Clinical trial results:
A Multicenter, Adaptive, Randomized, Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for Hospitalized Patients with COVID-19

Summary

EudraCT number	2020-003278-37
Trial protocol	DK GB SE PL GR IT
Global end of trial date	14 July 2023

Results information

Result version number	v1 (current)
This version publication date	06 December 2023
First version publication date	06 December 2023
Summary attachment (see zip file)	Efficacy & Safety of Ensovibep (MP0420) (ACTIV-3-TICO-AnnInternMed3-2022.pdf) Efficacy & safety of sotrovimab, BRII-196/BRII-198 (ACTIV-3-TICO-LancetInfectDis-2022.pdf) Tixa-cilga for COVID-19 (ACTIV-3-TICO-LancetRespirMed-2022.pdf) Neutralizing MAb LY-CoV555 (ACTIV-3-TICO-NEJM-2021.pdf) Results from final ACTIV-3 trial (Pfizer protease inhibitor) (CTgov_Results_Pfizer.xlsx)

Trial information

Trial identification

Sponsor protocol code	INSIGHT-014-ACTIV-3

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04501978
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regents of the University of Minnesota
Sponsor organisation address	Office of the Vice President for Research, 420 Johnston Hall, 101 Pleasant St. SE, Minneapolis, United States, MN 55455
Public contact	Jens Lundgren, CHIP - Rigshospitalet, University of Copenhagen, +45 3545 5757, jens.lundgren@regionh.dk
Scientific contact	Jens Lundgren, CHIP - Rigshospitalet, University of Copenhagen, +45 3545 5757, jens.lundgren@regionh.dk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No	No

1901/2006 apply to this trial?	
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	14 July 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 July 2023
Global end of trial reached?	Yes
Global end of trial date	14 July 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this protocol is to determine whether investigational agents, initially focusing on those that are aimed at enhancing the host immune response to SARS-CoV-2 infection are safe and superior to control (e.g., placebo) when given with SOC for the primary endpoint of time to sustained recovery evaluated up to 90 days after randomization.
SOC may be modified (updated based on data from this or other trials) during the course of evaluating different investigational agents with this master protocol.
Over the entire course of ACTIV-3/TICO, 6 different agents were evaluated. Detailed results are presented here for the first agent; results for the remaining 5 agents are provided in attachments to this record.

Protection of trial subjects:

To the extent possible, blood for study purposes was taken from the same stick as that for clinical care. Participants were monitored closely during study product infusion and for several hours afterward, with regular vital signs measurement and recording of adverse events.

Background therapy:

Remdesivir was provided to all study participants as standard of care (SOC) unless contraindicated for an individual patient; administered by IV infusion.

Evidence for comparator: -

Actual start date of recruitment	17 August 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	Denmark: 38
Country: Number of subjects enrolled	Singapore: 1
Country: Number of subjects enrolled	United States: 275
Worldwide total number of subjects	314
EEA total number of subjects	38

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)	181
From 65 to 84 years	122
85 years and over	11

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from participating hospitals between 05 August 2020 and 26 October 2020.

Pre-assignment

Screening details:

Hospitalized adults with COVID-19.

Period 1

Period 1 title	1st ACTIV-3 trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Carer, Assessor, Subject

Blinding implementation details:

Randomizer was given a treatment ID, which was sent to the pharmacy. The ID was decoded in the pharmacy. A saline placebo infusion was used. The infusion bag was covered with a colored sleeve to mask the slight different in color between the active product and placebo

Arms

Are arms mutually exclusive?	Yes
Arm title	LY3819253 plus SOC

Arm description:

LY3819253 7000 mg solution (10 vials of 20 mL solution containing 700 mg each); administered by IV infusion

Remdesivir is provided to all study participants as standard of care (SOC) unless contraindicated for an individual patient; administered by IV infusion

Arm type	Experimental
Investigational medicinal product name	LY3819253
Investigational medicinal product code	
Other name	LY-CoV555, bamlanivimab
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

LY3819253 was administered as a single dose of 7000 mg (200 mL)

Arm title	Placebo plus SOC

Arm description:

Normal saline was administered as a single dose of 200 mL by IV infusion.

Remdesivir is provided to all study participants unless contraindicated for an individual patient; administered by IV infusion.

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:

Normal saline was administered as a single dose of 200 mL.

Number of subjects in period 1	LY3819253 plus SOC	Placebo plus SOC
Started	163	151
Completed	163	151

Baseline characteristics

Reporting groups	
Reporting group title	LY3819253 plus SOC
Reporting group description:	
LY3819253 7000 mg solution (10 vials of 20 mL solution containing 700 mg each); administered by IV infusion Remdesivir is provided to all study participants as standard of care (SOC) unless contraindicated for an individual patient; administered by IV infusion	
Reporting group title	Placebo plus SOC
Reporting group description:	
Normal saline was administered as a single dose of 200 mL by IV infusion. Remdesivir is provided to all study participants unless contraindicated for an individual patient; administered by IV infusion.	

Reporting group values	LY3819253 plus SOC	Placebo plus SOC	Total
Number of subjects	163	151	314
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			
age in years			
Units: years			
arithmetic mean	60.4	58.9	
standard deviation	± 14.2	± 16.3	-
Gender categorical			
Gender at birth			
Units: Subjects			
Female	66	71	137
Male	97	80	177
Race/ethnicity			
Participants were asked to identify their race/ethnicity in a single question. Participants could choose multiple answers.			
Units: Subjects			
American Indian/Alaska Native	3	0	3
Asian	6	7	13
Native Hawaiian/Pacific Islander	1	1	2
Black/African American	32	34	66
White	90	88	178
More than one race	1	1	2

Other	4	4	8
Only ethnicity (Hispanic/Latino vs. not)reported	26	16	42

End points

End points reporting groups

Reporting group title	LY3819253 plus SOC

Reporting group description:

LY3819253 7000 mg solution (10 vials of 20 mL solution containing 700 mg each); administered by IV infusion

Remdesivir is provided to all study participants as standard of care (SOC) unless contraindicated for an individual patient; administered by IV infusion

Reporting group title	Placebo plus SOC

Reporting group description:

Normal saline was administered as a single dose of 200 mL by IV infusion.

Remdesivir is provided to all study participants unless contraindicated for an individual patient; administered by IV infusion.

Primary: Ordinal Outcome on Day 5

End point title	Ordinal Outcome on Day 5

End point description:

Ordinal outcome with 7 mutually exclusive categories

End point type	Primary

End point timeframe:

Through trial Day 5 (where Day 0 is randomization)

End point values	LY3819253 plus SOC	Placebo plus SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	151		
Units: Participants				
Death	1	0		
Inv. vent, ECMO, circ support, new renal repl tx	8	5		
Non-invasive vent or high-flow O2	25	22		
Supplemental O2 >=4L/min or 4L/min above BL	17	11		
Supplemental O2 <4L/min or <4L/min above BL	29	31		
Limiting symptoms d/t COVID-19, no new O2	50	48		
No limiting symptoms d/t COVID-19	31	33		

Statistical analyses

Statistical analysis title	Pulmonary ordinal outcome on Day 5

Statistical analysis description:

The analysis estimates the summary odds ratio of a better outcome with active treatment than with

placebo, using a proportional odds model that included the treatment group indicator

Comparison groups	LY3819253 plus SOC v Placebo plus SOC
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.45
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	1.29

Primary: Time to achieve sustained recovery

End point title	Time to achieve sustained recovery

End point description:

Sustained recovery defined as being discharged from the index hospitalization, followed by being alive and home for 14 consecutive days prior to Day 90

End point type	Primary

End point timeframe:

Through Day 90

End point values	LY3819253 plus SOC	Placebo plus SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	151		
Units: participants				
Achieved sustained recovery	144	136		

Statistical analyses

Statistical analysis title	Time to sustained recovery

Statistical analysis description:

This provides the recovery rate ratio comparing time to sustained recovery between treatment groups

Comparison groups	LY3819253 plus SOC v Placebo plus SOC
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Cox proportional hazard
Point estimate	1.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.47

Secondary: All-cause mortality

End point title	All-cause mortality

End point description:

End point type	Secondary

End point timeframe:

Through Day 90 (where Day 0 is randomization)

End point values	LY3819253 plus SOC	Placebo plus SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	151		
Units: participants				
Dead at Day 90	13	11		

Statistical analyses

Statistical analysis title	Time to death

Statistical analysis description:

Death through Day 90, hazard ratio estimated from Cox model with stratification by site pharmacy

Comparison groups	LY3819253 plus SOC v Placebo plus SOC
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.84
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	2.43

Secondary: Safety outcome through Day 5

End point title	Safety outcome through Day 5
End point description:	
Death, SAE, Grade 3 or 4 event, organ failure, or serious infection through Day 5	
End point type	Secondary
End point timeframe:	
Through Day 5 (where Day 0 is randomization)	

End point values	LY3819253 plus SOC	Placebo plus SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	151		
Units: participants				
Experienced safety outcome	45	28		

Statistical analyses

Statistical analysis title	Day 5 composite safety outcome
Comparison groups	LY3819253 plus SOC v Placebo plus SOC
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	3.29

Secondary: Safety outcome through Day 28	
End point title	Safety outcome through Day 28
End point description:	
Death, SAE, Grade 3 or 4 event, organ failure, or serious infection through Day 28	
End point type	Secondary
End point timeframe:	
Through Day 28 (where Day 0 is randomization)	

End point values	LY3819253 plus SOC	Placebo plus SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	151		
Units: participants				
Experienced safety event by Day 28	52	42		

Statistical analyses

Statistical analysis title	Day 28 composite safety outcome
Statistical analysis description: Hazard ratio estimated from Cox model with stratification by site pharmacy	
Comparison groups	LY3819253 plus SOC v Placebo plus SOC
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.35
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.82

Secondary: Safety outcome through Day 90

End point title	Safety outcome through Day 90
End point description: Death, SAE, organ failure, or serious infections through Day 90	
End point type	Secondary
End point timeframe: Through Day 90 (where Day 0 is randomization)	

End point values	LY3819253 plus SOC	Placebo plus SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	151		
Units: participants				
Experienced safety outcome by Day 90	45	41		

Statistical analyses

Statistical analysis title	Day 90 composite safety outcome
Statistical analysis description: hazard ratio estimated from Cox model with stratification by site pharmacy	
Comparison groups	LY3819253 plus SOC v Placebo plus SOC
Number of subjects included in analysis	314
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.83
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.6

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Through Day 90	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	LY3819253 plus SOC

Reporting group description:

LY3819253 7000 mg solution (10 vials of 20 mL solution containing 700 mg each); administered by IV infusion

Remdesivir is provided to all study participants as standard of care (SOC) unless contraindicated for an individual patient; administered by IV infusion

Reporting group title	Placebo plus SOC

Reporting group description:

Normal saline was administered as a single dose of 200 mL by IV infusion.

Remdesivir is provided to all study participants unless contraindicated for an individual patient; administered by IV infusion.

Serious adverse events	LY3819253 plus SOC	Placebo plus SOC	
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 163 (7.98%)	12 / 151 (7.95%)	
number of deaths (all causes)	13	11	
number of deaths resulting from adverse events			
Investigations			
Haemoglobin decreased			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Transitional cell carcinoma			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Injury, poisoning and procedural complications			
Infusion related reaction			

subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive urgency			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Arrhythmia supraventricular			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 163 (0.61%)	1 / 151 (0.66%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vomiting			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 163 (0.61%)	2 / 151 (1.32%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 163 (0.61%)	1 / 151 (0.66%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cholecystitis infective			

subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraspinal abscess			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0.01 %

Non-serious adverse events	LY3819253 plus SOC	Placebo plus SOC	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 163 (25.15%)	27 / 151 (17.88%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	6 / 163 (3.68%)	3 / 151 (1.99%)	
occurrences (all)	7	3	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences (all)	1	0	
Chills			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences (all)	1	0	
Fatigue			

subjects affected / exposed	9 / 163 (5.52%)	5 / 151 (3.31%)	
occurrences (all)	10	5	
Hypothermia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	1 / 163 (0.61%)	1 / 151 (0.66%)	
occurrences (all)	1	1	
Pyrexia			
subjects affected / exposed	2 / 163 (1.23%)	2 / 151 (1.32%)	
occurrences (all)	3	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 163 (0.00%)	3 / 151 (1.99%)	
occurrences (all)	0	3	
Dyspnoea			
subjects affected / exposed	15 / 163 (9.20%)	10 / 151 (6.62%)	
occurrences (all)	17	10	
Epistaxis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences (all)	0	1	
Hypoxia			
subjects affected / exposed	1 / 163 (0.61%)	2 / 151 (1.32%)	
occurrences (all)	1	2	
Pneumothorax			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences (all)	3	0	
Respiratory distress			
subjects affected / exposed	2 / 163 (1.23%)	0 / 151 (0.00%)	
occurrences (all)	2	0	
Respiratory failure			

subjects affected / exposed	4 / 163 (2.45%)	3 / 151 (1.99%)	
occurrences (all)	4	3	
Investigations			
Haemoglobin decreased			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences (all)	1	0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences (all)	1	0	
Liver function test increased			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	2 / 163 (1.23%)	0 / 151 (0.00%)	
occurrences (all)	2	0	
Arrhythmia supraventricular			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences (all)	1	0	
Atrial fibrillation			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences (all)	1	0	
Bradycardia			
subjects affected / exposed	2 / 163 (1.23%)	1 / 151 (0.66%)	
occurrences (all)	2	1	
Sinus bradycardia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences (all)	1	0	
Tachycardia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			

Anxiety			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences (all)	0	1	
Encephalopathy			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	1 / 163 (0.61%)	2 / 151 (1.32%)	
occurrences (all)	1	2	
Mental status changes			
subjects affected / exposed	7 / 163 (4.29%)	1 / 151 (0.66%)	
occurrences (all)	7	1	
Panic attack			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences (all)	1	0	
Seizure			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Coagulopathy			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences (all)	0	1	
Febrile neutropenia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences (all)	0	2	
Nausea			

subjects affected / exposed	0 / 163 (0.00%)	2 / 151 (1.32%)	
occurrences (all)	0	2	
Pancreatitis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	5 / 163 (3.07%)	1 / 151 (0.66%)	
occurrences (all)	7	1	
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	2 / 163 (1.23%)	0 / 151 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Candida infection			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences (all)	0	1	
Clostridium difficile colitis			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences (all)	0	1	
Paraspinal abscess			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	1 / 163 (0.61%)	1 / 151 (0.66%)	
occurrences (all)	1	1	
Pneumonia staphylococcal			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences (all)	0	1	

Pseudomonas infection			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences (all)	1	0	
Staphylococcal infection			
subjects affected / exposed	2 / 163 (1.23%)	0 / 151 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 163 (1.84%)	3 / 151 (1.99%)	
occurrences (all)	4	3	
Hyperglycaemia			
subjects affected / exposed	1 / 163 (0.61%)	1 / 151 (0.66%)	
occurrences (all)	1	1	
Hypoglycaemia			
subjects affected / exposed	0 / 163 (0.00%)	1 / 151 (0.66%)	
occurrences (all)	0	1	
Hyponatraemia			
subjects affected / exposed	1 / 163 (0.61%)	0 / 151 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
26 October 2020	The DSMB halted enrollment for futility.	-

Notes:

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33356051