Clinical trial results:
A randomised double-blind placebo-controlled trial of Brensocatib (INS1007) in patients with severe COVID-19

Summary

EudraCT number	2020-001643-13
Trial protocol	GB
Global end of trial date	28 February 2021

Results information

Result version number	v1 (current)
This version publication date	28 March 2023
First version publication date	28 March 2023

Trial information

Trial identification

Sponsor protocol code	01.01.20

Additional study identifiers

ISRCTN number	ISRCTN30564012
ClinicalTrials.gov id (NCT number)	NCT04817332
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Dundee
Sponsor organisation address	Ninewells Hospital and Medical School, Dundee, United Kingdom, DD1 9SY
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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	02 November 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 February 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The overall objective of the study is to evaluate the clinical efficacy of Brensocatib compared to placebo on top of standard care in adult patients hospitalized with COVID-19

Protection of trial subjects:

Participants (or legally authorized representative) were required to provide written informed consent. Participants were excluded if alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) > 5 times the upper limit of normal, history of sevefre liver disease, absolute neutrophil count <1.0 x10^9 cells/L, were currently treated with Itraconazole, Ketoconazole, diltiazem or verapamil, were pregnant or breast feeding.

Background therapy:

Patients in both arms received all other therapies required to manage their condition (standard of care) with the exception of other investigational products. Where participants had been enrolled into the RECOVERY (Randomised Evaluation of COVID-19 Therapy) trial and had been randomised to the standard care arm, co-enrolment to the STOP-COVID19 trial was allowed. Co-enrolment into RECOVERY RS (Respiratory support) a non-CTIMP intervention trial was allowed. Co-enrolment to other CTIMPs or non-CTIMP intervention trials was not be allowed.

Evidence for comparator:

Neutrophil serine proteases (NSPs) are involved in the pathogenesis of severe COVID-19 infection and are increased in severe and fatal infection (Seren, 2021). Neutrophil elastase, proteinase-3 and cathepsin-G are activated during neutrophil maturation in the bone marrow through dipeptidyl peptidase 1 (DPP1; also known as cathepsin C), which removes the N-terminal dipeptide sequence of neutrophil serine proteases allowing active enzymes to be packaged into granules prior to release of neutrophils into the circulation.(Palmer et al., 2018) Brensocatib (INS1007, formerly AZD7986) is an orally delivered selective, competitive, and reversible inhibitor of DPP1. Brensocatib has been shown to inhibit neutrophil serine protease activity in blood in both animal models and healthy volunteers.(Palmer et al., 2018) We recently conducted a large phase 2 study of Brensocatib in patients with bronchiectasis designed to test if treatment with Brensocatib could reduce infective exacerbations and reduce neutrophil elastase activity in the lung in bronchiectasis patients. The study met its primary endpoint of time to first exacerbation and key secondary endpoint of the frequency of exacerbations as well as showing marked reductions in neutrophil elastase concentrations in sputum (Chalmers, 2020).

Actual start date of recruitment	11 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	United Kingdom: 404

Worldwide total number of subjects	404
EEA total number of subjects	0

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)	226
From 65 to 84 years	158
85 years and over	20

Subject disposition

Recruitment

Recruitment details:

A total of 406 participants were randomised into the study across the 14 participating UK centres. Participants were recruited between 05th June 2020 and 25th January 2021.

Pre-assignment

Screening details:

Patients were screened for eligibility up to 24 hours prior to randomization and patients meeting the eligibility criteria were randomized within 96 hours of admission to hospital for COVID-19. 406 participants were randomised. There were two post-randomisation exclusions due to ineligibility in the Brensocatib arm.

Period 1

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

Blinding implementation details:

Double-blind, placebo-controlled. Participants were allocated via the randomisation system to receive either active treatment or matching placebo. The active treatment/placebo were packaged and labelled so as to not identify the contents. Trial staff and participants were blind to the allocation received. The final unblinding of the treatment allocation occurred after the creation of a final locked database.

