab 90 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6253 [128]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.72

Notes:

[128] - p-value is generated from a two-sided test.

Secondary: Part 1: Time to first discharge from investigator site up to Day 60

End point title	Part 1: Time to first discharge from investigator site up to Day 60[129]

End point description:

Time to first discharge from investigator site was defined as the time (days) from dosing to when the participant was first discharged from investigator site (IS) up to (and including) Day 60. Median and inter-quartile range (first quartile and third quartile) of time to first discharge from investigator site is presented. Only those participants with data available at the specified time points were analyzed. 99999 indicates that <75% of participants experienced the event within the treatment arm. Hence, third-quartile could not be derived.

End point type	Secondary

End point timeframe:

Up to Day 60

Notes:

[129] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 1: Placebo 1	Part 1: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	288[130]	294[131]		
Units: Days				
median (inter-quartile range (Q1-Q3))	18 (11 to 99999)	18 (10 to 99999)		

Notes:

[130] - mITT Population.

[131] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Model adjusted analysis performed using a Cox proportional hazards model adjusted by treatment, clinical status at Baseline as randomized and age group as randomized.

Comparison groups	Part 1: Placebo 1 v Part 1: Otilimab 90 mg
Number of subjects included in analysis	582
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1078 [132]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.3

Notes:

[132] - p-value is from a one-sided test.

Secondary: Part 1: Time to first discharge to non-hospitalized residence up to Day 60

End point title	Part 1: Time to first discharge to non-hospitalized residence up to Day 60[133]

End point description:

Time to first discharge to non-hospitalized residence was defined as the time (days) from dosing to when the participant was discharged to a non-hospitalized residence for the first time up to (and including) Day 60. Median and inter-quartile range (first quartile and third quartile) of time to first discharge to non-hospitalized residence is presented. Only those participants with data available at the specified time points were analyzed. 99999 indicates that <75% of participants experienced the event within the treatment arm. Hence, third-quartile could not be derived.

End point type	Secondary

End point timeframe:

Up to Day 60

Notes:

[133] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 1: Placebo 1	Part 1: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	269[134]	280[135]		
Units: Days				
median (inter-quartile range (Q1-Q3))	21 (12 to 99999)	20 (11 to 99999)		

Notes:

[134] - mITT Population.

[135] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Model adjusted analysis performed using a Cox proportional hazards model adjusted by treatment, clinical status at Baseline as randomized and age group as randomized.

Comparison groups	Part 1: Placebo 1 v Part 1: Otilimab 90 mg
Number of subjects included in analysis	549
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.114 [136]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.31

Notes:

[136] - p-value is from a one-sided test.

Secondary: Part 2: Time to first discharge from investigator site up to Day 60

End point title	Part 2: Time to first discharge from investigator site up to Day 60[137]

End point description:

Time to first discharge from investigator site was defined as the time (days) from dosing to when the participant was first discharged from investigator site up to (and including) Day 60. Median and inter-quartile range (first quartile and third quartile) of time to first discharge from investigator site is presented. Only those participants with data available at the specified time points were analyzed. 99999 indicates that <75% of participants experienced the event within the treatment arm. Hence, third-quartile could not be derived.

End point type	Secondary

End point timeframe:

Up to Day 60

Notes:

[137] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 2: Placebo 2	Part 2: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96[138]	99[139]		
Units: Days				
median (inter-quartile range (Q1-Q3))	36 (15 to 99999)	37 (15 to 99999)		

Notes:

[138] - mITT Population.

[139] - mITT Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Part 2: Placebo 2 v Part 2: Otilimab 90 mg
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	other[140]
P-value	= 0.7084 [141]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.4

Notes:

[140] - Model adjusted analysis performed using a Cox proportional hazards model adjusted by treatment, clinical status at Baseline as randomized, sex as randomized and age.

[141] - p-value is generated from a two-sided test.

Secondary: Part 2: Time to first discharge to non-hospitalized residence

End point title	Part 2: Time to first discharge to non-hospitalized residence[142]

End point description:

Time to first discharge to non-hospitalized residence was defined as the time (days) from dosing to when the participant (parti) was discharged to a non-hospitalized residence for the first time up to (and including) Day 60. Only those participants with data available at the specified time points were analyzed. In Part 2: Placebo 2 arm, 99999 indicates that <50% participants experienced event within treatment arm. Hence, median and third-quartile could not be derived. In Part 2: Otilimab 90 mg arm, 99999 indicates that <75%participants experienced event within the treatment arm. Hence, third-quartile could not be derived.

End point type	Secondary

End point timeframe:

Up to Day 60

Notes:

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

Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 2: Placebo 2	Part 2: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86[143]	90[144]		
Units: Days				
median (inter-quartile range (Q1-Q3))	99999 (18 to 99999)	53 (15 to 99999)		

Notes:

[143] - mITT Population

[144] - mITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Model adjusted analysis performed using a Cox proportional hazards model adjusted by treatment, clinical status at Baseline as randomized, sex as randomized and age.

Comparison groups	Part 2: Placebo 2 v Part 2: Otilimab 90 mg
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4085 [145]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.52

Notes:

[145] - p-value is generated from a two-sided test.

Secondary: Part 1: Number of participants with serious adverse events (SAEs) and common (>=5%) non-serious adverse events (non-SAEs)

End point title	Part 1: Number of participants with serious adverse events (SAEs) and common (>=5%) non-serious adverse events (non-SAEs)[146]

End point description:

An adverse event (AE) is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study intervention, whether or not considered related to the study intervention. An SAE is defined as any untoward medical occurrence that, at any dose may result in death or is life-threatening or requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability/incapacity or is a congenital anomaly/birth defect or any other situation according to medical or scientific judgment or is associated with liver injury and impaired liver function. Number of participants with any SAE and common (>=5%) non-SAEs are presented. Safety population comprised of all participants who received study intervention.

End point type	Secondary

End point timeframe:

Up to Day 60

Notes:

[146] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 1: Placebo 1	Part 1: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	396[147]	397[148]		
Units: Participants				
Non-SAEs	67	91		
SAEs	147	124		

Notes:

[147] - Safety Population

[148] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Number of participants with SAEs and common (>=5%) non-SAEs

End point title	Part 2: Number of participants with SAEs and common (>=5%) non-SAEs[149]

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study intervention, whether or not considered related to the study intervention. An SAE is defined as any untoward medical occurrence that, at any dose may result in death or is life-threatening or requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability/incapacity or is a congenital anomaly/birth defect or any other situation according to medical or scientific judgment or is associated with liver injury and impaired liver function. Number of participants with any SAE and common (>=5%) non-SAEs are presented.

End point type	Secondary

End point timeframe:

Up to Day 60

Notes:

[149] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoints are described part-wise; whereas the Baseline characteristics are for overall study.

End point values	Part 2: Placebo 2	Part 2: Otilimab 90 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173[150]	174[151]		
Units: Participants				
Non-SAEs	57	50		
SAEs	90	90		

Notes:

[150] - Safety Population

[151] - Safety Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality, SAEs, and non-SAEs were collected up to Day 60 in Part 1 and 2 of the study

Adverse event reporting additional description:

SAEs and non-serious AEs were reported for Safety Population (all participants who received study intervention). All-cause mortality was reported for Enrolled population(all participants who entered the study).Sixteen participants from Enrolled Population(N=1156) did not receive study treatment, hence were not included in Safety Population(N=1140)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Part 1: Placebo 1

Reporting group description:

Participants between the ages of greater than or equal to (>=)18 years and less than or equal to (<=)79 years received blinded 1-hour IV infusion of placebo (sterile 0.9 percent [%] weight by volume [w/v] sodium chloride solution) once along with standard of care.

Reporting group title	Part 1: Otilimab 90 mg

Reporting group description:

Participants between the ages of >=18 years and <=79 years received blinded otilimab 90 milligrams (mg) (solution in single-use vial diluted in sterile 0.9% w/v sodium chloride solution) once as 1-hour IV infusion along with standard of care.

Reporting group title	Part 2: Placebo 2

Reporting group description:

Participants aged 70 years or above received blinded 1-hour IV infusion of placebo (sterile 5% w/v dextrose solution) once along with standard of care.

Reporting group title	Part 2: Otilimab 90 mg

Reporting group description:

Participants aged 70 years or above received blinded otilimab 90 mg (solution in single-use vial diluted in sterile 5% dextrose solution) once as 1-hour IV infusion along with standard of care.

Serious adverse events	Part 1: Placebo 1	Part 1: Otilimab 90 mg	Part 2: Placebo 2
Total subjects affected by serious adverse events			
subjects affected / exposed	147 / 396 (37.12%)	124 / 397 (31.23%)	90 / 173 (52.02%)
number of deaths (all causes)	93	84	76
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal adenocarcinoma			

subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Shock			
subjects affected / exposed	4 / 396 (1.01%)	0 / 397 (0.00%)	3 / 173 (1.73%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 3
Hypotension			
subjects affected / exposed	3 / 396 (0.76%)	1 / 397 (0.25%)	2 / 173 (1.16%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Deep vein thrombosis			
subjects affected / exposed	2 / 396 (0.51%)	0 / 397 (0.00%)	2 / 173 (1.16%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock haemorrhagic			
subjects affected / exposed	5 / 396 (1.26%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 4	0 / 0	0 / 0
Circulatory collapse			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Embolism			
subjects affected / exposed	1 / 396 (0.25%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Peripheral artery thrombosis			
subjects affected / exposed	1 / 396 (0.25%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral ischaemia			

subjects affected / exposed	2 / 396 (0.51%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial haemorrhage			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extremity necrosis			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemic shock			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	15 / 396 (3.79%)	12 / 397 (3.02%)	8 / 173 (4.62%)
occurrences causally related to treatment / all	0 / 15	1 / 12	1 / 8
deaths causally related to treatment / all	0 / 15	1 / 10	1 / 8
Catheter site haemorrhage			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			

subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complication associated with device			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthermia			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Homeless			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			

subjects affected / exposed	18 / 396 (4.55%)	17 / 397 (4.28%)	8 / 173 (4.62%)
occurrences causally related to treatment / all	0 / 18	0 / 18	0 / 8
deaths causally related to treatment / all	0 / 14	0 / 13	0 / 7
Acute respiratory failure			
subjects affected / exposed	10 / 396 (2.53%)	9 / 397 (2.27%)	9 / 173 (5.20%)
occurrences causally related to treatment / all	0 / 10	1 / 9	0 / 9
deaths causally related to treatment / all	0 / 5	1 / 7	0 / 7
Acute respiratory distress syndrome			
subjects affected / exposed	9 / 396 (2.27%)	11 / 397 (2.77%)	3 / 173 (1.73%)
occurrences causally related to treatment / all	1 / 9	0 / 11	0 / 3
deaths causally related to treatment / all	0 / 8	0 / 8	0 / 2
Hypoxia			
subjects affected / exposed	5 / 396 (1.26%)	5 / 397 (1.26%)	7 / 173 (4.05%)
occurrences causally related to treatment / all	0 / 5	0 / 5	0 / 7
deaths causally related to treatment / all	0 / 3	0 / 4	0 / 7
Pneumothorax			
subjects affected / exposed	9 / 396 (2.27%)	8 / 397 (2.02%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 10	0 / 8	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 3	0 / 0
Pulmonary embolism			
subjects affected / exposed	11 / 396 (2.78%)	6 / 397 (1.51%)	3 / 173 (1.73%)
occurrences causally related to treatment / all	0 / 11	0 / 6	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 1
Respiratory distress			
subjects affected / exposed	2 / 396 (0.51%)	2 / 397 (0.50%)	5 / 173 (2.89%)
occurrences causally related to treatment / all	0 / 2	2 / 2	0 / 5
deaths causally related to treatment / all	0 / 1	2 / 2	0 / 4
Respiratory disorder			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	3 / 173 (1.73%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumomediastinum			

subjects affected / exposed	3 / 396 (0.76%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Organising pneumonia			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			
subjects affected / exposed	1 / 396 (0.25%)	1 / 397 (0.25%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Dyspnoea			
subjects affected / exposed	1 / 396 (0.25%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal oedema			
subjects affected / exposed	2 / 396 (0.51%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	2 / 396 (0.51%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax spontaneous			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute pulmonary oedema			

subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Bronchospasm			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemothorax			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercapnia			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory arrest			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Stridor			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachypnoea			

subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vocal cord dysfunction			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Organic brain syndrome			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Oxygen consumption increased			
subjects affected / exposed	2 / 396 (0.51%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Oxygen saturation decreased			
subjects affected / exposed	2 / 396 (0.51%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobin decreased			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Liver function test abnormal			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test increased			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary function test decreased			

subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin T increased			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Multiple injuries			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Subdural haematoma			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheal injury			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	4 / 396 (1.01%)	8 / 397 (2.02%)	7 / 173 (4.05%)
occurrences causally related to treatment / all	1 / 4	0 / 11	0 / 9
deaths causally related to treatment / all	1 / 2	0 / 6	0 / 6
Cardio-respiratory arrest			
subjects affected / exposed	1 / 396 (0.25%)	2 / 397 (0.50%)	4 / 173 (2.31%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 2

Atrial fibrillation			
subjects affected / exposed	3 / 396 (0.76%)	1 / 397 (0.25%)	2 / 173 (1.16%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 396 (0.00%)	2 / 397 (0.50%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Supraventricular tachycardia			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Cardiogenic shock			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiopulmonary failure			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Sinus node dysfunction			
subjects affected / exposed	1 / 396 (0.25%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			

subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiovascular insufficiency			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular failure			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paroxysmal atrioventricular block			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumopericardium			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulseless electrical activity			

subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Right ventricular failure			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	3 / 173 (1.73%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Cerebral haemorrhage			
subjects affected / exposed	1 / 396 (0.25%)	1 / 397 (0.25%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Intensive care unit acquired weakness			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	2 / 173 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Encephalopathy			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 396 (0.00%)	2 / 397 (0.50%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			

subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hypercapnic coma			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Coagulopathy			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 396 (0.25%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	1 / 396 (0.25%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Gastric ulcer			

subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric varices haemorrhage			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Rectal ulcer haemorrhage			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal haematoma			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal haemorrhage			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Ischaemic hepatitis			

subjects affected / exposed	2 / 396 (0.51%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Acute hepatic failure			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholestasis			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic cholecystitis			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis fulminant			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hepatocellular injury			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			

subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous emphysema			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Toxic epidermal necrolysis			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	10 / 396 (2.53%)	9 / 397 (2.27%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 11	1 / 9	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 1
Oliguria			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prerenal failure			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Haematoma muscle			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
Septic shock			
subjects affected / exposed	13 / 396 (3.28%)	14 / 397 (3.53%)	5 / 173 (2.89%)
occurrences causally related to treatment / all	2 / 14	4 / 14	1 / 5
deaths causally related to treatment / all	0 / 5	4 / 9	1 / 3
Pneumonia			
subjects affected / exposed	9 / 396 (2.27%)	7 / 397 (1.76%)	5 / 173 (2.89%)
occurrences causally related to treatment / all	3 / 9	3 / 7	1 / 5
deaths causally related to treatment / all	0 / 2	1 / 3	1 / 3
COVID-19 pneumonia			
subjects affected / exposed	3 / 396 (0.76%)	12 / 397 (3.02%)	4 / 173 (2.31%)
occurrences causally related to treatment / all	0 / 3	1 / 12	0 / 4
deaths causally related to treatment / all	0 / 3	1 / 11	0 / 3
COVID-19			
subjects affected / exposed	5 / 396 (1.26%)	3 / 397 (0.76%)	9 / 173 (5.20%)
occurrences causally related to treatment / all	0 / 5	0 / 3	0 / 9
deaths causally related to treatment / all	0 / 5	0 / 2	0 / 9
Sepsis			
subjects affected / exposed	7 / 396 (1.77%)	1 / 397 (0.25%)	2 / 173 (1.16%)
occurrences causally related to treatment / all	2 / 7	0 / 1	0 / 2
deaths causally related to treatment / all	1 / 5	0 / 1	0 / 2
Pneumonia staphylococcal			
subjects affected / exposed	6 / 396 (1.52%)	1 / 397 (0.25%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	2 / 6	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Pneumonia pseudomonal			
subjects affected / exposed	7 / 396 (1.77%)	2 / 397 (0.50%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 7	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 2	1 / 2	0 / 0
Klebsiella sepsis			
subjects affected / exposed	4 / 396 (1.01%)	1 / 397 (0.25%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	2 / 4	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	1 / 1
Staphylococcal bacteraemia			

subjects affected / exposed	1 / 396 (0.25%)	1 / 397 (0.25%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Staphylococcal sepsis			
subjects affected / exposed	2 / 396 (0.51%)	3 / 397 (0.76%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 396 (0.00%)	4 / 397 (1.01%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Bronchopulmonary aspergillosis			
subjects affected / exposed	3 / 396 (0.76%)	0 / 397 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Enterobacter pneumonia			
subjects affected / exposed	2 / 396 (0.51%)	1 / 397 (0.25%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 3	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia klebsiella			
subjects affected / exposed	2 / 396 (0.51%)	1 / 397 (0.25%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Bacterial sepsis			
subjects affected / exposed	2 / 396 (0.51%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	1 / 2	0 / 1	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 396 (0.25%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia haemophilus			

subjects affected / exposed	3 / 396 (0.76%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia serratia			
subjects affected / exposed	3 / 396 (0.76%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	2 / 396 (0.51%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Acinetobacter infection			
subjects affected / exposed	1 / 396 (0.25%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related bacteraemia			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal infection			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 396 (0.00%)	2 / 397 (0.50%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Lung abscess			

subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Pneumonia acinetobacter			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia proteus			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia streptococcal			
subjects affected / exposed	1 / 396 (0.25%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonal bacteraemia			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stenotrophomonas infection			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis bacterial			
subjects affected / exposed	1 / 396 (0.25%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	1 / 396 (0.25%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acinetobacter sepsis			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial infection			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Candida pneumonia			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Citrobacter infection			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Citrobacter sepsis			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Clostridium difficile colitis			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronavirus infection			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related sepsis			

subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterobacter sepsis			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Fusobacterium infection			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Lactobacillus infection			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mycetoma mycotic			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral candidiasis			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pneumococcal			

subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia escherichia			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pseudomembranous colitis			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Serratia bacteraemia			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superinfection			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheitis			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection enterococcal			

subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Failure to thrive			
subjects affected / exposed	0 / 396 (0.00%)	0 / 397 (0.00%)	1 / 173 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Metabolic acidosis			
subjects affected / exposed	3 / 396 (0.76%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypernatraemia			
subjects affected / exposed	1 / 396 (0.25%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acidosis			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Gout			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 396 (0.25%)	0 / 397 (0.00%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lactic acidosis			
subjects affected / exposed	0 / 396 (0.00%)	1 / 397 (0.25%)	0 / 173 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 2: Otilimab 90		

	mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	90 / 174 (51.72%)		
number of deaths (all causes)	74		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oesophageal adenocarcinoma			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Shock			
subjects affected / exposed	2 / 174 (1.15%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Hypotension			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Shock haemorrhagic			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Circulatory collapse			

subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Embolism				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral artery thrombosis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral ischaemia				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arterial haemorrhage				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Extremity necrosis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematoma				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypovolaemic shock				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Orthostatic hypotension				

subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Multiple organ dysfunction syndrome				
subjects affected / exposed	6 / 174 (3.45%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 6			
Catheter site haemorrhage				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Complication associated with device				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperthermia				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Systemic inflammatory response syndrome				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Immune system disorders				

Haemophagocytic lymphohistiocytosis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Social circumstances				
Homeless				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Respiratory failure				
subjects affected / exposed	6 / 174 (3.45%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 6			
Acute respiratory failure				
subjects affected / exposed	6 / 174 (3.45%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 6			
Acute respiratory distress syndrome				
subjects affected / exposed	3 / 174 (1.72%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 3			
Hypoxia				
subjects affected / exposed	4 / 174 (2.30%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 4			
Pneumothorax				
subjects affected / exposed	3 / 174 (1.72%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Pulmonary embolism				

subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				
subjects affected / exposed	5 / 174 (2.87%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 5			
Respiratory disorder				
subjects affected / exposed	3 / 174 (1.72%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 3			
Pneumomediastinum				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Organising pneumonia				
subjects affected / exposed	2 / 174 (1.15%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pulmonary fibrosis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Laryngeal oedema				

subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax spontaneous				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute pulmonary oedema				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchospasm				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemothorax				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypercapnia				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pulmonary oedema				

subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory arrest				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stridor				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tachypnoea				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vocal cord dysfunction				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Organic brain syndrome				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Oxygen consumption increased				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oxygen saturation decreased				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoglobin decreased				

subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Liver function test abnormal				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Liver function test increased				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary function test decreased				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transaminases increased				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Troponin T increased				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Multiple injuries				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tracheal injury				

subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	4 / 174 (2.30%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 3		
Cardio-respiratory arrest			
subjects affected / exposed	7 / 174 (4.02%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 5		
Atrial fibrillation			
subjects affected / exposed	2 / 174 (1.15%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Myocardial infarction			
subjects affected / exposed	2 / 174 (1.15%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Supraventricular tachycardia			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bradycardia			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiogenic shock			

subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiopulmonary failure				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus node dysfunction				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiovascular insufficiency				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Left ventricular failure				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocarditis				

subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Paroxysmal atrioventricular block				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumopericardium				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulseless electrical activity				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Right ventricular failure				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Nervous system disorders				
Ischaemic stroke				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intensive care unit acquired weakness				
subjects affected / exposed	3 / 174 (1.72%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				

subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Subarachnoid haemorrhage				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhage intracranial				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic stroke				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypercapnic coma				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoxic-ischaemic encephalopathy				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Coagulopathy				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				

Gastrointestinal haemorrhage				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal ischaemia				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal haemorrhage				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer haemorrhage				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastric varices haemorrhage				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal perforation				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal ulcer haemorrhage				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Retroperitoneal haematoma				

subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Retroperitoneal haemorrhage				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Ischaemic hepatitis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute hepatic failure				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholestasis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic cholecystitis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis				

subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis fulminant				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatocellular injury				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Rash				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subcutaneous emphysema				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Toxic epidermal necrolysis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	6 / 174 (3.45%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 2			
Oliguria				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prerenal failure				

subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Haematoma muscle				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Septic shock				
subjects affected / exposed	8 / 174 (4.60%)			
occurrences causally related to treatment / all	0 / 8			
deaths causally related to treatment / all	0 / 6			
Pneumonia				
subjects affected / exposed	6 / 174 (3.45%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 3			
COVID-19 pneumonia				
subjects affected / exposed	5 / 174 (2.87%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 5			
COVID-19				
subjects affected / exposed	6 / 174 (3.45%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 6			
Sepsis				
subjects affected / exposed	4 / 174 (2.30%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 3			

Pneumonia staphylococcal			
subjects affected / exposed	4 / 174 (2.30%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Pneumonia pseudomonal			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Klebsiella sepsis			
subjects affected / exposed	2 / 174 (1.15%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Staphylococcal bacteraemia			
subjects affected / exposed	4 / 174 (2.30%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 2		
Staphylococcal sepsis			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	1 / 174 (0.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterobacter pneumonia			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia klebsiella			

subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial sepsis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia haemophilus				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia serratia				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Acinetobacter infection				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Device related bacteraemia				

subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Enterococcal infection				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia sepsis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung abscess				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia acinetobacter				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pneumonia proteus				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia streptococcal				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pseudomonal bacteraemia				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary sepsis				

subjects affected / exposed	2 / 174 (1.15%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Stenotrophomonas infection				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Tracheobronchitis bacterial				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acinetobacter sepsis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial infection				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Candida pneumonia				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Citrobacter infection				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Citrobacter sepsis				

subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile colitis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronavirus infection				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device related sepsis				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterobacter sepsis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fusobacterium infection				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lactobacillus infection				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mycetoma mycotic				

subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Oral candidiasis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia pneumococcal				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia escherichia				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pseudomembranous colitis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Serratia bacteraemia				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Soft tissue infection				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Superinfection				

subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tracheitis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tracheobronchitis				
subjects affected / exposed	1 / 174 (0.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Urinary tract infection enterococcal				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Failure to thrive				
subjects affected / exposed	2 / 174 (1.15%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Metabolic acidosis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypernatraemia				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acidosis				
subjects affected / exposed	0 / 174 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gout				

subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lactic acidosis			
subjects affected / exposed	0 / 174 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part 1: Placebo 1	Part 1: Otilimab 90 mg	Part 2: Placebo 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	97 / 396 (24.49%)	115 / 397 (28.97%)	57 / 173 (32.95%)
Vascular disorders			
Hypotension			
subjects affected / exposed	13 / 396 (3.28%)	13 / 397 (3.27%)	11 / 173 (6.36%)
occurrences (all)	17	14	13
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	15 / 396 (3.79%)	11 / 397 (2.77%)	10 / 173 (5.78%)
occurrences (all)	15	13	11
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	22 / 396 (5.56%)	18 / 397 (4.53%)	10 / 173 (5.78%)
occurrences (all)	22	19	10
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	35 / 396 (8.84%)	39 / 397 (9.82%)	15 / 173 (8.67%)
occurrences (all)	35	42	16
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	17 / 396 (4.29%)	15 / 397 (3.78%)	11 / 173 (6.36%)
occurrences (all)	18	16	13
Infections and infestations			
Pneumonia			
subjects affected / exposed	21 / 396 (5.30%)	37 / 397 (9.32%)	12 / 173 (6.94%)
occurrences (all)	21	43	12
Urinary tract infection			
subjects affected / exposed	13 / 396 (3.28%)	12 / 397 (3.02%)	10 / 173 (5.78%)
occurrences (all)	13	13	10
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	14 / 396 (3.54%)	12 / 397 (3.02%)	4 / 173 (2.31%)
occurrences (all)	15	13	5
Hypernatraemia			
subjects affected / exposed	9 / 396 (2.27%)	20 / 397 (5.04%)	0 / 173 (0.00%)
occurrences (all)	9	22	0
Fluid overload			
subjects affected / exposed	2 / 396 (0.51%)	1 / 397 (0.25%)	5 / 173 (2.89%)
occurrences (all)	2	1	5

Non-serious adverse events	Part 2: Otilimab 90 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 174 (29.31%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	9 / 174 (5.17%)		
occurrences (all)	11		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	7 / 174 (4.02%)		
occurrences (all)	7		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	11 / 174 (6.32%)		
occurrences (all)	11		
Gastrointestinal disorders			

Constipation subjects affected / exposed occurrences (all)	16 / 174 (9.20%) 16		
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all)	8 / 174 (4.60%) 9		
Infections and infestations Pneumonia subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	6 / 174 (3.45%) 7 5 / 174 (2.87%) 5		
Metabolism and nutrition disorders Hyperglycaemia subjects affected / exposed occurrences (all) Hypernatraemia subjects affected / exposed occurrences (all) Fluid overload subjects affected / exposed occurrences (all)	10 / 174 (5.75%) 14 0 / 174 (0.00%) 0 9 / 174 (5.17%) 10		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 May 2020	Amendment 1: Modifications to the protocol in response to regulatory feedback, and clarifications based on investigator feedback. The key change is revision of the primary endpoint (where definition of "free of respiratory failure" is participants in categories 1-4 on GlaxoSmithKline [GSK] Ordinal Scale). Other changes are (1) to revise recording of blood pressure and pulse rate; (2) to add details of randomization caps; (3) to simplify/clarify some Inclusion and Exclusion Criteria; (4) to clarify medications permitted during the study.
02 July 2020	Amendment 2: Modifications to the protocol in response to regulatory and ethics committee feedback, and clarifications based on investigator feedback. The main changes are (1) clarification that Day 1 pre-dose assessments do not need to be repeated if Screening and Randomization are within 24 hours; (2) expedited reporting of cytokine release syndrome (CRS) as an adverse event of special interest (AESI); (3) clarification that organ transplant participants are excluded per Exclusion Criteria #11; (4) clarification of conditions by which convalescent plasma is permitted or not during the study; (5) removed specific mention of chloroquine and hydroxychloroquine; (6) expanded the null hypothesis; (7) consent may be collected before the 48hour screening window.
25 January 2021	Amendment 3: Before the last of 806 participants completed the study (Last Subject Last Visit, Day 60), an interim analysis of the primary endpoint and all-cause mortality data at Day 28 showed that substantial clinical benefit was evident in one of the pre-defined stratification subgroups "Age 70 to less than (<)80 years", with no safety concerns in any subgroup. Given the ongoing pandemic and particularly high mortality of Coronavirus Disease-2019 (COVID-19) disease in participants over 70 years old, together with recent publications that support the hypothesis that the severity of the disease is driven by a maladaptive innate immune response in which Granulocyte-macrophage colony stimulating factor (GM-CSF) plays a key role and which is more commonly elevated in older participants. GSK has therefore determined to urgently confirm these subgroup findings by amending the protocol to allow the enrolment of an additional cohort of participants aged 70 years and above with no upper age limit. GSK has reviewed the results from what is now considered as the first part of the study (Part 1) and decided that a second part will be added to the study (Part 2) which has less frequent assessments to decrease the burden on sites

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported