Clinical trial results:
A Phase 1/2a Trial of the Inhaled Administration of the SARS-CoV-2-Neutralizing Monoclonal Antibody DZIF-10c in SARS-CoV-2-Infected and -Uninfected Individuals

Summary

EudraCT number	2020-004448-27
Trial protocol	DE
Global end of trial date	23 September 2021

Results information

Result version number	v1 (current)
This version publication date	05 November 2022
First version publication date	05 November 2022

Trial information

Trial identification

Sponsor protocol code	Uni-Koeln-4370

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04631705
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Cologne
Sponsor organisation address	Albertus-Magnus-Platz, Cologne, Germany,
Public contact	Florian Klein, Institute of Virology, 49 22147885800,
Scientific contact	Florian Klein, Institute of Virology, 49 22147885800,

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	19 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 September 2021
Global end of trial reached?	Yes
Global end of trial date	23 September 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the safety and tolerability of a single inhaled application of DZIF-10c in SARS-CoV-2-uninfected and SARS-CoV-2-infected individuals.
- To evaluate the safety and tolerability of a single combined inhaled and intravenous application of DZIF-10c in SARS-CoV-2-infected individuals.

Protection of trial subjects:

- Frequent safety labs
- Safety Monitoring Committee
- Hospitalization and monitoring for open-label dose escalation phase

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 December 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	Germany: 45
Worldwide total number of subjects	45
EEA total number of subjects	45

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)	45
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Groups 1A-1C: Generally healthy volunteers negative for SARS-CoV-2 RNA in swab and negative for SARS-CoV-2 antibodies by serology.
Groups 2A-2D: SARS-CoV-2-infected volunteers positive for SARS-CoV-2 RNA in swab within 3 days of study drug administration, and within 7 days of symptom onset and/or negative SARS-CoV-2 antibody serology

Period 1

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

Blinding implementation details:

- Groups 1A-1C were open label and sequentially enrolled
- Groups 2A-2C were open label and sequentially enrolled
- Group 2D was randomised and double blind

Arms

Are arms mutually exclusive?	Yes
Arm title	1A: Healthy, 50 mg inh.

Arm description: -

Arm type	Experimental
Investigational medicinal product name	DZIF-10c
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

DZIF-10c for inhalation in nebuliser solution; see arm title for dosage

Arm title	1B: Healthy, 100 mg inh.

Arm description: -

Arm type	Experimental
Investigational medicinal product name	DZIF-10c
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

DZIF-10c for inhalation in nebuliser solution; see arm title for dosage

Arm title	1C: Healthy, 250 mg inh.

Arm description: -

Arm type	Experimental

Investigational medicinal product name	DZIF-10c
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

DZIF-10c for inhalation in nebuliser solution; see arm title for dosage

Arm title	2A: Infected, 50 mg inh.

Arm description: -

Arm type	Experimental
Investigational medicinal product name	DZIF-10c
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

DZIF-10c for inhalation in nebuliser solution; see arm title for dosage

Arm title	2B: Infected, 100 mg inh.

Arm description: -

Arm type	Experimental
Investigational medicinal product name	DZIF-10c
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

DZIF-10c for inhalation in nebuliser solution; see arm title for dosage

Arm title	2C: Infected, 250 mg inh.

Arm description: -

Arm type	Experimental
Investigational medicinal product name	DZIF-10c
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

DZIF-10c for inhalation in nebuliser solution; see arm title for dosage

Arm title	2D: Infected, placebo inh., placebo i.v.

Arm description: -

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

Dosage and administration details:

Sterile normal saline (0.9% NaCl) used as placebo for infusion

Investigational medicinal product name	Diluent solution for DZIF-10c
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

Diluent for DZIF-10c used as placebo for nebuliser solution

Arm title	2D: Infected, 250 mg inh., placebo i.v.

Arm description: -

Arm type	Experimental
Investigational medicinal product name	DZIF-10c (inhalation)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

DZIF-10c for inhalation in nebuliser solution; see arm title for dosage

Investigational medicinal product name	Normal saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Sterile normal saline (0.9% NaCl) used as placebo for infusion

Arm title	2D: Infected, 250 mg inh., 40 mg/kg i.v.