Arms

Are arms mutually exclusive?	Yes
Arm title	Brensocatib

Arm description:

Brensocatib 25mg once daily for 28 days

Arm type	Experimental
Investigational medicinal product name	INS1007
Investigational medicinal product code	
Other name	Brensocatib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Brensocatib is an oral tablet with a strength dose of 25mg, administered once a day.

Arm title	Placebo

Arm description:

Oral placebo tablet

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo tablet contains microcrystalline cellulose and sodium fumarate and is coated. Dosage is 25mg once daily

Number of subjects in period 1	Brensocatib	Placebo
Started	190	214
Completed	187	211
Not completed	3	3
Lost to follow-up	3	3

Baseline characteristics

Reporting groups	
Reporting group title	Brensocatib
Reporting group description:	
Brensocatib 25mg once daily for 28 days	
Reporting group title	Placebo
Reporting group description:	
Oral placebo tablet	

Reporting group values	Brensocatib	Placebo	Total
Number of subjects	190	214	404
Age categorical			
Age (years)			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	104	122	226
From 65-84 years	80	78	158
85 years and over	6	14	20
Age continuous			
Age, years (standard deviation)			
Units: years			
arithmetic mean	62.3	62.0	
standard deviation	± 12.5	± 14.9	-
Gender categorical			
Sex: male, female			
Units: Subjects			
Female	65	87	152
Male	125	127	252
Ethnicity			
Ethnicity			
Units: Subjects			
White British	167	189	356
Irish	2	1	3
Any other White background	6	5	11
White and Black Caribbean	0	1	1
White and Black African	0	1	1
Any other Mixed/Multiple ethnic background	0	1	1
Indian	1	5	6
Pakistan	4	3	7
Bangladeshi	0	1	1
Any other Asian background	4	2	6

African	1	0	1
Any other Black/African/Caribbean background	0	1	1
Arab	1	1	2
Any other ethnic group	2	3	5
Unknown	2	0	2
Smoking Status			
Smoking Status at enrolment			
Units: Subjects			
Current smoker	9	12	21
Never smoked	93	98	191
Former smoker	67	72	139
Unknown	21	32	53
Clinical status			
Clinical status at randomisation			
Units: Subjects			
Hospitalized, not requiring supplemental oxygen	42	50	92
Hospitalized, requiring supplemental oxygen	128	140	268
Hospitalized, on non-invasive ventilation or high	20	24	44
SARS-CoV-2 PCR status			
SARS-CoV-2 PCR status			
Units: Subjects			
Confirmed positive SARS CoV-2 PCR test	186	204	390
Clinically suspected without confirmed SARS-CoV-2	4	10	14
Duration of symptoms			
Median duration of symptoms (25th, 75th centile)			
Units: days			
median	9	8	
inter-quartile range (Q1-Q3)	6 to 12	6 to 11	-

End points

End points reporting groups

Reporting group title	Brensocatib
Reporting group description: Brensocatib 25mg once daily for 28 days	
Reporting group title	Placebo
Reporting group description: Oral placebo tablet	

Primary: 1. Comparison of participant clinical status between treatment arms

End point title	1. Comparison of participant clinical status between treatment arms

End point description:

To determine the participant clinical status on a 7-point ordinal scale:
1. Not hospitalised, no limitations on activities
2. Not hospitalised, limitation on activities;
3. Hospitalised, not requiring supplemental oxygen;
4. Hospitalised, requiring supplemental oxygen;
5. Hospitalised, on non-invasive ventilation or high flow oxygen devices;
6. Hospitalised, on invasive mechanical ventilation or Extracorporeal membrane oxygenation (ECMO)
7. Death.

End point type	Primary

End point timeframe:

Up to 29 days

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	214		
Units: Participants				
Not hospitalised, no limitations on activities	28	40		
Not hospitalised, limitation on activities	112	129		
Hospitalised, not requiring supplemental oxygen	7	11		
Hospitalised, requiring supplemental oxygen	6	1		
Hospitalised, on non-invasive ventilation or high	0	1		
Hospitalised, on invasive mechanical ventilation o	5	6		
Death	29	23		

Statistical analyses

Statistical analysis title	Ordinal logistic regression- primary outcome

Statistical analysis description:

Ordinal logistic regression- primary outcome

Comparison groups	Brensocatib v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	0.92

Secondary: 2. Time to an Improvement of One Category From Admission Using 7-point Ordinal Scale

End point title	2. Time to an Improvement of One Category From Admission Using 7-point Ordinal Scale

End point description:

Evaluation of the clinical efficacy of Brensocatib relative to standard care: 7-point ordinal scale.

End point type	Secondary

End point timeframe:

Up to 29 days

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	214		
Units: Participants	159	186		

Statistical analyses

Statistical analysis title	Regression, cox - secondary outcome

Statistical analysis description:

Baseline CSTAT compared to follow-up CSTAT. Days to improvement derived as
1.days from randomization to first follow-up day where CSTAT improved
2.those who died before improvement were censored at date of death
3.those who withdrew or were loss to follow-up before improvement, if their day 29 status was unknown, they were censored at the date of loss to follow-up/withdrawal
4.other participants were censored at day 29 from randomisation in study time if there were no improvement

Comparison groups	Placebo v Brensocatib

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.058 [1]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1

Notes:

[1] - Adjusted hazard ratio

Secondary: 3. Participant Clinical Status on 7-point Ordinal Scale

End point title	3. Participant Clinical Status on 7-point Ordinal Scale

End point description:

Evaluation of the clinical efficacy of Brensocatib relative to standard care: 7-point ordinal scale

End point type	Secondary

End point timeframe:

Up to 29 days

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	214		
Units: Participants				
Not hospitalised, no limitations on activities	22	26		
Not hospitalised, limitations on activities	103	124		
Hospitalised, not requiring supplemental oxygen	12	19		
Hospitalised, requiring supplemental oxygen	16	13		
Hospitalised, on non-invasive ventilation or high	3	5		
Hospitalised, on invasive mechanical ventilation o	9	6		
Death	20	18		
Missing	5	3		

Statistical analyses

No statistical analyses for this end point

Secondary: 4. Mean Change in the 7-point Ordinal Scale

End point title	4. Mean Change in the 7-point Ordinal Scale

End point description:

Evaluation of the clinical efficacy of Brensocatib relative to standard care: 7-point ordinal scale.

End point type	Secondary

End point timeframe:

Baseline to days 3, 5, 8, 11, 15 and 29

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	187	211		
Units: Units on WHO Scale				
arithmetic mean (standard deviation)	1.0 (± 2.0)	1.3 (± 2.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: 5. Time to Discharge or to a National Early Warning Score (NEWS) of ≤ 2 and Maintained for 24 Hours, Whichever Occurs First

End point title	5. Time to Discharge or to a National Early Warning Score (NEWS) of ≤ 2 and Maintained for 24 Hours, Whichever Occurs First

End point description:

Evaluation of the clinical efficacy of Brensocatib relative to standard care: National Early Warning Score

End point type	Secondary

End point timeframe:

Up to 29 days

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	195		
Units: Participants	172	195		

Statistical analyses

Statistical analysis title	Hazard ratio -secondary outcome

Statistical analysis description:

Time to discharge or NEWS of ≤ 2 was calculated as days from randomization to date of discharged or NEWS of ≤ 2, whichever occurs first. Some patients had multiple admission during the study period and the first date of discharged was used for this analysis.

Comparison groups	Brensocatib v Placebo

Number of subjects included in analysis	385
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.75
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.13

Notes:

[2] - Adjusted hazard ratio

Secondary: 6. Change From Baseline of National Early Warning Score (NEWS)

End point title	6. Change From Baseline of National Early Warning Score (NEWS)

End point description:

Evaluation of the clinical efficacy of Brensocatib relative to standard care: National Early Warning Score.Minimum value 0, maximum value 20. Higher scores mean worse outcome.

End point type	Secondary

End point timeframe:

Days 8, 15 and 29

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	214		
Units: Participants				
-11	1	0		
-9	2	0		
-8	0	1		
-7	1	0		
-6	0	2		
-5	1	0		
-4	1	3		
-3	4	1		
-2	1	1		
-1	3	3		
0.0	15	24		
1.0	22	24		
2.0	36	34		
3.0	28	36		
4.0	21	28		
5.0	10	14		
6.0	11	6		
7.0	3	4		
8.0	1	4		

9.0	0	2		
10.0	0	1		
Missing	29	26		

Statistical analyses

No statistical analyses for this end point

Secondary: 7. Number of Oxygen Therapy Free Days

End point title	7. Number of Oxygen Therapy Free Days
End point description:	
Evaluation of the clinical efficacy of Brensocatib relative to standard care: oxygenation	
End point type	Secondary
End point timeframe:	
Up to day 29	

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	214		
Units: days				
median (inter-quartile range (Q1-Q3))	24 (11 to 27)	24.5 (17 to 27)		

Statistical analyses

Statistical analysis title	Negative binomial regression
Statistical analysis description:	
Number of days free from oxygen support (CSTAT = 1, 2, 3) were compared between the treatment arms using negative binomial regression, results are expressed as incidence rate ratios (with 95% confidence intervals).	
Comparison groups	Brensocatib v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.027
Method	Rate ratio
Parameter estimate	Rate ratio
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	0.99

Secondary: 8. Incidence and Duration of New Oxygen Therapy Use During the Trial	
End point title	8. Incidence and Duration of New Oxygen Therapy Use During the Trial
End point description: Evaluation of the clinical efficacy of Brensocatib relative to standard care: oxygenation	
End point type	Secondary
End point timeframe: Up to day 29	

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	214		
Units: Days				
median (inter-quartile range (Q1-Q3))	0 (0 to 2)	0 (0 to 1)		

Statistical analyses

Statistical analysis title	Incidence and Duration of New Oxygen Therapy Use
Statistical analysis description: Evaluation of the clinical efficacy of Brensocatib relative to standard care: oxygenation	
Comparison groups	Brensocatib v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.058
Method	Rate ratio
Parameter estimate	Rate ratio
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.74

Secondary: 9. Number of Mechanical Ventilator Free Days	
End point title	9. Number of Mechanical Ventilator Free Days
End point description: Evaluation of the clinical efficacy of Brensocatib relative to standard care: Mechanical ventilation	
End point type	Secondary

End point timeframe:

Up to day 29

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	214		
Units: Days				
median (inter-quartile range (Q1-Q3))	28 (22 to 28)	28 (26 to 28)		

Statistical analyses

Statistical analysis title	Negative binomial regression

Statistical analysis description:

Number of days free from ventilator (CSTAT = 1, 2, 3, 4) were compared between the treatment arms using negative binomial regression results are expressed as incidence rate ratios (with 95% confidence intervals).

Comparison groups	Brensocatib v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.021
Method	Rate ratio
Parameter estimate	Rate ratio
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	0.99

Secondary: 10. Incidence and Duration of New Mechanical Ventilation Use During the Trial

End point title	10. Incidence and Duration of New Mechanical Ventilation Use During the Trial

End point description:

Evaluation of the clinical efficacy of Brensocatib relative to standard care: Mechanical ventilation

End point type	Secondary

End point timeframe:

Up to day 29

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	214		
Units: Days				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	0 (0 to 0)		

Statistical analyses

Statistical analysis title	Negative binomial regression
Comparison groups	Brensocatib v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.018
Method	Rate ratio
Parameter estimate	Rate ratio
Point estimate	1.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.09
upper limit	2.58

Secondary: 11. Duration of Hospitalisation

End point title	11. Duration of Hospitalisation

End point description:

n:
Evaluation of the clinical efficacy of Brensocatib relative to standard care: hospitalisation

End point type	Secondary

End point timeframe:

Duration between date of admission and discharge assessed up to 29 days.

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	214		
Units: Days				
arithmetic mean (standard deviation)	8.4 (± 8.3)	8.2 (± 8.3)		

Statistical analyses

Statistical analysis title	Negative binomial regression

Statistical analysis description:

Duration of hospitalisation was calculated from date of randomisation to date of discharged. If a participant had more than one admission during the study period, the total duration of hospitalisation was calculated. Participants who died in the hospital and participants who withdrew and date of discharged were not recorded were excluded in the analysis.

Comparison groups	Brensocatib v Placebo
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.602
Method	Rate ratio
Parameter estimate	Rate ratio
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.15

Secondary: 12. 28-day Mortality

End point title	12. 28-day Mortality

End point description:

Evaluation of the clinical efficacy of Brensocatib relative to standard care: mortality

End point type	Secondary

End point timeframe:

Date of death up to 20 days

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	214		
Units: Participants	29	23		

Statistical analyses

Statistical analysis title	Regression, cox

Statistical analysis description:

Survival analysis was used to compare 28-day mortality between the treatment arms. Participants who did not die will be censored on the last study day. Those who withdrew or were loss to follow-up and their day 29 status was unknown were censored at the date of loss to follow-up/withdrawal. Other participants were censored 28 days from randomisation in study time.

Comparison groups	Brensocatib v Placebo

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	1.88

Secondary: 13. Cumulative Incidence of Serious Adverse Events (SAEs)

End point title	13. Cumulative Incidence of Serious Adverse Events (SAEs)
End point description:	
Evaluation of the safety of the intervention through 29 days of follow-up as compared to the control arm	
End point type	Secondary
End point timeframe:	
1-29 days	

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	214		
Units: Participants	40	35		

Statistical analyses

No statistical analyses for this end point

Secondary: 14. Discontinuation or Temporary Suspension of Treatment

End point title	14. Discontinuation or Temporary Suspension of Treatment
End point description:	
Evaluation of the safety of the intervention through 28 days of follow-up as compared to the control arm	
End point type	Secondary
End point timeframe:	
1-29 days	

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	214		
Units: Participants	13	12		

Statistical analyses

No statistical analyses for this end point

Secondary: 15. Changes in White 15. Cell Count (x10^9/L) Over Time (Hospitalised Participants Only)

End point title	15. Changes in White 15. Cell Count (x10^9/L) Over Time (Hospitalised Participants Only)

End point description:

Evaluation of the safety of the intervention through 28 days of follow-up as compared to the control arm

End point type	Secondary

End point timeframe:

Days 0/1, 3, 5, 8, 11, 15, 29

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	18		
Units: cells/millilitre				
arithmetic mean (standard deviation)	8.9 (± 4.7)	8.5 (± 3.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: 16. Changes in Haemoglobin (g/L) Over Time (Hospitalised Participants Only)

End point title	16. Changes in Haemoglobin (g/L) Over Time (Hospitalised Participants Only)

End point description:

Evaluation of the safety of the intervention through 28 days of follow-up as compared to the control arm

End point type	Secondary

End point timeframe:

Days 0/1, 3, 5, 8, 11, 15, 29

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	18		
Units: g/L				
arithmetic mean (standard deviation)	195.4 (± 264)	105.5 (± 21.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: 17. Changes in Platelets (x10^9/L) Over Time (Hospitalised Participants Only)

End point title	17. Changes in Platelets (x10^9/L) Over Time (Hospitalised Participants Only)

End point description:

Evaluation of the safety of the intervention through 28 days of follow-up as compared to the control arm

End point type	Secondary

End point timeframe:

Days 0/1, 3, 5, 8, 11, 15, 29

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	18		
Units: x10(7) cell/L				
arithmetic mean (standard deviation)	270 (± 94.3)	269 (± 117)		

Statistical analyses

No statistical analyses for this end point

Secondary: 18. Changes in Creatinine (Umol/L) Over Time (Hospitalised Participants Only)

End point title	18. Changes in Creatinine (Umol/L) Over Time (Hospitalised Participants Only)

End point description:

Evaluation of the safety of the intervention through 28 days of follow-up as compared to the control arm

End point type	Secondary

End point timeframe:

Days 0/1, 3, 5, 8, 11, 15, 29

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	19		
Units: umol/L				
arithmetic mean (standard deviation)	84.9 (± 39)	84.1 (± 52)		

Statistical analyses

No statistical analyses for this end point

Secondary: 19. Changes in Total Bilirubin (Umol/L) Over Time (Hospitalised Participants Only)

End point title	19. Changes in Total Bilirubin (Umol/L) Over Time (Hospitalised Participants Only)

End point description:

Evaluation of the safety of the intervention through 28 days of follow-up as compared to the control arm

End point type	Secondary

End point timeframe:

Days 0/1, 3, 5, 8, 11, 15, 29

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	16		
Units: umol/L				
arithmetic mean (standard deviation)	8.4 (± 3.9)	9.3 (± 9.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: 20. Changes in Alanine Aminotransferase (U/L) Over Time (Hospitalised Participants Only)

End point title	20. Changes in Alanine Aminotransferase (U/L) Over Time (Hospitalised Participants Only)

End point description:

Evaluation of the safety of the intervention through 28 days of follow-up as compared to the control arm

End point type	Secondary

End point timeframe:

Days 0/1, 3, 5, 8, 11, 15, 29

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	15		
Units: U/L				
arithmetic mean (standard deviation)	62.8 (± 43.2)	52.3 (± 92.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: 21. Changes in Aspartate Aminotransferase U/L Over Time (Hospitalised Participants Only)

End point title	21. Changes in Aspartate Aminotransferase U/L Over Time (Hospitalised Participants Only)

End point description:

Evaluation of the safety of the intervention through 28 days of follow-up as compared to the control arm

End point type	Secondary

End point timeframe:

Days 0/1, 3, 5, 8, 11, 15, 29

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	4		
Units: U/L				
arithmetic mean (standard deviation)	22 (± 11.4)	28.8 (± 14.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: 22. Adverse Events of Special Interest- Hyperkeratosis, Infections and Dental Complications

End point title	22. Adverse Events of Special Interest- Hyperkeratosis, Infections and Dental Complications

End point description:

Evaluation of the safety of the intervention through 29 days of follow-up as compared to the control arm

End point type	Secondary

End point timeframe:

1-29 days

End point values	Brensocatib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	214		
Units: Participants				
Hyperkeratosis	0	0		
Dental complications	0	1		
Secondary infections	6	7		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

29 days

Adverse event reporting additional description:

Adverse events were reported by the participant, site principal investigators or delegated staff responsible for detecting documenting and recording events that met the definition of an adverse event. Participants discharged from hospital before the end of the trial were given a diary to record adverse events up to day 28. Site principal investigat

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.0

Reporting groups

Reporting group title	Brensocatib

Reporting group description:

Brensocatib 25mg once daily for 28 days

Reporting group title	Placebo

Reporting group description:

Oral placebo tablet

Serious adverse events	Brensocatib	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	40 / 190 (21.05%)	35 / 214 (16.36%)	
number of deaths (all causes)	29	23	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to liver			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
Cerebellar infarction			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary embolism			

subjects affected / exposed	3 / 190 (1.58%)	2 / 214 (0.93%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Syncope			
subjects affected / exposed	0 / 190 (0.00%)	2 / 214 (0.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration			

site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic cyst			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hypoxia			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			

subjects affected / exposed	1 / 190 (0.53%)	1 / 214 (0.47%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax spontaneous			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug eruption			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 190 (0.00%)	2 / 214 (0.93%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	14 / 190 (7.37%)	17 / 214 (7.94%)	
occurrences causally related to treatment / all	0 / 14	0 / 17	
deaths causally related to treatment / all	0 / 13	0 / 17	
Lower respiratory tract infection			

subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Diverticulitis intestinal haemorrhagic			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arthritis bacterial			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 190 (0.53%)	1 / 214 (0.47%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
COVID-19 pneumonia			
subjects affected / exposed	9 / 190 (4.74%)	3 / 214 (1.40%)	
occurrences causally related to treatment / all	0 / 9	0 / 3	
deaths causally related to treatment / all	0 / 9	0 / 2	
Urosepsis			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Brensocatib	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	86 / 190 (45.26%)	99 / 214 (46.26%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Chronic lymphocytic leukaemia			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Peripheral ischaemia			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 190 (0.00%)	3 / 214 (1.40%)	
occurrences (all)	0	3	
Cold sweat			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Chest discomfort			
subjects affected / exposed	2 / 190 (1.05%)	0 / 214 (0.00%)	
occurrences (all)	2	0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Swelling face			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	1 / 190 (0.53%)	1 / 214 (0.47%)	
occurrences (all)	1	1	
Extravasation			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	

Feeling hot			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Peripheral swelling			
subjects affected / exposed	2 / 190 (1.05%)	0 / 214 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 190 (0.53%)	4 / 214 (1.87%)	
occurrences (all)	1	4	
Hiccups			
subjects affected / exposed	2 / 190 (1.05%)	1 / 214 (0.47%)	
occurrences (all)	2	1	
Pneumothorax			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Epistaxis			
subjects affected / exposed	3 / 190 (1.58%)	0 / 214 (0.00%)	
occurrences (all)	3	0	
Rhinorrhoea			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Pulmonary embolism			
subjects affected / exposed	1 / 190 (0.53%)	3 / 214 (1.40%)	
occurrences (all)	1	3	
Psychiatric disorders			
Hallucination, visual			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	0 / 190 (0.00%)	2 / 214 (0.93%)	
occurrences (all)	0	2	
Delirium			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Nightmare			

subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Suicidal ideation			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Investigations			
Electrocardiogram abnormal			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Alanine aminotransferase increased			
subjects affected / exposed	2 / 190 (1.05%)	2 / 214 (0.93%)	
occurrences (all)	2	4	
Liver function test abnormal			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Glycosylated haemoglobin increased			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Blood glucose abnormal			
subjects affected / exposed	1 / 190 (0.53%)	1 / 214 (0.47%)	
occurrences (all)	1	1	
Blood glucose increased			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Transaminases increased			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 190 (0.53%)	1 / 214 (0.47%)	
occurrences (all)	1	1	
Palpitations			

subjects affected / exposed	2 / 190 (1.05%)	0 / 214 (0.00%)	
occurrences (all)	2	0	
Atrial fibrillation			
subjects affected / exposed	0 / 190 (0.00%)	2 / 214 (0.93%)	
occurrences (all)	0	2	
Tachyarrhythmia			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Acute coronary syndrome			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Sinus bradycardia			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 190 (1.58%)	5 / 214 (2.34%)	
occurrences (all)	3	5	
Headache			
subjects affected / exposed	2 / 190 (1.05%)	2 / 214 (0.93%)	
occurrences (all)	2	2	
Memory impairment			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Syncope			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Hypoaesthesia			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Dysarthria			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	

Paraesthesia			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Eye disorders			
Vision blurred			
subjects affected / exposed	2 / 190 (1.05%)	1 / 214 (0.47%)	
occurrences (all)	2	1	
Eye pruritus			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 190 (0.00%)	4 / 214 (1.87%)	
occurrences (all)	0	4	
Dyspepsia			
subjects affected / exposed	3 / 190 (1.58%)	4 / 214 (1.87%)	
occurrences (all)	3	4	
Diarrhoea			
subjects affected / exposed	0 / 190 (0.00%)	2 / 214 (0.93%)	
occurrences (all)	0	2	
Dry mouth			
subjects affected / exposed	1 / 190 (0.53%)	2 / 214 (0.93%)	
occurrences (all)	1	2	
Nausea			
subjects affected / exposed	3 / 190 (1.58%)	3 / 214 (1.40%)	
occurrences (all)	3	3	
Vomiting			
subjects affected / exposed	1 / 190 (0.53%)	4 / 214 (1.87%)	
occurrences (all)	1	4	
Constipation			
subjects affected / exposed	1 / 190 (0.53%)	4 / 214 (1.87%)	
occurrences (all)	1	4	
Flatulence			

subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Rectal haemorrhage			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Gastritis erosive			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 190 (0.53%)	1 / 214 (0.47%)	
occurrences (all)	1	1	
Oral mucosal eruption			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Gingival bleeding			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Glossodynia			
subjects affected / exposed	1 / 190 (0.53%)	1 / 214 (0.47%)	
occurrences (all)	1	1	
Tongue blistering			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Oral mucosal blistering			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Swollen tongue			
subjects affected / exposed	1 / 190 (0.53%)	1 / 214 (0.47%)	
occurrences (all)	1	1	
Oral pain			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Hypoaesthesia oral			

subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Gingival pain			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Lip pain			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Lip swelling			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Paraesthesia oral			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Tongue erythema			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Tongue discolouration			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Rash macular			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Pruritus	Additional description: Pruritis soles of feet		
subjects affected / exposed	1 / 190 (0.53%)	1 / 214 (0.47%)	
occurrences (all)	1	1	
Rash pustular	Additional description: Pustules on palms of hands		

subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	5 / 190 (2.63%)	7 / 214 (3.27%)	
occurrences (all)	5	7	
Eczema			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Mouth ulceration			
subjects affected / exposed	2 / 190 (1.05%)	1 / 214 (0.47%)	
occurrences (all)	2	1	
Night sweats			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Subcutaneous emphysema	Additional description: Widespread surgical emphysema in arms and neck, shown in CXR.		
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Dry skin			
subjects affected / exposed	2 / 190 (1.05%)	1 / 214 (0.47%)	
occurrences (all)	2	1	
Rash pruritic			
subjects affected / exposed	1 / 190 (0.53%)	1 / 214 (0.47%)	
occurrences (all)	1	1	
Acne			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Hyperhidrosis			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 190 (1.05%)	0 / 214 (0.00%)	
occurrences (all)	2	0	
Cholelithiasis			

subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Pollakiuria			
subjects affected / exposed	0 / 190 (0.00%)	2 / 214 (0.93%)	
occurrences (all)	0	2	
Dysuria			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 190 (1.05%)	4 / 214 (1.87%)	
occurrences (all)	2	4	
Plantar fasciitis			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Neck pain			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Pain in jaw			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Infections and infestations			
Clostridium difficile colitis			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection			

subjects affected / exposed	2 / 190 (1.05%)	2 / 214 (0.93%)	
occurrences (all)	2	2	
Oral candidiasis			
subjects affected / exposed	0 / 190 (0.00%)	3 / 214 (1.40%)	
occurrences (all)	0	3	
Candida infection			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 190 (0.00%)	2 / 214 (0.93%)	
occurrences (all)	0	2	
Urinary tract infection			
subjects affected / exposed	1 / 190 (0.53%)	1 / 214 (0.47%)	
occurrences (all)	1	1	
Pharyngitis			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Serratia infection			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	4 / 190 (2.11%)	2 / 214 (0.93%)	
occurrences (all)	4	2	
Gout			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Steroid diabetes	Additional description: Undiagnosed Diabetes (new presentation) - steroid induced		

subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Hypomagnesaemia			
subjects affected / exposed	0 / 190 (0.00%)	1 / 214 (0.47%)	
occurrences (all)	0	1	
Hypokalaemia			
subjects affected / exposed	1 / 190 (0.53%)	0 / 214 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported