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

Summary

EudraCT number	2020-003503-34
Trial protocol	DE
Global end of trial date	11 August 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-4288

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04631666
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	08 August 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 July 2021
Global end of trial reached?	Yes
Global end of trial date	11 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 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: 57
Worldwide total number of subjects	57
EEA total number of subjects	57

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)	57
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Groups 1A, 1B, 1C, 1D: Generally healthy volunteers negative for SARS-CoV-2 RNA in swab and negative for SARS-CoV-2 antibodies by serology.
Groups 2C and 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, 1B, 1C, 1D, and 2C were open label and sequentially enrolled
- Group 2D was randomised and double blind

Arms

Are arms mutually exclusive?	Yes
Arm title	1A: Healthy, 2.5 mg/kg

Arm description:

Open label

Arm type	Experimental
Investigational medicinal product name	DZIF-10c
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

i.v. Infusion - see Arm title for dosage

Arm title	1B: Healthy, 10 mg/kg

Arm description:

Open label

Arm type	Experimental
Investigational medicinal product name	DZIF-10c
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

i.v. Infusion - see Arm title for dosage

Arm title	1C: Healthy, 40 mg/kg

Arm description:

Open label

Arm type	Experimental

Investigational medicinal product name	DZIF-10c
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Infusion
Dosage and administration details: i.v. Infusion - see Arm title for dosage	
Arm title	1D: Healthy, 80 mg/kg
Arm description: Open label	
Arm type	Experimental
Investigational medicinal product name	DZIF-10c
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Infusion
Dosage and administration details: i.v. Infusion - see Arm title for dosage	
Arm title	2C: Infected, 40 mg/kg
Arm description: Open label	
Arm type	Experimental
Investigational medicinal product name	DZIF-10c
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Infusion
Dosage and administration details: i.v. Infusion - see Arm title for dosage	
Arm title	2D: Infected, DZIF-10c, 40 mg/kg
Arm description: Randomised and double blind	
Arm type	Experimental
Investigational medicinal product name	DZIF-10c
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Infusion
Dosage and administration details: i.v. Infusion - see Arm title for dosage	
Arm title	2D: Infected, Placebo i.v.
Arm description: Randomised and double-blind	
Arm type	Placebo
Investigational medicinal product name	Normal saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
Sterile normale saline 0.9% used as placebo

Number of subjects in period 1	1A: Healthy, 2.5 mg/kg	1B: Healthy, 10 mg/kg	1C: Healthy, 40 mg/kg
Started	3	3	3
Completed	3	3	3

Number of subjects in period 1	1D: Healthy, 80 mg/kg	2C: Infected, 40 mg/kg	2D: Infected, DZIF-10c, 40 mg/kg
Started	6	3	26
Completed	6	3	26

Number of subjects in period 1	2D: Infected, Placebo i.v.
Started	13
Completed	13

Baseline characteristics

Reporting groups	
Reporting group title	1A: Healthy, 2.5 mg/kg
Reporting group description:	
Open label	
Reporting group title	1B: Healthy, 10 mg/kg
Reporting group description:	
Open label	
Reporting group title	1C: Healthy, 40 mg/kg
Reporting group description:	
Open label	
Reporting group title	1D: Healthy, 80 mg/kg
Reporting group description:	
Open label	
Reporting group title	2C: Infected, 40 mg/kg
Reporting group description:	
Open label	
Reporting group title	2D: Infected, DZIF-10c, 40 mg/kg
Reporting group description:	
Randomised and double blind	
Reporting group title	2D: Infected, Placebo i.v.
Reporting group description:	
Randomised and double-blind	

Reporting group values	1A: Healthy, 2.5 mg/kg	1B: Healthy, 10 mg/kg	1C: Healthy, 40 mg/kg
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	26	28	28
inter-quartile range (Q1-Q3)	22 to 34	27 to 39	28 to 28
Gender categorical			
Units: Subjects			
Female	0	3	1
Male	3	0	2

Reporting group values	1D: Healthy, 80 mg/kg	2C: Infected, 40 mg/kg	2D: Infected, DZIF-10c, 40 mg/kg
Number of subjects	6	3	26
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	26.5	43	40
inter-quartile range (Q1-Q3)	26 to 28	41 to 48	30 to 52
Gender categorical			
Units: Subjects			
Female	5	2	11
Male	1	1	15

Reporting group values	2D: Infected, Placebo i.v.	Total	
Number of subjects	13	57	
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	32		
inter-quartile range (Q1-Q3)	25 to 47	-	
Gender categorical			
Units: Subjects			
Female	5	27	
Male	8	30	

End points

End points reporting groups	
Reporting group title	1A: Healthy, 2.5 mg/kg
Reporting group description: Open label	
Reporting group title	1B: Healthy, 10 mg/kg
Reporting group description: Open label	
Reporting group title	1C: Healthy, 40 mg/kg
Reporting group description: Open label	
Reporting group title	1D: Healthy, 80 mg/kg
Reporting group description: Open label	
Reporting group title	2C: Infected, 40 mg/kg
Reporting group description: Open label	
Reporting group title	2D: Infected, DZIF-10c, 40 mg/kg
Reporting group description: Randomised and double blind	
Reporting group title	2D: Infected, Placebo i.v.
Reporting group description: Randomised and double-blind	

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

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, 2.5 mg/kg	1B: Healthy, 10 mg/kg	1C: Healthy, 40 mg/kg	1D: Healthy, 80 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: % individuals				
number (not applicable)	66.7	33.3	0	0

End point values	2C: Infected, 40 mg/kg	2D: Infected, DZIF-10c, 40	2D: Infected, Placebo i.v.	

		mg/kg		
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	26	13	
Units: % individuals				
number (not applicable)	0	42.3	61.5	

Statistical analyses

No statistical analyses for this end point

Secondary: DZIF-10c elimination half life

End point title	DZIF-10c elimination half life[2]

End point description:

End point type	Secondary

End point timeframe:

Study period

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	1A: Healthy, 2.5 mg/kg	1B: Healthy, 10 mg/kg	1C: Healthy, 40 mg/kg	1D: Healthy, 80 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: days				
geometric mean (geometric coefficient of variation)	28.4 (± 17.5)	24.2 (± 12.8)	20.1 (± 9.53)	20.9 (± 25.4)

End point values	2C: Infected, 40 mg/kg	2D: Infected, DZIF-10c, 40 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	26		
Units: days				
geometric mean (geometric coefficient of variation)	16.8 (± 45)	21.8 (± 12.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: DZIF-10c peak serum concentration

End point title	DZIF-10c peak serum concentration[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, 2.5 mg/kg	1B: Healthy, 10 mg/kg	1C: Healthy, 40 mg/kg	1D: Healthy, 80 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: µg/ml				
geometric mean (geometric coefficient of variation)	54.3 (± 12.6)	207 (± 8.92)	738 (± 7.94)	1480 (± 10.2)

End point values	2C: Infected, 40 mg/kg	2D: Infected, DZIF-10c, 40 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	26		
Units: µg/ml				
geometric mean (geometric coefficient of variation)	983 (± 8.9)	970 (± 21.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: DZIF-10c Area under the Curve

End point title	DZIF-10c Area under the Curve[4]

End point description:

End point type	Secondary

End point timeframe:

Study period

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: Descriptive end point

End point values	1A: Healthy, 2.5 mg/kg	1B: Healthy, 10 mg/kg	1C: Healthy, 40 mg/kg	1D: Healthy, 80 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: µg h/ml				
geometric mean (geometric coefficient of variation)	15400 (± 5.79)	61700 (± 14.3)	212000 (± 18.9)	358000 (± 14.0)

End point values	2C: Infected, 40 mg/kg	2D: Infected, DZIF-10c, 40 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	26		
Units: µg h/ml				
geometric mean (geometric coefficient of variation)	236000 (± 24.4)	235000 (± 15.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: DZIF-10c clearance

End point title	DZIF-10c clearance[5]

End point description:

End point type	Secondary

End point timeframe:

Study period

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: Descriptive end point

End point values	1A: Healthy, 2.5 mg/kg	1B: Healthy, 10 mg/kg	1C: Healthy, 40 mg/kg	1D: Healthy, 80 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: ml/d				
geometric mean (geometric coefficient of variation)	311 (± 10.6)	242 (± 26.8)	282 (± 40.8)	341 (± 14.1)

End point values	2C: Infected, 40 mg/kg	2D: Infected, DZIF-10c, 40 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	26		
Units: ml/d				

geometric mean (geometric coefficient of variation)	280 (± 24.2)	339 (± 20.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: DZIF-10c volume of distribution Vz

End point title	DZIF-10c volume of distribution Vz[6]

End point description:

End point type	Secondary

End point timeframe:

Study period

Notes:

[6] - 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, 2.5 mg/kg	1B: Healthy, 10 mg/kg	1C: Healthy, 40 mg/kg	1D: Healthy, 80 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: ml				
geometric mean (geometric coefficient of variation)	12800 (± 11.7)	8460 (± 18.0)	8160 (± 45.7)	10300 (± 21.8)

End point values	2C: Infected, 40 mg/kg	2D: Infected, DZIF-10c, 40 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	26		
Units: ml				
geometric mean (geometric coefficient of variation)	6790 (± 29.6)	10700 (± 19.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Drug Antibody Development

End point title	Anti-Drug Antibody Development[7]

End point description:

Individuals developing anti-drug antibodies

End point type	Secondary

End point timeframe:

Study period

Notes:

[7] - 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, 2.5 mg/kg	1B: Healthy, 10 mg/kg	1C: Healthy, 40 mg/kg	1D: Healthy, 80 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: individuals	0	0	0	0

End point values	2C: Infected, 40 mg/kg	2D: Infected, DZIF-10c, 40 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	26		
Units: individuals	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Drug Antibody Peak Titer

End point title	Anti-Drug Antibody Peak Titer[8]

End point description:

Peak serum anti-drug antibody titer in individuals developing anti-drug antibodies

End point type	Secondary

End point timeframe:

Study period

Notes:

[8] - 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	2C: Infected, 40 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Reciprocal serum titer				
number (not applicable)	960			

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)[9]

End point description:

Time-weighted average change

End point type	Secondary

End point timeframe:

Up to day 28 visit

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: Only randomized and controlled phase shown; preplanned as hypothesis-generating analysis

End point values	2D: Infected, DZIF-10c, 40 mg/kg	2D: Infected, Placebo i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	13		
Units: Adjusted mean AOC				
number (not applicable)				
Over 7 days	-2.035	-1.449		
Over 14 days	-3.273	-2.668		
Over 28 days	-3.938	-3.576		

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)[10]

End point description:

Mixed model for repeated measures

End point type	Secondary

End point timeframe:

Day 1 to Day 29

Notes:

[10] - 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, DZIF-10c, 40 mg/kg	2D: Infected, Placebo i.v.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	13		
Units: Adjusted mean				
number (not applicable)				
Over 7 days	-4.3	-3.3		
Over 14 days	-4.5	-4.3		
Over 28 days	-4.7	-4.6		

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, 2.5 mg/kg
Reporting group description: Open label	
Reporting group title	1B: Healthy, 10 mg/kg
Reporting group description: Open label	
Reporting group title	1C: Healthy, 40 mg/kg
Reporting group description: Open label	
Reporting group title	1D: Healthy, 80 mg/kg
Reporting group description: Open label	
Reporting group title	2C: Infected, 40 mg/kg
Reporting group description: Open label	
Reporting group title	2D: Infected, DZIF-10c, 40 mg/kg
Reporting group description: Randomised and double blind	
Reporting group title	2D: Infected, Placebo i.v.
Reporting group description: Randomised and double-blind	

Serious adverse events	1A: Healthy, 2.5 mg/kg	1B: Healthy, 10 mg/kg	1C: Healthy, 40 mg/kg
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	1D: Healthy, 80 mg/kg	2C: Infected, 40 mg/kg	2D: Infected, DZIF-10c, 40 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from			

adverse events

Serious adverse events	2D: Infected, Placebo i.v.		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	1A: Healthy, 2.5 mg/kg	1B: Healthy, 10 mg/kg	1C: Healthy, 40 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	2 / 3 (66.67%)
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
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	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hyposmia			
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
Hypogeusia			
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
Ageusia			
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			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
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
Non-cardiac chest pain			
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%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Malaise			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tympanic membrane perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Proctalgia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	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
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vomiting			
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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Thyroid mass			
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			
Myalgia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Cystitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	1D: Healthy, 80 mg/kg	2C: Infected, 40 mg/kg	2D: Infected, DZIF-10c, 40 mg/kg
Total subjects affected by non-serious adverse events			

subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	18 / 26 (69.23%)
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	8 / 26 (30.77%)
occurrences (all)	0	0	9
Hyposmia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Disturbance in attention			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Hypogeusia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Parosmia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Ageusia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	4 / 26 (15.38%)
occurrences (all)	0	0	4
Chest discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Tympanic membrane perforation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Proctalgia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	3 / 26 (11.54%)
occurrences (all)	0	0	3
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	8 / 26 (30.77%)
occurrences (all)	0	0	10
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	4 / 26 (15.38%)
occurrences (all)	0	0	4
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Endocrine disorders			
Thyroid mass			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1

Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1

Non-serious adverse events	2D: Infected, Placebo i.v.		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 13 (76.92%)		
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			

subjects affected / exposed	5 / 13 (38.46%)		
occurrences (all)	5		
Hyposmia			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		
Dysgeusia			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		
Disturbance in attention			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Hypogeusia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Parosmia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Ageusia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Neutropenia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pain			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		
Chest discomfort			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Fatigue			

subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Non-cardiac chest pain			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Tympanic membrane perforation			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Proctalgia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			

Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Cough subjects affected / exposed occurrences (all)	4 / 13 (30.77%) 5		
Dyspnoea subjects affected / exposed occurrences (all)	3 / 13 (23.08%) 3		
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Pruritus subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Endocrine disorders			
Thyroid mass subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Musculoskeletal and connective tissue disorders			
Myalgia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Arthralgia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Infections and infestations			
COVID-19 subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Rhinitis subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Cystitis			

subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Tonsillitis			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Tooth abscess			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 April 2021	Addition of higher dose open label group and 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.

Notes: