



Clinical trial results:

A Multi-Center, Phase 2, Open-label, Parallel Cohort Study of Efficacy and Safety of Duvelisib in Patients with Relapsed or Refractory Peripheral T-cell Lymphoma (PTCL)

Summary

EudraCT number	2019-001123-13
Trial protocol	DE GB IT
Global end of trial date	22 December 2023

Results information

Result version number	v2 (current)
This version publication date	20 April 2025
First version publication date	04 January 2025
Version creation reason	<ul style="list-style-type: none">• New data added to full data set• Correction of full data set Updated to align with another database.

Trial information

Trial identification

Sponsor protocol code	VS-0145-225
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03372057
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Secura Bio, Inc.
Sponsor organisation address	1995 Village Center Circle, Suite 128, Las Vegas, NV, United States, 89134
Public contact	Ohad Bentur, MD, MHA, MSc/Senior Medical Director, Secura Bio, Inc., 1 702-254-0011, obentur@securabio.com
Scientific contact	Ohad Bentur, MD, MHA, MSc/Senior Medical Director, Secura Bio, Inc., 1 702-254-0011, obentur@securabio.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	22 December 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	22 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Dose Optimization Phase: To determine the optimal duvelisib dose for utilization in the Expansion Phase by evaluating the ORR supported by safety, additional efficacy, and pharmacokinetics parameters as well as any other available data in the population of participants receiving the optimal dose of duvelisib for at least one cycle in participants with relapsed or refractory PTCL.

Expansion Phase: To determine the efficacy of the optimal dose of duvelisib in participants with relapsed or refractory PTCL.

Protection of trial subjects:

This study was conducted in accordance with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which the study was conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 May 2018
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	United Kingdom: 6
Country: Number of subjects enrolled	United States: 117
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Italy: 21
Country: Number of subjects enrolled	Japan: 10
Worldwide total number of subjects	156
EEA total number of subjects	23

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)	70
From 65 to 84 years	83
85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Regardless of study phase, all participants underwent screening assessments up to 30 days before the first study drug dose.

Period 1

Period 1 title	Dose Optimization Phase (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Dose Optimization Phase: Cohort 1

Arm description:

Duvelisib was administered orally (PO) twice daily (BID) at a starting dose of 25 milligrams (mg), with potential escalation on a per-participant basis to 50 mg and then 75 mg, based on the participant's response to and tolerance of therapy, in 28-day cycles.

Arm type	Experimental
Investigational medicinal product name	Duvelisib
Investigational medicinal product code	
Other name	IPI-145
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Duvelisib PO 25 mg BID or 50 mg BID or 75 mg BID in 28-day cycles.

Arm title	Dose Optimization Phase: Cohort 2
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Arm description:

Duvelisib 75 mg PO BID was administered in 28-day cycles.

Arm type	Experimental
Investigational medicinal product name	Duvelisib
Investigational medicinal product code	
Other name	IPI-145
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Duvelisib PO 75 mg BID in 28-day cycles.

Arm title	Expansion Phase
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Arm description:

Duvelisib PO BID at a starting dose of 75 mg was administered for the first 2 cycles (28-day cycles), followed by a mandatory reduction to 25 mg BID thereafter for those participants with complete response (CR), partial response (PR) or stable disease (SD), in 28-day cycles (dose determined in Optimization Phase).

Arm type	Experimental
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Investigational medicinal product name	Duvelisib
Investigational medicinal product code	
Other name	IPI-145
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Duvelisib PO BID in 28-day cycles (dose determined in Optimization Phase).

Number of subjects in period 1	Dose Optimization Phase: Cohort 1	Dose Optimization Phase: Cohort 2	Expansion Phase
Started	20	13	123
Received at Least 1 Dose of Study Drug	20	13	123
Completed	0	0	0
Not completed	20	13	123
Consent withdrawn by subject	1	1	4
Adverse event, non-fatal	-	-	1
Death	16	11	78
Progressive Disease	-	-	1
Closure Of The Study By The Sponsor	3	1	39

Baseline characteristics

Reporting groups

Reporting group title	Dose Optimization Phase: Cohort 1
Reporting group description:	
Duvelisib was administered orally (PO) twice daily (BID) at a starting dose of 25 milligrams (mg), with potential escalation on a per-participant basis to 50 mg and then 75 mg, based on the participant's response to and tolerance of therapy, in 28-day cycles.	
Reporting group title	Dose Optimization Phase: Cohort 2
Reporting group description:	
Duvelisib 75 mg PO BID was administered in 28-day cycles.	
Reporting group title	Expansion Phase
Reporting group description:	
Duvelisib PO BID at a starting dose of 75 mg was administered for the first 2 cycles (28-day cycles), followed by a mandatory reduction to 25 mg BID thereafter for those participants with complete response (CR), partial response (PR) or stable disease (SD), in 28-day cycles (dose determined in Optimization Phase).	

Reporting group values	Dose Optimization Phase: Cohort 1	Dose Optimization Phase: Cohort 2	Expansion Phase
Number of subjects	20	13	123
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			
arithmetic mean	64.0	65.0	62.9
standard deviation	± 14.81	± 7.22	± 13.59
Gender categorical			
Units: Subjects			
Female	6	4	56
Male	14	9	67
Ethnicity (NIH/OMB)			
National Institutes of Health/Office of Management and Budget (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	2	0	12
Not Hispanic or Latino	18	12	111
Unknown or Not Reported	0	1	0
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	1	18

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	0	9
White	16	12	92
More than one race	0	0	0
Unknown or Not Reported	1	0	4
Eastern Cooperative Oncology Group (ECOG) Performance Status			
ECOG Performance Status is a scale that measures how cancer affects a participant's daily living abilities. The scale ranges from 0 (fully active) to 5 (dead). 0 = fully active without restriction; 1 = Restricted in physically strenuous activity; 2 = Ambulatory, capable of all selfcare; 3 = Capable of limited selfcare; 4 = Completely disabled; 5 = Dead.			
Units: Subjects			
Status - 0	8	5	49
Status - 1	8	7	64
Status - 2	3	1	10
Status - 3	0	0	0
Status - 4	0	0	0
Status - 5	0	0	0
Missing	1	0	0

Reporting group values	Total		
Number of subjects	156		
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			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	66		
Male	90		
Ethnicity (NIH/OMB)			
National Institutes of Health/Office of Management and Budget (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	14		
Not Hispanic or Latino	141		
Unknown or Not Reported	1		
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0		

Asian	20		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	11		
White	120		
More than one race	0		
Unknown or Not Reported	5		
Eastern Cooperative Oncology Group (ECOG) Performance Status			
ECOG Performance Status is a scale that measures how cancer affects a participant's daily living abilities. The scale ranges from 0 (fully active) to 5 (dead). 0 = fully active without restriction; 1 = Restricted in physically strenuous activity; 2 = Ambulatory, capable of all selfcare; 3 = Capable of limited selfcare; 4 = Completely disabled; 5 = Dead.			
Units: Subjects			
Status - 0	62		
Status - 1	79		
Status - 2	14		
Status - 3	0		
Status - 4	0		
Status - 5	0		
Missing	1		

End points

End points reporting groups

Reporting group title	Dose Optimization Phase: Cohort 1
Reporting group description: Duvelisib was administered orally (PO) twice daily (BID) at a starting dose of 25 milligrams (mg), with potential escalation on a per-participant basis to 50 mg and then 75 mg, based on the participant's response to and tolerance of therapy, in 28-day cycles.	
Reporting group title	Dose Optimization Phase: Cohort 2
Reporting group description: Duvelisib 75 mg PO BID was administered in 28-day cycles.	
Reporting group title	Expansion Phase
Reporting group description: Duvelisib PO BID at a starting dose of 75 mg was administered for the first 2 cycles (28-day cycles), followed by a mandatory reduction to 25 mg BID thereafter for those participants with complete response (CR), partial response (PR) or stable disease (SD), in 28-day cycles (dose determined in Optimization Phase).	
Subject analysis set title	Dose Optimization Efficacy Set
Subject analysis set type	Sub-group analysis
Subject analysis set description: All participants who received at least one dose of study drug, completed at least one cycle of treatment, and have at least one scan to assess disease response after completion of one cycle of treatment.	
Subject analysis set title	Modified Intent-to-treat (mITT)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: All participants who receive at least one dose of study drug.	
Subject analysis set title	All Participants
Subject analysis set type	Full analysis
Subject analysis set description: Every study participant that received at least 1 dose of study drug and had evaluable data.	
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis
Subject analysis set description: All participants who receive at least one dose of study drug.	

Primary: Overall Response Rate (ORR) as Assessed by the Investigator Using the Lugano Criteria

End point title	Overall Response Rate (ORR) as Assessed by the Investigator Using the Lugano Criteria ^{[1][2]}
End point description: ORR was defined as the percentage of participants with complete response (CR) + partial response (PR), as assessed by the investigator using the Lugano criteria, for participants receiving the optimal dose of duvelisib for at least one cycle of study therapy. Here, 'Number of subjects analysed' signifies those participants who were evaluable for this end point.	
End point type	Primary
End point timeframe: 56 days (2 cycles; 28-day cycles)	

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 descriptive statistics (percentage of participants plus confidence interval) are reported for this primary end point, as prespecified in the statistical analysis plan.

[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: As pre-specified, efficacy analysis using investigator assessment reported for the Dose

End point values	Dose Optimization Phase: Cohort 1	Dose Optimization Phase: Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13 ^[3]	13 ^[4]		
Units: percentage of participants				
number (confidence interval 95%)	53.8 (26.7 to 80.9)	53.8 (26.7 to 80.9)		

Notes:

[3] - Dose Optimization Efficacy Set

[4] - Dose Optimization Efficacy Set

Statistical analyses

No statistical analyses for this end point

Primary: ORR as Assessed by the Independent Review Committee (IRC) Using the Lugano Criteria

End point title	ORR as Assessed by the Independent Review Committee (IRC) Using the Lugano Criteria ^[5] ^[6]
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End point description:

ORR was defined as the percentage of participants with CR + PR, as assessed by the IRC using the Lugano criteria, for participants receiving the optimal dose of duvelisib for at least one cycle of study therapy. Here, 'Number of subjects analysed' signifies those participants who were evaluable for this end point.

End point type	Primary
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End point timeframe:

56 days (2 cycles; 28-day cycles)

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: As pre-specified, efficacy analysis using IRC assessment reported for the Expansion Phase only.

[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: Only descriptive statistics (percentage of participants plus confidence interval) are reported for this primary end point, as prespecified in the statistical analysis plan.

End point values	Expansion Phase			
Subject group type	Reporting group			
Number of subjects analysed	123 ^[7]			
Units: percentage of participants				
number (confidence interval 95%)	48.0 (39.1 to 56.8)			

Notes:

[7] - Modified Intent-to-treat (mITT)

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) as Assessed by the Investigator Using the Lugano Criteria

End point title	Duration of Response (DOR) as Assessed by the Investigator Using the Lugano Criteria ^[8]
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End point description:

DOR was defined for participants with CR or PR as the time from the date of the first documentation of response (CR or PR) to the date of the first documentation of progressive disease (PD) or death due to any cause. Participants who withdrew from the study for any reason prior to PD and participants who had ongoing response at the time of the data cut were censored at the date of their last response assessment. Here, 'Number of subjects analysed' signifies those participants who were evaluable for this end point. '9999' = Insufficient number of participants with events to calculate upper confidence intervals.

End point type	Secondary
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End point timeframe:

Up to 70 months

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: As pre-specified, efficacy analysis using investigator assessment reported for the Dose Optimization Phase only.

End point values	Dose Optimization Phase: Cohort 1	Dose Optimization Phase: Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5 ^[9]	5 ^[10]		
Units: month				
median (confidence interval 95%)	4.22 (1.87 to 9999)	3.32 (1.77 to 9999)		

Notes:

[9] - Dose Optimization Efficacy Set

[10] - Dose Optimization Efficacy Set

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS) as Assessed by the Investigator Using the Lugano Criteria

End point title	Progression-free Survival (PFS) as Assessed by the Investigator Using the Lugano Criteria ^[11]
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End point description:

PFS was defined as the time from the date of first treatment to the date of the first radiographic disease progression or death due to any cause, whichever occurred first. Here, 'Number of subjects analysed' signifies those participants who were evaluable for this end point.

End point type	Secondary
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End point timeframe:

Up to 70 months

Notes:

[11] - 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: As pre-specified, efficacy analysis using investigator assessment reported for the Dose Optimization Phase only.

End point values	Dose Optimization Phase: Cohort 1	Dose Optimization Phase: Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10 ^[12]	11 ^[13]		
Units: month				
median (confidence interval 95%)	3.55 (1.05 to 8.54)	3.55 (1.81 to 13.14)		

Notes:

[12] - Dose Optimization Efficacy Set

[13] - Dose Optimization Efficacy Set

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR) as Assessed by the Investigator Using the Lugano Criteria

End point title	Disease Control Rate (DCR) as Assessed by the Investigator Using the Lugano Criteria ^[14]
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End point description:

DCR was defined as the percentage of participants with a best overall response of CR or PR or with a best overall response of stable disease (SD) sustained for at least 8 weeks. Here, 'Number of subjects analysed' signifies those participants who were evaluable for this end point.

End point type	Secondary
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End point timeframe:

Up to 8 weeks

Notes:

[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: As pre-specified, efficacy analysis using investigator assessment reported for the Dose Optimization Phase only.

End point values	Dose Optimization Phase: Cohort 1	Dose Optimization Phase: Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13 ^[15]	13 ^[16]		
Units: percentage of participants				
median (confidence interval 95%)	61.5 (35.1 to 88.0)	61.5 (35.1 to 88.0)		

Notes:

[15] - Dose Optimization Efficacy Set

[16] - Dose Optimization Efficacy Set

Statistical analyses

No statistical analyses for this end point

Secondary: DOR as Assessed by the IRC Using the Lugano Criteria

End point title	DOR as Assessed by the IRC Using the Lugano Criteria ^[17]
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End point description:

DOR was defined for participants with CR or PR as the time from the date of the first documentation of response (CR or PR) to the date of the first documentation of progressive disease or death due to any

cause. Participants who withdrew from the study for any reason prior to PD and participants who had ongoing response at the time of the data cut were censored at the date of their last response assessment. Here, 'Number of subjects analysed' signifies those participants who were evaluable for this end point.

End point type	Secondary
End point timeframe:	
Up to 70 months	

Notes:

[17] - 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: As pre-specified, efficacy analysis using IRC assessment reported for the Expansion Phase only.

End point values	Expansion Phase			
Subject group type	Reporting group			
Number of subjects analysed	25 ^[18]			
Units: month				
median (confidence interval 95%)	7.9 (6.4 to 21.00)			

Notes:

[18] - Modified Intent-to-treat (mITT)

Statistical analyses

No statistical analyses for this end point

Secondary: PFS as Assessed by the IRC Using the Lugano Criteria

End point title	PFS as Assessed by the IRC Using the Lugano Criteria ^[19]
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End point description:

PFS was defined as the time from the date of first treatment to the date of the first radiographic disease progression or death due to any cause, whichever occurred first. Here, 'Number of subjects analysed' signifies those participants who were evaluable for this end point.

End point type	Secondary
End point timeframe:	
Up to 70 months	

Notes:

[19] - 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: As pre-specified, efficacy analysis using IRC assessment reported for the Expansion Phase only.

End point values	Expansion Phase			
Subject group type	Reporting group			
Number of subjects analysed	74 ^[20]			
Units: month				
median (confidence interval 95%)	3.4 (1.8 to 3.9)			

Notes:

[20] - Modified Intent-to-treat (mITT)

Statistical analyses

No statistical analyses for this end point

Secondary: DCR as Assessed by the IRC Using the Lugano Criteria

End point title	DCR as Assessed by the IRC Using the Lugano Criteria ^[21]
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End point description:

DCR was defined as the participants with a best overall response of CR or PR or with a best overall response of SD sustained for at least 8 weeks. Here, 'Number of subjects analysed' signifies those participants who were evaluable for this end point.

End point type	Secondary
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End point timeframe:

Up to 8 weeks

Notes:

[21] - 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: As pre-specified, efficacy analysis using IRC assessment reported for the Expansion Phase only.

End point values	Expansion Phase			
Subject group type	Reporting group			
Number of subjects analysed	123 ^[22]			
Units: percentage of participants				
number (confidence interval 95%)	49.6 (40.8 to 58.4)			

Notes:

[22] - Modified Intent-to-treat (mITT)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
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End point description:

OS was defined as the time from the date of first treatment to the date of death due to any cause. Participants without documented death were censored at last alive date. Here, 'Number of subjects analysed' signifies those participants who were evaluable for this end point. '9999' = Insufficient number of participants with events to calculate the upper confidence interval.

End point type	Secondary
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End point timeframe:

Up to 70 months

End point values	Dose Optimization Phase: Cohort 1	Dose Optimization Phase: Cohort 2	Expansion Phase	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9 ^[23]	11 ^[24]	78 ^[25]	
Units: month				
median (confidence interval 95%)	6.70 (5.22 to 9999)	10.58 (6.67 to 44.62)	12.4 (8.4 to 22.7)	

Notes:

[23] - Dose Optimization Efficacy Set

[24] - Dose Optimization Efficacy Set

[25] - Modified Intent-to-treat (mITT)

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of IPI-145 (Duvelisib) and IPI-656 (Metabolite)

End point title	Plasma Concentration of IPI-145 (Duvelisib) and IPI-656 (Metabolite)
End point description: Blood samples were taken for the analyses of duvelisib and IPI-656 in plasma at the designated time points. Results are reported as nanograms/millilitre (ng/mL). Here, 'Number of subjects analysed' signifies those participants who were evaluable for this end point. '9999' = data not available due to no participants evaluable at the specified timepoint.	
End point type	Secondary
End point timeframe: Day 15 of Cycles 1 and 2 (28-day cycles)	

End point values	Dose Optimization Phase: Cohort 1	Dose Optimization Phase: Cohort 2	Expansion Phase	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14 ^[26]	12 ^[27]	100 ^[28]	
Units: ng/mL				
arithmetic mean (standard deviation)				
Duvelisib: Cycle 1, Day 15	1238.1 (± 787.53)	2070.0 (± 889.39)	2873.7 (± 1709.15)	
Duvelisib: Cycle 2, Day 15	1492.5 (± 1019.10)	9999 (± 9999)	2648.2 (± 1336.94)	
Metabolite (IPI-156): Cycle 1, Day 15	1310.4 (± 1408.99)	1580.9 (± 772.13)	2387.5 (± 1919.33)	
Metabolite (IPI-156): Cycle 2, Day 15	894.8 (± 441.55)	9999 (± 9999)	2427.0 (± 1655.89)	

Notes:

[26] - Safety Analysis Set; Cycle 1, Day 15: N=14; Cycle 2, Day 15: N=4

[27] - Safety Analysis Set; Cycle 1, Day 15: N=12; Cycle 2, Day 15: N=0

[28] - Safety Analysis Set; Cycle 1, Day 15: N=100; Cycle 2, Day 15: N=68

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of treatment (Day 1) to end of study (70 months).

Adverse event reporting additional description:

All reported safety data based upon Safety Analysis Set: all participants who received at least one dose of study drug. All-cause mortality reported as occurrence of death due to any cause during the study and after study discontinuation.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24
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Reporting groups

Reporting group title	Dose Optimization Phase: Cohort 1
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Reporting group description:

Duvelisib PO BID at a starting dose of 25 mg, with potential escalation on a per-participant basis to 50 mg and then 75 mg, based on the participant's response to and tolerance of therapy, in 28-day cycles.

Reporting group title	Expansion Phase
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Reporting group description:

Duvelisib PO BID at a starting dose of 75 mg for the first 2 cycles, followed by a mandatory reduction to 25 mg BID thereafter for those participants with CR, PR or SD, in 28-day cycles (dose determined in Optimization Phase).

Reporting group title	Dose Optimization Phase: Cohort 2
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Reporting group description:

Duvelisib 75 mg PO BID, administered in 28-day cycles.

Serious adverse events	Dose Optimization Phase: Cohort 1	Expansion Phase	Dose Optimization Phase: Cohort 2
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 20 (70.00%)	60 / 123 (48.78%)	9 / 13 (69.23%)
number of deaths (all causes)	16	78	11
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Epstein-Barr virus associated lymphoproliferative disorder			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Post transplant lymphoproliferative disorder			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Allogenic stem cell transplantation			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 20 (5.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Chills			
subjects affected / exposed	1 / 20 (5.00%)	0 / 123 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	3 / 20 (15.00%)	10 / 123 (8.13%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 10	0 / 0
deaths causally related to treatment / all	0 / 3	0 / 10	0 / 0
Pyrexia			

subjects affected / exposed	1 / 20 (5.00%)	6 / 123 (4.88%)	3 / 13 (23.08%)
occurrences causally related to treatment / all	0 / 1	3 / 6	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 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	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 20 (5.00%)	0 / 123 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 20 (5.00%)	1 / 123 (0.81%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Hypoxia			
subjects affected / exposed	1 / 20 (5.00%)	2 / 123 (1.63%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Dyspnoea			
subjects affected / exposed	2 / 20 (10.00%)	0 / 123 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory failure			
subjects affected / exposed	2 / 20 (10.00%)	1 / 123 (0.81%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 20 (10.00%)	3 / 123 (2.44%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	2 / 2	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 123 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 20 (5.00%)	3 / 123 (2.44%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	1 / 1	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 20 (0.00%)	2 / 123 (1.63%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			

subjects affected / exposed	1 / 20 (5.00%)	1 / 123 (0.81%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 20 (5.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 123 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular dementia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cerebrovascular accident			

subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 20 (0.00%)	2 / 123 (1.63%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 123 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 20 (5.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 20 (5.00%)	1 / 123 (0.81%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 20 (5.00%)	2 / 123 (1.63%)	2 / 13 (15.38%)
occurrences causally related to treatment / all	1 / 1	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			

subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Vomiting			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal inflammation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 123 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 20 (5.00%)	9 / 123 (7.32%)	2 / 13 (15.38%)
occurrences causally related to treatment / all	1 / 1	9 / 11	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 123 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cholecystitis acute			

subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 123 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash morbilliform			
subjects affected / exposed	0 / 20 (0.00%)	0 / 123 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	1 / 20 (5.00%)	1 / 123 (0.81%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	1 / 1	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythema			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eczema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 123 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin lesion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	1 / 20 (5.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	1 / 20 (5.00%)	2 / 123 (1.63%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Synovial cyst			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	3 / 20 (15.00%)	3 / 123 (2.44%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	2 / 3	3 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia			
subjects affected / exposed	4 / 20 (20.00%)	4 / 123 (3.25%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	4 / 6	2 / 4	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 20 (0.00%)	2 / 123 (1.63%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 20 (0.00%)	2 / 123 (1.63%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Enterocolitis infectious			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex viraemia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective spondylitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cryptococcosis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Coronavirus infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 123 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 123 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	1 / 20 (5.00%)	0 / 123 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic candida			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 20 (0.00%)	2 / 123 (1.63%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			

subjects affected / exposed	1 / 20 (5.00%)	0 / 123 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 123 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 123 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 20 (5.00%)	2 / 123 (1.63%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 1	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour lysis syndrome			
subjects affected / exposed	1 / 20 (5.00%)	0 / 123 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 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	Dose Optimization Phase: Cohort 1	Expansion Phase	Dose Optimization Phase: Cohort 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 20 (95.00%)	120 / 123 (97.56%)	13 / 13 (100.00%)
Vascular disorders			
Thrombophlebitis superficial			
subjects affected / exposed	0 / 20 (0.00%)	0 / 123 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hypertension			

subjects affected / exposed	1 / 20 (5.00%)	16 / 123 (13.01%)	1 / 13 (7.69%)
occurrences (all)	2	27	1
Hypotension			
subjects affected / exposed	3 / 20 (15.00%)	12 / 123 (9.76%)	2 / 13 (15.38%)
occurrences (all)	4	13	2
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	2 / 20 (10.00%)	3 / 123 (2.44%)	0 / 13 (0.00%)
occurrences (all)	2	4	0
Generalised oedema			
subjects affected / exposed	2 / 20 (10.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences (all)	2	1	0
Fatigue			
subjects affected / exposed	7 / 20 (35.00%)	38 / 123 (30.89%)	6 / 13 (46.15%)
occurrences (all)	12	40	6
Face oedema			
subjects affected / exposed	4 / 20 (20.00%)	1 / 123 (0.81%)	1 / 13 (7.69%)
occurrences (all)	4	1	1
Chills			
subjects affected / exposed	2 / 20 (10.00%)	8 / 123 (6.50%)	1 / 13 (7.69%)
occurrences (all)	2	11	1
Swelling face			
subjects affected / exposed	0 / 20 (0.00%)	0 / 123 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	6 / 20 (30.00%)	28 / 123 (22.76%)	6 / 13 (46.15%)
occurrences (all)	9	49	6
Oedema peripheral			
subjects affected / exposed	6 / 20 (30.00%)	19 / 123 (15.45%)	3 / 13 (23.08%)
occurrences (all)	6	23	8
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 123 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Drug hypersensitivity			

subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 123 (0.00%) 0	1 / 13 (7.69%) 1
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 20 (0.00%)	0 / 123 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	2 / 20 (10.00%)	6 / 123 (4.88%)	1 / 13 (7.69%)
occurrences (all)	4	6	2
Productive cough			
subjects affected / exposed	1 / 20 (5.00%)	5 / 123 (4.07%)	2 / 13 (15.38%)
occurrences (all)	1	5	3
Pulmonary oedema			
subjects affected / exposed	1 / 20 (5.00%)	2 / 123 (1.63%)	1 / 13 (7.69%)
occurrences (all)	1	2	1
Hypoxia			
subjects affected / exposed	0 / 20 (0.00%)	2 / 123 (1.63%)	1 / 13 (7.69%)
occurrences (all)	0	2	2
Upper-airway cough syndrome			
subjects affected / exposed	1 / 20 (5.00%)	2 / 123 (1.63%)	1 / 13 (7.69%)
occurrences (all)	1	2	1
Wheezing			
subjects affected / exposed	2 / 20 (10.00%)	2 / 123 (1.63%)	1 / 13 (7.69%)
occurrences (all)	2	2	1
Oropharyngeal pain			
subjects affected / exposed	0 / 20 (0.00%)	11 / 123 (8.94%)	0 / 13 (0.00%)
occurrences (all)	0	15	0
Cough			
subjects affected / exposed	5 / 20 (25.00%)	15 / 123 (12.20%)	4 / 13 (30.77%)
occurrences (all)	7	17	4
Dyspnoea			
subjects affected / exposed	3 / 20 (15.00%)	17 / 123 (13.82%)	1 / 13 (7.69%)
occurrences (all)	4	19	1
Rhinorrhoea			

subjects affected / exposed	0 / 20 (0.00%)	3 / 123 (2.44%)	1 / 13 (7.69%)
occurrences (all)	0	3	1
Respiratory failure			
subjects affected / exposed	0 / 20 (0.00%)	0 / 123 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 20 (20.00%)	10 / 123 (8.13%)	0 / 13 (0.00%)
occurrences (all)	4	11	0
Confusional state			
subjects affected / exposed	2 / 20 (10.00%)	1 / 123 (0.81%)	0 / 13 (0.00%)
occurrences (all)	2	2	0
Anxiety			
subjects affected / exposed	1 / 20 (5.00%)	5 / 123 (4.07%)	2 / 13 (15.38%)
occurrences (all)	1	6	2
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 20 (20.00%)	47 / 123 (38.21%)	7 / 13 (53.85%)
occurrences (all)	8	98	18
Amylase increased			
subjects affected / exposed	2 / 20 (10.00%)	9 / 123 (7.32%)	0 / 13 (0.00%)
occurrences (all)	4	18	0
Blood alkaline phosphatase increased			
subjects affected / exposed	4 / 20 (20.00%)	12 / 123 (9.76%)	1 / 13 (7.69%)
occurrences (all)	7	15	1
Lymphocyte count decreased			
subjects affected / exposed	4 / 20 (20.00%)	17 / 123 (13.82%)	2 / 13 (15.38%)
occurrences (all)	9	43	2
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 20 (20.00%)	45 / 123 (36.59%)	5 / 13 (38.46%)
occurrences (all)	5	99	7
Blood bilirubin increased			
subjects affected / exposed	1 / 20 (5.00%)	10 / 123 (8.13%)	1 / 13 (7.69%)
occurrences (all)	1	14	2
Blood culture positive			

subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Blood immunoglobulin G decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 123 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood lactate dehydrogenase			
subjects affected / exposed	0 / 20 (0.00%)	2 / 123 (1.63%)	1 / 13 (7.69%)
occurrences (all)	0	2	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	2 / 20 (10.00%)	20 / 123 (16.26%)	1 / 13 (7.69%)
occurrences (all)	2	23	1
Immunoglobulins decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 123 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Lipase increased			
subjects affected / exposed	3 / 20 (15.00%)	13 / 123 (10.57%)	0 / 13 (0.00%)
occurrences (all)	5	15	0
Neutrophil count decreased			
subjects affected / exposed	8 / 20 (40.00%)	41 / 123 (33.33%)	3 / 13 (23.08%)
occurrences (all)	17	101	9
Platelet count decreased			
subjects affected / exposed	11 / 20 (55.00%)	34 / 123 (27.64%)	6 / 13 (46.15%)
occurrences (all)	14	67	10
Urine output decreased			
subjects affected / exposed	2 / 20 (10.00%)	0 / 123 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Weight decreased			
subjects affected / exposed	3 / 20 (15.00%)	8 / 123 (6.50%)	3 / 13 (23.08%)
occurrences (all)	3	11	5
Weight increased			
subjects affected / exposed	2 / 20 (10.00%)	4 / 123 (3.25%)	0 / 13 (0.00%)
occurrences (all)	2	5	0
Blood creatinine increased			
subjects affected / exposed	3 / 20 (15.00%)	16 / 123 (13.01%)	0 / 13 (0.00%)
occurrences (all)	3	23	0

White blood cell count decreased subjects affected / exposed occurrences (all)	7 / 20 (35.00%) 13	25 / 123 (20.33%) 41	3 / 13 (23.08%) 6
Cardiac disorders			
Sinus tachycardia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	7 / 123 (5.69%) 9	2 / 13 (15.38%) 2
Tachycardia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	4 / 123 (3.25%) 4	2 / 13 (15.38%) 2
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	8 / 123 (6.50%) 9	3 / 13 (23.08%) 3
Presyncope subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 123 (0.00%) 0	1 / 13 (7.69%) 1
Dizziness subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3	9 / 123 (7.32%) 12	2 / 13 (15.38%) 2
Sciatica subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 123 (0.81%) 1	1 / 13 (7.69%) 1
Hypoaesthesia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	2 / 123 (1.63%) 3	1 / 13 (7.69%) 1
Dysgeusia subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2	10 / 123 (8.13%) 11	1 / 13 (7.69%) 2
Paraesthesia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	9 / 123 (7.32%) 9	0 / 13 (0.00%) 0
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	8 / 123 (6.50%) 9	0 / 13 (0.00%) 0
Blood and lymphatic system disorders			

Normocytic anaemia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 123 (0.00%) 0	1 / 13 (7.69%) 1
Eosinophilia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	7 / 123 (5.69%) 8	0 / 13 (0.00%) 0
Anaemia subjects affected / exposed occurrences (all)	7 / 20 (35.00%) 7	34 / 123 (27.64%) 56	5 / 13 (38.46%) 13
Autoimmune haemolytic anaemia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 123 (0.00%) 0	1 / 13 (7.69%) 1
Ear and labyrinth disorders Ear discomfort subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	2 / 123 (1.63%) 2	1 / 13 (7.69%) 1
Eye disorders Periorbital oedema subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 123 (0.00%) 0	1 / 13 (7.69%) 5
Cataract subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 123 (0.00%) 0	1 / 13 (7.69%) 1
Dry eye subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	5 / 123 (4.07%) 5	1 / 13 (7.69%) 1
Eye irritation subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 123 (0.00%) 0	1 / 13 (7.69%) 1
Vitreous floaters subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	2 / 123 (1.63%) 2	1 / 13 (7.69%) 1
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)	6 / 20 (30.00%) 7	16 / 123 (13.01%) 18	2 / 13 (15.38%) 2
Oral pain			

subjects affected / exposed	0 / 20 (0.00%)	3 / 123 (2.44%)	2 / 13 (15.38%)
occurrences (all)	0	3	2
Colitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Constipation			
subjects affected / exposed	5 / 20 (25.00%)	22 / 123 (17.89%)	2 / 13 (15.38%)
occurrences (all)	5	24	3
Stomatitis			
subjects affected / exposed	1 / 20 (5.00%)	15 / 123 (12.20%)	3 / 13 (23.08%)
occurrences (all)	1	21	5
Diarrhoea			
subjects affected / exposed	9 / 20 (45.00%)	41 / 123 (33.33%)	9 / 13 (69.23%)
occurrences (all)	13	63	18
Haemorrhoids			
subjects affected / exposed	0 / 20 (0.00%)	1 / 123 (0.81%)	2 / 13 (15.38%)
occurrences (all)	0	1	2
Nausea			
subjects affected / exposed	9 / 20 (45.00%)	31 / 123 (25.20%)	6 / 13 (46.15%)
occurrences (all)	12	37	6
Gastrointestinal inflammation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 123 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 123 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	1 / 20 (5.00%)	5 / 123 (4.07%)	1 / 13 (7.69%)
occurrences (all)	1	5	1
Dyspepsia			
subjects affected / exposed	1 / 20 (5.00%)	9 / 123 (7.32%)	2 / 13 (15.38%)
occurrences (all)	1	9	3
Dry mouth			
subjects affected / exposed	1 / 20 (5.00%)	8 / 123 (6.50%)	0 / 13 (0.00%)
occurrences (all)	1	8	0
Abdominal pain			

subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2	13 / 123 (10.57%) 17	4 / 13 (30.77%) 4
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 123 (0.00%) 0	1 / 13 (7.69%) 1
Skin and subcutaneous tissue disorders			
Rash erythematous			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	3 / 123 (2.44%) 3	4 / 13 (30.77%) 6
Dermatitis acneiform			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 123 (0.81%) 1	1 / 13 (7.69%) 1
Dry skin			
subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2	13 / 123 (10.57%) 18	3 / 13 (23.08%) 6
Eczema			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	2 / 123 (1.63%) 3	1 / 13 (7.69%) 1
Erythema			
subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3	6 / 123 (4.88%) 12	2 / 13 (15.38%) 2
Hyperhidrosis			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	4 / 123 (3.25%) 4	1 / 13 (7.69%) 1
Night sweats			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	4 / 123 (3.25%) 4	2 / 13 (15.38%) 3
Pain of skin			
subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 123 (0.00%) 0	1 / 13 (7.69%) 2
Rash pruritic			
subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	2 / 123 (1.63%) 3	2 / 13 (15.38%) 2
Rash maculo-papular			

subjects affected / exposed occurrences (all)	7 / 20 (35.00%) 7	21 / 123 (17.07%) 37	2 / 13 (15.38%) 7
Rash macular subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 123 (0.81%) 2	1 / 13 (7.69%) 2
Photosensitivity reaction subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	2 / 123 (1.63%) 2	1 / 13 (7.69%) 1
Pruritus subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 4	20 / 123 (16.26%) 29	3 / 13 (23.08%) 4
Rash subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3	14 / 123 (11.38%) 31	3 / 13 (23.08%) 3
Psoriasis subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 123 (0.00%) 0	1 / 13 (7.69%) 1
Renal and urinary disorders Urinary retention subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 123 (0.00%) 0	1 / 13 (7.69%) 1
Acute kidney injury subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3	2 / 123 (1.63%) 2	1 / 13 (7.69%) 1
Musculoskeletal and connective tissue disorders Neck pain subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 3	4 / 123 (3.25%) 4	0 / 13 (0.00%) 0
Pain in extremity subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3	5 / 123 (4.07%) 5	1 / 13 (7.69%) 1
Arthralgia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	17 / 123 (13.82%) 24	2 / 13 (15.38%) 2
Muscular weakness			

subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 2	3 / 123 (2.44%) 4	2 / 13 (15.38%) 2
Bursitis subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	2 / 123 (1.63%) 2	1 / 13 (7.69%) 1
Back pain subjects affected / exposed occurrences (all)	4 / 20 (20.00%) 4	9 / 123 (7.32%) 9	1 / 13 (7.69%) 1
Myalgia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	7 / 123 (5.69%) 7	1 / 13 (7.69%) 1
Infections and infestations			
COVID-19 subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	7 / 123 (5.69%) 7	0 / 13 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	5 / 123 (4.07%) 5	1 / 13 (7.69%) 1
Oral candidiasis subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	2 / 123 (1.63%) 2	2 / 13 (15.38%) 3
Mucosal infection subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	2 / 123 (1.63%) 2	1 / 13 (7.69%) 1
Clostridium difficile colitis subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 123 (0.00%) 0	1 / 13 (7.69%) 1
Pneumonia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	1 / 123 (0.81%) 1	1 / 13 (7.69%) 1
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	5 / 123 (4.07%) 5	1 / 13 (7.69%) 1
Adenovirus infection subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 123 (0.00%) 0	1 / 13 (7.69%) 1

Oesophageal candidiasis subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 123 (0.81%) 1	1 / 13 (7.69%) 1
Influenza subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 123 (0.00%) 0	1 / 13 (7.69%) 2
Eye infection subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 123 (0.00%) 0	2 / 13 (15.38%) 2
Metabolism and nutrition disorders			
Dehydration subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	4 / 123 (3.25%) 4	4 / 13 (30.77%) 5
Decreased appetite subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	11 / 123 (8.94%) 12	2 / 13 (15.38%) 2
Glucose tolerance impaired subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2	2 / 123 (1.63%) 2	0 / 13 (0.00%) 0
Hypophosphataemia subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 4	1 / 123 (0.81%) 1	2 / 13 (15.38%) 2
Hyponatraemia subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3	15 / 123 (12.20%) 20	2 / 13 (15.38%) 3
Hypomagnesaemia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	6 / 123 (4.88%) 10	1 / 13 (7.69%) 1
Hypokalaemia subjects affected / exposed occurrences (all)	6 / 20 (30.00%) 7	13 / 123 (10.57%) 20	4 / 13 (30.77%) 4
Hypocalcaemia subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3	5 / 123 (4.07%) 5	1 / 13 (7.69%) 2
Hyperglycaemia			

subjects affected / exposed	1 / 20 (5.00%)	12 / 123 (9.76%)	0 / 13 (0.00%)
occurrences (all)	3	18	0
Hypoalbuminaemia			
subjects affected / exposed	2 / 20 (10.00%)	10 / 123 (8.13%)	3 / 13 (23.08%)
occurrences (all)	2	12	4
Hypercalcaemia			
subjects affected / exposed	1 / 20 (5.00%)	2 / 123 (1.63%)	1 / 13 (7.69%)
occurrences (all)	2	2	1
Lactic acidosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 123 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hyperuricaemia			
subjects affected / exposed	2 / 20 (10.00%)	7 / 123 (5.69%)	1 / 13 (7.69%)
occurrences (all)	2	7	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 March 2019	<ul style="list-style-type: none">- Objective/endpoint alignment- Population clarification- Expansion Phase dose determination
09 August 2019	<ul style="list-style-type: none">- Revised vital sign collection to occur at every visit, including C1D8, C1D15 and C2D15 visits- Added new sections with details related to participant data protection and quality assurance
16 September 2019	<ul style="list-style-type: none">- Modified text to indicate the optimal dose for the Expansion Phase has been selected and that the optimal dose was selected based on the interim results of the Dose Optimization Phase- Added new section: "End of Study Definition"- Modified text to indicate that live vaccines are prohibited for 3 months after last dose of study drug

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported