Clinical trial results:
A participant and investigator-blinded, randomized, placebo-controlled Phase 2a study to investigate the pharmacokinetics, pharmacodynamics, safety and tolerability of TIN816 in patients with sepsis-associated acute kidney injury

Summary

EudraCT number	2022-000887-23
Trial protocol	ES FR DE BE HU
Global end of trial date	25 April 2024

Results information

Result version number	v1 (current)
This version publication date	30 April 2025
First version publication date	30 April 2025

Trial information

Trial identification

Sponsor protocol code	CTIN816B12201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05507437
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Novartis Pharma AG, Clinical Disclosure Office, 41 613241111, novartis.email@novartis.com
Scientific contact	Novartis Pharma AG, Clinical Disclosure Office, 41 613241111, novartis.email@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 April 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 April 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the pharmacokinetics (PK) of TIN816 with a single dose of intravenous (IV) infusion in hospitalized adult participants with diagnosis of sepsis-associated acute kidney injury.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 November 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Germany: 1
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	7
From 65 to 84 years	12
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants took part in 7 investigative sites in 5 countries.

Pre-assignment

Screening details:

The study consisted of a screening period up to 48 hours.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	TIN816

Arm description:

TIN816 2 mg/kg intravenous dose on Day 1.

Arm type	Experimental
Investigational medicinal product name	TIN816
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single i.v. infusion of TIN816 administered at a dose of 2 mg/kg.

Arm title	Placebo

Arm description:

Placebo intravenous dose on Day 1

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

Dosage and administration details:

Single i.v. infusion of placebo.

Number of subjects in period 1	TIN816	Placebo
Started	16	4
Completed	12	3
Not completed	4	1
Consent withdrawn by subject	1	1

Adverse event	3	-

Baseline characteristics

Reporting groups	
Reporting group title	TIN816
Reporting group description:	
TIN816 2 mg/kg intravenous dose on Day 1.	
Reporting group title	Placebo
Reporting group description:	
Placebo intravenous dose on Day 1	

Reporting group values	TIN816	Placebo	Total
Number of subjects	16	4	20
Age categorical 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)	6	1	7
From 65-84 years	10	2	12
85 years and over	0	1	1
Age Continuous Units: years			
arithmetic mean	66.25	68.0	
standard deviation	± 12.250	± 19.950	-
Sex: Female, Male Units: participants			
Female	3	1	4
Male	13	3	16
Race/Ethnicity, Customized Units: Subjects			
White	2	1	3
Not Reported	14	3	17

End points

End points reporting groups

Reporting group title	TIN816
Reporting group description: TIN816 2 mg/kg intravenous dose on Day 1.	
Reporting group title	Placebo
Reporting group description: Placebo intravenous dose on Day 1	

Primary: Maximum serum concentration (Cmax) of TIN816

End point title	Maximum serum concentration (Cmax) of TIN816[1][2]
End point description: Cmax is defined as the maximum (peak) observed concentration following a dose. TIN816 serum concentrations were determined using the actual recorded sampling times and non-compartmental method with Phoenix WinNonlin (Version 8.3). TIN816 concentrations were determined by a validated ligand binding assay with a lower limit of quantification (LLOQ) of 10 ng/mL.	
End point type	Primary
End point timeframe: Day 1 (Pre-dose and 2 hours), Day 2, Day 3, Day 5, Day 8, Day 14, Day 30, Day 60 and Day 90	

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: only analyzed descriptively.

[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: PK Endpoint not analyzed for participants on placebo

End point values	TIN816			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: ug/mL				
geometric mean (geometric coefficient of variation)	40.8 (± 36.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Area under serum concentration-time curve from time zero to the last measurable concentration sampling time (AUClast) of TIN816

End point title	Area under serum concentration-time curve from time zero to the last measurable concentration sampling time (AUClast) of TIN816[3][4]
End point description: AUClast is the area under the serum concentration-time curve from time zero to the time of last quantifiable concentration (tlast) of TIN816. TIN816 serum concentrations were determined using the actual recorded sampling times and non-compartmental method with Phoenix WinNonlin (Version 8.3). TIN816 concentrations were determined by a validated ligand binding assay with a lower limit of	

quantification (LLOQ) of 10 ng/mL.

End point type	Primary

End point timeframe:

Day 1 (Pre-dose and 2 hours), Day 2, Day 3, Day 5, Day 8, Day 14, Day 30, Day 60 and Day 90

Notes:

[3] - 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: only analyzed descriptively.

[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: PK Endpoint not analyzed for participants on placebo

End point values	TIN816			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: day*ug/mL				
geometric mean (geometric coefficient of variation)	99.9 (± 49.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Terminal elimination half-life (T1/2) of TIN816

End point title	Terminal elimination half-life (T1/2) of TIN816[5][6]

End point description:

T1/2 is the elimination half-life associated with the terminal slope. TIN816 serum concentrations were determined using the actual recorded sampling times and non-compartmental method with Phoenix WinNonlin (Version 8.3). TIN816 concentrations were determined by a validated ligand binding assay with a lower limit of quantification (LLOQ) of 10 ng/mL.

End point type	Primary

End point timeframe:

Day 1 (Pre-dose and 2 hours), Day 2, Day 3, Day 5, Day 8, Day 14, Day 30, Day 60 and Day 90

Notes:

[5] - 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: only analyzed descriptively.

[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: PK Endpoint not analyzed for participants on placebo

End point values	TIN816			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Day				
geometric mean (geometric coefficient of variation)	5.70 (± 14.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Total body clearance (CL) of TIN816

End point title	Total body clearance (CL) of TIN816[7][8]

End point description:

CL is the total body clearance of TIN816 from the serum following intravenous administration (volume x time-1). TIN816 serum concentrations were determined using the actual recorded sampling times and non-compartmental method with Phoenix WinNonlin (Version 8.3). TIN816 concentrations were determined by a validated ligand binding assay with a lower limit of quantification (LLOQ) of 10 ng/mL.

End point type	Primary

End point timeframe:

Day 1 (Pre-dose and 2 hours), Day 2, Day 3, Day 5, Day 8, Day 14, Day 30, Day 60 and Day 90

Notes:

[7] - 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: only analyzed descriptively.

[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: PK Endpoint not analyzed for participants on placebo

End point values	TIN816			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Liter/day/kg				
geometric mean (geometric coefficient of variation)	0.0189 (± 24.7)			

Statistical analyses

No statistical analyses for this end point

Primary: The apparent volume of distribution (Vz) of TIN816

End point title	The apparent volume of distribution (Vz) of TIN816[9][10]

End point description:

Vz is the apparent volume of distribution during terminal phase following intravenous administration. TIN816 serum concentrations were determined using the actual recorded sampling times and non-compartmental method with Phoenix WinNonlin (Version 8.3). TIN816 concentrations were determined by a validated ligand binding assay with a lower limit of quantification (LLOQ) of 10 ng/mL.

End point type	Primary

End point timeframe:

Day 1 (Pre-dose and 2 hours), Day 2, Day 3, Day 5, Day 8, Day 14, Day 30, Day 60 and Day 90

Notes:

[9] - 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: only analyzed descriptively.

[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: PK Endpoint not analyzed for participants on placebo

End point values	TIN816			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Liter/kg				
geometric mean (geometric coefficient of variation)	0.155 (± 31.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Area under the serum concentration-time curve from time zero extrapolated to infinity (AUC[0-inf]) of TIN816

End point title	Area under the serum concentration-time curve from time zero extrapolated to infinity (AUC[0-inf]) of TIN816[11][12]

End point description:

The AUC from time zero to infinity (mass x time x volume-1). TIN816 serum concentrations were determined using the actual recorded sampling times and non-compartmental method with Phoenix WinNonlin (Version 8.3). TIN816 concentrations were determined by a validated ligand binding assay with a lower limit of quantification (LLOQ) of 10 ng/mL.

End point type	Primary

End point timeframe:

Day 1 (Pre-dose and 2 hours), Day 2, Day 3, Day 5, Day 8, Day 14, Day 30, Day 60 and Day 90

Notes:

[11] - 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: only analyzed descriptively.

[12] - 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: PK Endpoint not analyzed for participants on placebo

End point values	TIN816			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: day*ug/mL				
geometric mean (geometric coefficient of variation)	104 (± 47.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Time to reach maximum serum concentration (Tmax) of TIN816

End point title	Time to reach maximum serum concentration (Tmax) of TIN816[13][14]

End point description:

Tmax is the time to reach maximum (peak) drug concentration after single-dose administration (time). TIN816 serum concentrations were determined using the actual recorded sampling times and non-compartmental method with Phoenix WinNonlin (Version 8.3). TIN816 concentrations were determined

by a validated ligand binding assay with a lower limit of quantification (LLOQ) of 10 ng/mL.

End point type	Primary

End point timeframe:

Day 1 (Pre-dose and 2 hours), Day 2, Day 3, Day 5, Day 8, Day 14, Day 30, Day 60 and Day 90

Notes:

[13] - 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: only analyzed descriptively.

[14] - 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: PK Endpoint not analyzed for participants on placebo

End point values	TIN816			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Day				
median (full range (min-max))	0.0868 (0.0597 to 0.163)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with treatment emergent adverse events (AEs) and serious adverse events (SAEs)

End point title	Number of participants with treatment emergent adverse events (AEs) and serious adverse events (SAEs)

End point description:

Number of participants with treatment emergent AEs (any AE regardless of seriousness) and SAEs.

End point type	Secondary

End point timeframe:

Adverse events were reported from first dose of study treatment until end of study treatment plus follow up period, up to a maximum duration of approximately 90 days.

End point values	TIN816	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	4		
Units: Participants				
Adverse events	14	4		
Serious Adverse events	11	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study treatment until end of study treatment plus follow up period, up to a maximum duration of approximately 90 days.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	TIN816

Reporting group description:

TIN816

Reporting group title	All Patients

Reporting group description:

All Patients

Reporting group title	Placebo

Reporting group description:

Placebo

Serious adverse events	TIN816	All Patients	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 16 (68.75%)	12 / 20 (60.00%)	1 / 4 (25.00%)
number of deaths (all causes)	3	3	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Distributive shock			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders			
Cerebral haematoma			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Anaemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Acute respiratory failure			

subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Toxic epidermal necrolysis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal tubular necrosis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	2 / 16 (12.50%)	2 / 20 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 16 (12.50%)	2 / 20 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Peritonitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious pleural effusion			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	2 / 16 (12.50%)	2 / 20 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	TIN816	All Patients	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 16 (87.50%)	18 / 20 (90.00%)	4 / 4 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasma cell myeloma			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Transitional cell carcinoma			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 16 (6.25%)	2 / 20 (10.00%)	1 / 4 (25.00%)
occurrences (all)	1	2	1
Haemorrhage			

subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Haemodynamic instability			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Deep vein thrombosis			
subjects affected / exposed	1 / 16 (6.25%)	2 / 20 (10.00%)	1 / 4 (25.00%)
occurrences (all)	1	2	1
Pelvic venous thrombosis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Jugular vein thrombosis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Hypotension			
subjects affected / exposed	2 / 16 (12.50%)	2 / 20 (10.00%)	0 / 4 (0.00%)
occurrences (all)	2	2	0
Shock haemorrhagic			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Hyperthermia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	2	2	0
Chest pain			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Respiratory, thoracic and mediastinal disorders			

Respiratory distress			
subjects affected / exposed	2 / 16 (12.50%)	2 / 20 (10.00%)	0 / 4 (0.00%)
occurrences (all)	2	2	0
Respiratory acidosis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Pulmonary embolism			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Hypercapnia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	2 / 16 (12.50%)	2 / 20 (10.00%)	0 / 4 (0.00%)
occurrences (all)	2	2	0
Confusional state			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Delirium			
subjects affected / exposed	2 / 16 (12.50%)	3 / 20 (15.00%)	1 / 4 (25.00%)
occurrences (all)	2	3	1
Insomnia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 16 (12.50%)	2 / 20 (10.00%)	0 / 4 (0.00%)
occurrences (all)	2	2	0
Alanine aminotransferase increased			
subjects affected / exposed	2 / 16 (12.50%)	2 / 20 (10.00%)	0 / 4 (0.00%)
occurrences (all)	2	2	0
Cardiac disorders			

Stress cardiomyopathy			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Atrioventricular block first degree			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Atrial fibrillation			
subjects affected / exposed	2 / 16 (12.50%)	2 / 20 (10.00%)	0 / 4 (0.00%)
occurrences (all)	2	2	0
Nervous system disorders			
Extrapyramidal disorder			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Intensive care unit acquired weakness			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Myoclonus			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 16 (18.75%)	5 / 20 (25.00%)	2 / 4 (50.00%)
occurrences (all)	4	6	2
Lymphopenia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Thrombocytopenia			
subjects affected / exposed	2 / 16 (12.50%)	2 / 20 (10.00%)	0 / 4 (0.00%)
occurrences (all)	2	2	0
Ear and labyrinth disorders			
Ear haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Eye disorders			
Phlyctenular keratoconjunctivitis			

subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Constipation			
subjects affected / exposed	3 / 16 (18.75%)	3 / 20 (15.00%)	0 / 4 (0.00%)
occurrences (all)	3	3	0
Diarrhoea			
subjects affected / exposed	1 / 16 (6.25%)	3 / 20 (15.00%)	2 / 4 (50.00%)
occurrences (all)	1	3	2
Faecaloma			
subjects affected / exposed	2 / 16 (12.50%)	2 / 20 (10.00%)	0 / 4 (0.00%)
occurrences (all)	2	2	0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 16 (12.50%)	2 / 20 (10.00%)	0 / 4 (0.00%)
occurrences (all)	2	2	0
Impaired gastric emptying			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Nausea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Oesophagitis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Oral mucosal blistering			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Pancreatitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1

Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Hepatic cytolysis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Cholecystitis acute			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Pruritus			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Decubitus ulcer			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Renal failure			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Urinary retention			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Gouty arthritis			

subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Musculoskeletal pain			
subjects affected / exposed	2 / 16 (12.50%)	2 / 20 (10.00%)	0 / 4 (0.00%)
occurrences (all)	2	2	0
Rhabdomyolysis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Bacteraemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
COVID-19			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Endocarditis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Herpes simplex reactivation			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Oral candidiasis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Oral herpes			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Pneumonia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Skin bacterial infection			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0

Systemic candida			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Urinary tract candidiasis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Urinary tract infection			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	2	2	0
Urosepsis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Clostridium difficile infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Hyperglycaemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Hyperferritinaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Folate deficiency			
subjects affected / exposed	0 / 16 (0.00%)	1 / 20 (5.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Hypernatraemia			
subjects affected / exposed	3 / 16 (18.75%)	4 / 20 (20.00%)	1 / 4 (25.00%)
occurrences (all)	3	4	1
Hyperphosphataemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Hypertriglyceridaemia			

subjects affected / exposed	3 / 16 (18.75%)	3 / 20 (15.00%)	0 / 4 (0.00%)
occurrences (all)	3	3	0
Hyperuricaemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Hypervolaemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Hypocalcaemia			
subjects affected / exposed	3 / 16 (18.75%)	3 / 20 (15.00%)	0 / 4 (0.00%)
occurrences (all)	3	3	0
Hypokalaemia			
subjects affected / exposed	2 / 16 (12.50%)	3 / 20 (15.00%)	1 / 4 (25.00%)
occurrences (all)	2	4	2
Hypomagnesaemia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Hypophosphataemia			
subjects affected / exposed	3 / 16 (18.75%)	4 / 20 (20.00%)	1 / 4 (25.00%)
occurrences (all)	3	4	1
Malnutrition			
subjects affected / exposed	1 / 16 (6.25%)	2 / 20 (10.00%)	1 / 4 (25.00%)
occurrences (all)	1	2	1
Metabolic acidosis			
subjects affected / exposed	1 / 16 (6.25%)	2 / 20 (10.00%)	1 / 4 (25.00%)
occurrences (all)	1	2	1
Vitamin C deficiency			
subjects affected / exposed	1 / 16 (6.25%)	1 / 20 (5.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Vitamin D deficiency			
subjects affected / exposed	1 / 16 (6.25%)	2 / 20 (10.00%)	1 / 4 (25.00%)
occurrences (all)	1	2	1

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