Arm description: -

Arm type	Experimental
Investigational medicinal product name	DZIF-10c (inhalation)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

DZIF-10c for inhalation in nebuliser solution; see arm title for dosage

Investigational medicinal product name	DZIF-10c (infusion)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

DZIF-10c for intravenous infusion; see arm title for dosage

Number of subjects in period 1	1A: Healthy, 50 mg inh.	1B: Healthy, 100 mg inh.	1C: Healthy, 250 mg inh.
Started	3	3	3
Completed	3	3	3
Not completed	0	0	0
Consent withdrawn by subject	-	-	-

Number of subjects in period 1	2A: Infected, 50 mg inh.	2B: Infected, 100 mg inh.	2C: Infected, 250 mg inh.
Started	3	3	3
Completed	3	3	3
Not completed	0	0	0
Consent withdrawn by subject	-	-	-

Number of subjects in period 1	2D: Infected, placebo inh., placebo i.v.	2D: Infected, 250 mg inh., placebo i.v.	2D: Infected, 250 mg inh., 40 mg/kg i.v.
Started	10	8	9
Completed	9	8	9
Not completed	1	0	0
Consent withdrawn by subject	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	1A: Healthy, 50 mg inh.
Reporting group description: -	
Reporting group title	1B: Healthy, 100 mg inh.
Reporting group description: -	
Reporting group title	1C: Healthy, 250 mg inh.
Reporting group description: -	
Reporting group title	2A: Infected, 50 mg inh.
Reporting group description: -	
Reporting group title	2B: Infected, 100 mg inh.
Reporting group description: -	
Reporting group title	2C: Infected, 250 mg inh.
Reporting group description: -	
Reporting group title	2D: Infected, placebo inh., placebo i.v.
Reporting group description: -	
Reporting group title	2D: Infected, 250 mg inh., placebo i.v.
Reporting group description: -	
Reporting group title	2D: Infected, 250 mg inh., 40 mg/kg i.v.
Reporting group description: -	

Reporting group values	1A: Healthy, 50 mg inh.	1B: Healthy, 100 mg inh.	1C: Healthy, 250 mg inh.
Number of subjects	3	3	3
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
median	43	33	27
inter-quartile range (Q1-Q3)	29 to 44	32 to 44	20 to 29
Gender categorical Units: Subjects			
Female	0	1	2
Male	3	2	1

Reporting group values	2A: Infected, 50 mg inh.	2B: Infected, 100 mg inh.	2C: Infected, 250 mg inh.
Number of subjects	3	3	3

Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
median	35	39	41
inter-quartile range (Q1-Q3)	30 to 62	25 to 42	32 to 46
Gender categorical Units: Subjects			
Female	1	2	1
Male	2	1	2

Reporting group values	2D: Infected, placebo inh., placebo i.v.	2D: Infected, 250 mg inh., placebo i.v.	2D: Infected, 250 mg inh., 40 mg/kg i.v.
Number of subjects	10	8	9
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
median	34	32	28
inter-quartile range (Q1-Q3)	28 to 36	29 to 46	27 to 38
Gender categorical Units: Subjects			
Female	2	2	4
Male	8	6	5

Reporting group values	Total		
Number of subjects	45		
Age categorical Units: Subjects			
In utero	0		

Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
median			
inter-quartile range (Q1-Q3)	-		
Gender categorical			
Units: Subjects			
Female	15		
Male	30		

End points

End points reporting groups	
Reporting group title	1A: Healthy, 50 mg inh.
Reporting group description: -	
Reporting group title	1B: Healthy, 100 mg inh.
Reporting group description: -	
Reporting group title	1C: Healthy, 250 mg inh.
Reporting group description: -	
Reporting group title	2A: Infected, 50 mg inh.
Reporting group description: -	
Reporting group title	2B: Infected, 100 mg inh.
Reporting group description: -	
Reporting group title	2C: Infected, 250 mg inh.
Reporting group description: -	
Reporting group title	2D: Infected, placebo inh., placebo i.v.
Reporting group description: -	
Reporting group title	2D: Infected, 250 mg inh., placebo i.v.
Reporting group description: -	
Reporting group title	2D: Infected, 250 mg inh., 40 mg/kg i.v.
Reporting group description: -	

Primary: Proportion of patients with any AE within 7 d of study drug administration	
End point title	Proportion of patients with any AE within 7 d of study drug administration[1]
End point description:	
End point type	Primary
End point timeframe:	
Over first 7 days after study drug administration	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive end point.

End point values	1A: Healthy, 50 mg inh.	1B: Healthy, 100 mg inh.	1C: Healthy, 250 mg inh.	2A: Infected, 50 mg inh.
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: % individuals				
number (not applicable)	66.7	33.3	33.3	100

End point values	2B: Infected, 100 mg inh.	2C: Infected, 250 mg inh.	2D: Infected, placebo inh., placebo i.v.	2D: Infected, 250 mg inh., placebo i.v.
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	10	8

Units: % individuals				
number (not applicable)	33.3	0	60.0	37.5

End point values	2D: Infected, 250 mg inh., 40 mg/kg i.v.			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: % individuals				
number (not applicable)	33			

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the Curve (AUC) for DZIF-10c serum levels from day 1 to day 29

End point title	Area under the Curve (AUC) for DZIF-10c serum levels from day 1 to day 29[2]

End point description:

Only for individuals with detectable antibody levels and with n of at least 3 individuals with values enabling analysis

End point type	Secondary

End point timeframe:

Day 1 to Day 29

Notes:

[2] - 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: Descriptive end point.

End point values	1C: Healthy, 250 mg inh.	2D: Infected, 250 mg inh., placebo i.v.	2D: Infected, 250 mg inh., 40 mg/kg i.v.	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	4	9	
Units: µg*h/ml				
geometric mean (geometric coefficient of variation)	284 (± 18.2)	225 (± 39.2)	174000 (± 14.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Individuals developing anti-drug antibodies

End point title	Individuals developing anti-drug antibodies[3]

End point description:

End point type	Secondary

End point timeframe:

Study period

Notes:

[3] - 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: Descriptive end point.

End point values	1A: Healthy, 50 mg inh.	1B: Healthy, 100 mg inh.	1C: Healthy, 250 mg inh.	2A: Infected, 50 mg inh.
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: individuals	0	0	0	0

End point values	2B: Infected, 100 mg inh.	2C: Infected, 250 mg inh.	2D: Infected, 250 mg inh., placebo i.v.	2D: Infected, 250 mg inh., 40 mg/kg i.v.
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	8	9
Units: individuals	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: SARS-CoV-2 viral load absolute change from baseline (NP swabs, E gene, time-weighted average change)

End point title	SARS-CoV-2 viral load absolute change from baseline (NP swabs, E gene, time-weighted average change)[4]

End point description:

Time-weighted average change

End point type	Secondary

End point timeframe:

Day 1 to Day 29

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only randomized and controlled phase shown; preplanned as hypothesis-generating analysis.

End point values	2D: Infected, placebo inh., placebo i.v.	2D: Infected, 250 mg inh., placebo i.v.	2D: Infected, 250 mg inh., 40 mg/kg i.v.	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: Adjusted mean AOC				
number (not applicable)				
Over 7 days	-1.932	-2.100	-1.716	
Over 14 days	-2.780	-3.044	-2.786	
Over 28 days	-3.616	-3.652	-3.652	

Statistical analyses

No statistical analyses for this end point

Secondary: SARS-CoV-2 viral load absolute change from baseline (NP swabs, E gene, MMRM)

End point title	SARS-CoV-2 viral load absolute change from baseline (NP swabs, E gene, MMRM)[5]
End point description:	
Mixed model for repeated measures	
End point type	Secondary
End point timeframe:	
Day 1 to Day 29	

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only randomized and controlled phase shown; preplanned as hypothesis-generating analysis.

End point values	2D: Infected, placebo inh., placebo i.v.	2D: Infected, 250 mg inh., placebo i.v.	2D: Infected, 250 mg inh., 40 mg/kg i.v.	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	9	
Units: Adjusted mean				
number (not applicable)				
Over 7 days	-3.4	-3.4	-3.2	
Over 14 days	-4.4	-4.1	-4.4	
Over 28 days	-4.4	-4.3	-4.4	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Treatment-emergent adverse events: All adverse events after drug intake until final study visit	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups	
Reporting group title	1A: Healthy, 50 mg inh.
Reporting group description: -	
Reporting group title	1B: Healthy, 100 mg inh.
Reporting group description: -	
Reporting group title	1C: Healthy, 250 mg inh.
Reporting group description: -	
Reporting group title	2A: Infected, 50 mg inh.
Reporting group description: -	
Reporting group title	2B: Infected, 100 mg inh.
Reporting group description: -	
Reporting group title	2C: Infected, 250 mg inh.
Reporting group description: -	
Reporting group title	2D: Infected, placebo inh., placebo i.v.
Reporting group description: -	
Reporting group title	2D: Infected, 250 mg inh., placebo i.v.
Reporting group description: -	
Reporting group title	2D: Infected, 250 mg inh., 40 mg/kg i.v.
Reporting group description: -	

Serious adverse events	1A: Healthy, 50 mg inh.	1B: Healthy, 100 mg inh.	1C: Healthy, 250 mg inh.
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	2A: Infected, 50 mg inh.	2B: Infected, 100 mg inh.	2C: Infected, 250 mg inh.
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	2D: Infected, placebo inh., placebo i.v.	2D: Infected, 250 mg inh., placebo i.v.	2D: Infected, 250 mg inh., 40 mg/kg i.v.
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

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

Non-serious adverse events	1A: Healthy, 50 mg inh.	1B: Healthy, 100 mg inh.	1C: Healthy, 250 mg inh.
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	2 / 3 (66.67%)
General disorders and administration site conditions			
Inflammation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Dyspnoea			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Aphasia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Ventricular arrhythmia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Sciatica			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Disturbance in attention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Parosmia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Infections and infestations			
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gonococcal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	2A: Infected, 50 mg inh.	2B: Infected, 100 mg inh.	2C: Infected, 250 mg inh.
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	2 / 3 (66.67%)	2 / 3 (66.67%)
General disorders and administration site conditions			
Inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Aphasia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lipase increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Ventricular arrhythmia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Headache			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Disturbance in attention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Parosmia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Leukopenia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue			

disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Sinusitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gonococcal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	2D: Infected, placebo inh., placebo i.v.	2D: Infected, 250 mg inh., placebo i.v.	2D: Infected, 250 mg inh., 40 mg/kg i.v.
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 10 (70.00%)	5 / 8 (62.50%)	4 / 9 (44.44%)
General disorders and administration site conditions			
Inflammation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	2 / 10 (20.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
Pain			
subjects affected / exposed	2 / 10 (20.00%)	0 / 8 (0.00%)	2 / 9 (22.22%)
occurrences (all)	3	0	2
Fatigue			
subjects affected / exposed	0 / 10 (0.00%)	1 / 8 (12.50%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Chest pain			

subjects affected / exposed	0 / 10 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 10 (0.00%)	1 / 8 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Dyspnoea			
subjects affected / exposed	1 / 10 (10.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 10 (20.00%)	1 / 8 (12.50%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
Cough			
subjects affected / exposed	5 / 10 (50.00%)	2 / 8 (25.00%)	1 / 9 (11.11%)
occurrences (all)	6	2	1
Dyspnoea exertional			
subjects affected / exposed	0 / 10 (0.00%)	1 / 8 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
Psychiatric disorders			
Aphasia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Lipase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			

Ventricular arrhythmia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 10 (20.00%)	2 / 8 (25.00%)	3 / 9 (33.33%)
occurrences (all)	3	2	6
Sciatica			
subjects affected / exposed	0 / 10 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	2 / 10 (20.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	1
Disturbance in attention			
subjects affected / exposed	0 / 10 (0.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Parosmia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 8 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 10 (0.00%)	1 / 8 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 10 (0.00%)	1 / 8 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Renal and urinary disorders			

Haematuria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Sinusitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 8 (12.50%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Gonococcal infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	1 / 10 (10.00%)	0 / 8 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 January 2021	- Reduced frequency of post inhalation pulmonary function testing
20 April 2021	- Changes in description of study drug administration procedure

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Limited sample size and early termination of enrolment.

Notes: