Clinical trial results:
A Phase 2, Randomized, Open-label, 2-Arm Study Comparing 2 Intermittent Dosing Schedules of Duvelisib in Subjects with Indolent Non-Hodgkin Lymphoma (iNHL)

Summary

EudraCT number	2019-001381-14
Trial protocol	CZ GB IT
Global end of trial date	24 July 2023

Results information

Result version number	v1 (current)
This version publication date	09 August 2024
First version publication date	09 August 2024

Trial information

Trial identification

Sponsor protocol code	VS-0145-229

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04038359
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	24 July 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 July 2023
Global end of trial reached?	Yes
Global end of trial date	24 July 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the efficacy of duvelisib administered with prescribed drug holidays in participants with iNHL, according to the 2007 revised International Working Group (IWG) Criteria.

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	01 November 2019
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	Korea, Republic of: 23
Country: Number of subjects enrolled	Russian Federation: 29
Country: Number of subjects enrolled	United States: 9
Country: Number of subjects enrolled	Poland: 15
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Czechia: 5
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Italy: 15
Worldwide total number of subjects	103
EEA total number of subjects	36

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	57
From 65 to 84 years	45
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

One participant withdrew consent prior to receiving any study drug.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Duvelisib, Continuous and Intermittent Dosing

Arm description:

Duvelisib 25 milligrams twice daily continuously for 10 weeks, followed by 25 milligrams twice daily dosed 2 weeks off and 2 weeks on of each subsequent 4-week cycle.

Arm type	Experimental
Investigational medicinal product name	Duvelisib
Investigational medicinal product code	
Other name	Copiktra, VS-0145, IPI-145
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Duvelisib was administered orally as a capsule at the dose and frequency described in the arm description.

Arm title	Duvelisib, Intermittent Dosing

Arm description:

Duvelisib 25 milligrams twice daily dosed 2 weeks on and 2 weeks off.

Arm type	Experimental
Investigational medicinal product name	Duvelisib
Investigational medicinal product code	
Other name	Copiktra, VS-0145, IPI-145
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Duvelisib was administered orally as a capsule at the dose and frequency described in the arm description.

Number of subjects in period 1[1]	Duvelisib, Continuous and Intermittent Dosing	Duvelisib, Intermittent Dosing
Started	51	51
Received At Least 1 Dose of Study Drug	51	51
Completed	32	36
Not completed	19	15

Participant moved	1	-
Physician decision	3	2
Consent withdrawn by subject	4	3
Adverse event, non-fatal	-	2
Death	8	7
Lost to follow-up	3	-
Progressive disease	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: One participant in the 'Duvelisib, Continuous and Intermittent Dosing' study arm withdrew consent prior to receiving any study drug.

Baseline characteristics

Reporting groups	
Reporting group title	Duvelisib, Continuous and Intermittent Dosing
Reporting group description:	
Duvelisib 25 milligrams twice daily continuously for 10 weeks, followed by 25 milligrams twice daily dosed 2 weeks off and 2 weeks on of each subsequent 4-week cycle.	
Reporting group title	Duvelisib, Intermittent Dosing
Reporting group description:	
Duvelisib 25 milligrams twice daily dosed 2 weeks on and 2 weeks off.	

Reporting group values	Duvelisib, Continuous and Intermittent Dosing	Duvelisib, Intermittent Dosing	Total
Number of subjects	51	51	102
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	60.5	63.9	
standard deviation	± 12.15	± 11.40	-
Gender categorical Units: Subjects			
Female	28	27	55
Male	23	24	47
Race Units: Subjects			
Asian	14	9	23
White	36	42	78
Black or African American	1	0	1
Ethnicity Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	48	50	98
Not Reported	2	0	2
Unknown	0	1	1

End points

End points reporting groups

Reporting group title	Duvelisib, Continuous and Intermittent Dosing
Reporting group description:	
Duvelisib 25 milligrams twice daily continuously for 10 weeks, followed by 25 milligrams twice daily dosed 2 weeks off and 2 weeks on of each subsequent 4-week cycle.	
Reporting group title	Duvelisib, Intermittent Dosing
Reporting group description:	
Duvelisib 25 milligrams twice daily dosed 2 weeks on and 2 weeks off.	
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 1 dose of duvelisib.	
Subject analysis set title	All-treated (AT) Analysis Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All participants who received at least 1 dose of study drug.	

Primary: Overall Response Rate (ORR) According to the 2007 Revised IWG Criteria

End point title	Overall Response Rate (ORR) According to the 2007 Revised IWG Criteria[1]
End point description:	
ORR was defined as the percentage of participants achieving a complete response (CR) or partial response (PR) and assessed using the 2007 revised IWG criteria. The 2007 revised IWG criteria defined CR as the disappearance of all evidence of disease and PR as the regression of measurable disease and no new sites. Here, 'Number of subjects analyzed' signifies those participants who were evaluable for this end point.	
End point type	Primary
End point timeframe:	
Up to 14 months	

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 pre-specified in the statistical analysis plan.

End point values	Duvelisib, Continuous and Intermittent Dosing	Duvelisib, Intermittent Dosing		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49[2]	51[3]		
Units: percentage of participants				
number (confidence interval 95%)				
mITT	65.3 (50.4 to 78.3)	52.9 (38.5 to 67.1)		
PP	62.2 (46.5 to 76.2)	54.3 (39.0 to 69.1)		

Notes:

[2] - mITT (N=49); PP (N=45)

[3] - mITT (N=51); PP (N=46)

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS)

End point title	Progression-free Survival (PFS)

End point description:

PFS was defined as the time from first dose to first progressive disease (PD) or death (progression date/death date - treatment start date + 1) or, for participants without PD or documented death, as the time from first dose to censoring date (censoring date – treatment start date + 1). The 2007 revised IWG criteria defined PD as any new lesion or increase by ≥50% of previously involved sites from nadir. The 2014 Lugano criteria defined PD as a progressive metabolic response (according to positron emission tomography-computed tomography [PET-CT]) and progressive disease (according to computed tomography [CT]). Results reported as months. Here, 'Number of subjects analyzed' signifies those participants who were evaluable for this end point.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	Duvelisib, Continuous and Intermittent Dosing	Duvelisib, Intermittent Dosing		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49[4]	51[5]		
Units: months				
median (confidence interval 95%)				
2007 Revised IWG Criteria	16.0 (8.5 to 27.2)	23.0 (12.5 to 34.3)		
2014 Lugano Criteria	16.0 (8.5 to 27.2)	23.0 (12.5 to 34.3)		

Notes:

[4] - mITT

[5] - mITT

Statistical analyses

No statistical analyses for this end point

Secondary: ORR at Specific Timepoints

End point title	ORR at Specific Timepoints

End point description:

ORR at 6, 12, 18, and 24 months after first dose of study intervention was defined as the percentage of participants achieving CR or PR at each timepoint and was assessed using both the 2007 revised IWG criteria and the 2014 Lugano criteria. The 2007 revised IWG criteria defined CR as the disappearance of all evidence of disease and PR as the regression of measurable disease and no new sites. The 2014 Lugano criteria defined CR as a complete metabolic response (according to PET-CT) and a complete radiologic response (according to CT) and PR as partial metabolic response (according to PET-CT) and partial remission (according to CT). The response was cumulative for each timepoint; a participant was considered a responder if their first response occurred up to the end of that timepoint. Here, 'Number of subjects analyzed' signifies those participants who were evaluable for this end point.

End point type	Secondary

End point timeframe:

6, 12, 18, and 24 months after first dose of study intervention

End point values	Duvelisib, Continuous and Intermittent Dosing	Duvelisib, Intermittent Dosing		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49[6]	51[7]		
Units: percentage of participants				
number (confidence interval 95%)				
6 months: 2007 Revised IWG Criteria	63.3 (48.3 to 76.6)	49.0 (34.8 to 63.4)		
12 months: 2007 Revised IWG Criteria	65.3 (50.4 to 78.3)	52.9 (38.5 to 67.1)		
18 months: 2007 Revised IWG Criteria	65.3 (50.4 to 78.3)	52.9 (38.5 to 67.1)		
24 months: 2007 Revised IWG Criteria	65.3 (50.4 to 78.3)	52.9 (38.5 to 67.1)		
6 months: 2014 Lugano Criteria	63.3 (48.3 to 76.6)	47.1 (32.9 to 61.5)		
12 months: 2014 Lugano Criteria	65.3 (50.4 to 78.3)	51.0 (36.6 to 65.2)		
18 months: 2014 Lugano Criteria	65.3 (50.4 to 78.3)	51.0 (36.6 to 65.2)		
24 months: 2014 Lugano Criteria	65.3 (50.4 to 78.3)	51.0 (36.6 to 65.2)		

Notes:

[6] - mITT

[7] - mITT

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

DOR was defined for participants with CR or PR as the time from the date of first documentation of response (CR or PR) to date of the first documentation of PD or death. The 2007 revised IWG criteria defined CR as the disappearance of all evidence of disease, PR as the regression of measurable disease and no new sites, and PD as any new lesion or increase by ≥50% of previously involved sites from nadir. The 2014 Lugano criteria defined CR as a complete metabolic response (according to PET-CT) and a complete radiologic response (according to CT), PR as partial metabolic response (according to PET-CT) and partial remission (according to CT), and PD as a progressive metabolic response (according to PET-CT) and progressive disease (according to CT). Results are reported as months. 9999=insufficient data available to generate summary-level data using prespecified method of analysis. Here, 'Number of subjects analyzed' signifies those participants who were evaluable for this end point.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	Duvelisib, Continuous and Intermittent Dosing	Duvelisib, Intermittent Dosing		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49[8]	51[9]		
Units: months				
median (confidence interval 95%)				
2007 Revised IWG Criteria	21.4 (13.7 to 9999)	32.2 (17.5 to 9999)		
2014 Lugano Criteria	21.4 (13.7 to 9999)	32.2 (13.8 to 9999)		

Notes:

[8] - mITT

[9] - mITT

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was the time from first dose to death (death date - treatment start date + 1). Participants without documented death were censored at their last known alive date (last known alive date - treatment start date + 1). Results reported as months. 9999=insufficient data available to generate summary-level data using prespecified method of analysis. Here, 'Number of subjects analyzed' signifies those participants who were evaluable for this end point.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	Duvelisib, Continuous and Intermittent Dosing	Duvelisib, Intermittent Dosing		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49[10]	51[11]		
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)		

Notes:

[10] - mITT

[11] - mITT

Statistical analyses

No statistical analyses for this end point

Secondary: Lymph Node Response Rate (LNRR)

End point title	Lymph Node Response Rate (LNRR)

End point description:

LNRR was calculated as the percentage of participants achieving ≥50% decrease in the sum of the

product of the diameters of target lymph nodes. The confidence interval for LNRR was calculated only for participants who had at least 1 nodal target lesion, using the Clopper-Pearson exact method for binomial proportions. Participants whose target lesions were all extranodal were excluded from this analysis. Here, 'Number of subjects analyzed' signifies those participants who were evaluable for this end point.

End point type	Secondary
End point timeframe:	
14 months	

End point values	Duvelisib, Continuous and Intermittent Dosing	Duvelisib, Intermittent Dosing		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49[12]	51[13]		
Units: percentage of participants				
number (confidence interval 95%)	64.3 (48.0 to 78.4)	60.9 (45.4 to 74.9)		

Notes:

[12] - mITT

[13] - mITT

Statistical analyses

No statistical analyses for this end point

Secondary: Time To First Response (TTFR)

End point title	Time To First Response (TTFR)

End point description:

For participants with CR or PR, TTFR was defined as the time from first dose of study intervention to time of first CR or PR and was calculated as: the date of first CR or PR – randomization date + 1. The 2007 revised IWG criteria defined CR as the disappearance of all evidence of disease and PR as the regression of measurable disease and no new sites. The 2014 Lugano criteria defined CR as a complete metabolic response (according to PET-CT) and a complete radiologic response (according to CT) and PR as partial metabolic response (according to PET-CT) and partial remission (according to CT). Results are reported as months. Here, 'Number of subjects analyzed' signifies those participants who were evaluable for this end point.

End point type	Secondary
End point timeframe:	
Up to 14 months	

End point values	Duvelisib, Continuous and Intermittent Dosing	Duvelisib, Intermittent Dosing		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32[14]	27[15]		
Units: months				
median (full range (min-max))				
2007 Revised IWG Criteria	2.30 (2.1 to 12.9)	2.30 (2.1 to 12.5)		

2014 Lugano Criteria	2.30 (2.1 to 12.9)	2.30 (2.1 to 12.5)		

Notes:

[14] - 2007 Revised IWG Criteria and 2014 Lugano Criteria: mITT (N=32)

[15] - 2007 Revised IWG Criteria: mITT (N=27); 2014 Lugano Criteria: mITT (N=26)

Statistical analyses

No statistical analyses for this end point

Secondary: Time To Treatment Failure (TTF)

End point title	Time To Treatment Failure (TTF)

End point description:

TTF was calculated as the time from first dose of study treatment to discontinuation for any reason (discontinuation date - treatment start date + 1). Participants who were still ongoing treatment at time of data cut were censored (last dose date - treatment start date + 1). Results reported as months. Here, 'Number of subjects analyzed' signifies those participants who were evaluable for this end point.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	Duvelisib, Continuous and Intermittent Dosing	Duvelisib, Intermittent Dosing		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49[16]	51[17]		
Units: months				
median (confidence interval 95%)	12.6 (6.2 to 17.1)	14.3 (8.0 to 23.0)		

Notes:

[16] - mITT

[17] - mITT

Statistical analyses

No statistical analyses for this end point

Secondary: ORR According to 2014 Lugano Criteria

End point title	ORR According to 2014 Lugano Criteria

End point description:

ORR was defined as the percentage of participants achieving a CR or PR and was assessed using the 2014 Lugano criteria. The 2014 Lugano criteria defined CR as a complete metabolic response (according to PET-CT) and a complete radiologic response (according to CT) and PR as partial metabolic response (according to PET-CT) and partial remission (according to CT). Here, 'Number of subjects analyzed' signifies those participants who were evaluable for this end point.

End point type	Secondary

End point timeframe:

Up to 14 months

End point values	Duvelisib, Continuous and Intermittent Dosing	Duvelisib, Intermittent Dosing		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49[18]	51[19]		
Units: percentage of participants				
number (confidence interval 95%)				
mITT	65.3 (50.4 to 78.3)	51.0 (36.6 to 65.2)		
PP	62.2 (46.5 to 76.2)	52.2 (36.9 to 67.1)		

Notes:

[18] - mITT (N=49); PP (N=45)

[19] - mITT (N=51); PP (N=46)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 37 months

Adverse event reporting additional description:

All reported safety data based upon All-treated (AT) Analysis Set: all participants who received at least 1 dose of duvelisib.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Duvelisib, Continuous and Intermittent Dosing

Reporting group description:

Duvelisib 25 milligrams twice daily continuously for 10 weeks, followed by 25 milligrams twice daily dosed 2 weeks off and 2 weeks on of each subsequent 4-week cycle.

Reporting group title	Duvelisib, Intermittent Dosing

Reporting group description:

Duvelisib 25 milligrams twice daily dosed 2 weeks on and 2 weeks off.

Serious adverse events	Duvelisib, Continuous and Intermittent Dosing	Duvelisib, Intermittent Dosing	
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 51 (25.49%)	16 / 51 (31.37%)	
number of deaths (all causes)	8	7	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Pelvic venous thrombosis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
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			
Disease progression			

subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Asthenia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
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			
Dyspnoea			
subjects affected / exposed	0 / 51 (0.00%)	2 / 51 (3.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 51 (0.00%)	2 / 51 (3.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Major depression			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			

subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Pylorospasm			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	3 / 51 (5.88%)	3 / 51 (5.88%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
COVID-19			

subjects affected / exposed	2 / 51 (3.92%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 51 (1.96%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 51 (1.96%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 51 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

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

Non-serious adverse events	Duvelisib, Continuous and Intermittent Dosing	Duvelisib, Intermittent Dosing	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 51 (96.08%)	50 / 51 (98.04%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	15 / 51 (29.41%)	8 / 51 (15.69%)	
occurrences (all)	61	15	
Aspartate aminotransferase increased			
subjects affected / exposed	15 / 51 (29.41%)	6 / 51 (11.76%)	
occurrences (all)	55	13	
Neutrophil count decreased			
subjects affected / exposed	3 / 51 (5.88%)	2 / 51 (3.92%)	
occurrences (all)	16	4	
Platelet count decreased			
subjects affected / exposed	3 / 51 (5.88%)	2 / 51 (3.92%)	
occurrences (all)	3	2	
Weight decreased			
subjects affected / exposed	3 / 51 (5.88%)	4 / 51 (7.84%)	
occurrences (all)	3	4	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 51 (0.00%)	6 / 51 (11.76%)	
occurrences (all)	0	7	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 51 (3.92%)	3 / 51 (5.88%)	
occurrences (all)	2	4	
Headache			
subjects affected / exposed	8 / 51 (15.69%)	1 / 51 (1.96%)	
occurrences (all)	13	1	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	4 / 51 (7.84%)	5 / 51 (9.80%)	
occurrences (all)	5	7	
Neutropenia			
subjects affected / exposed	10 / 51 (19.61%)	17 / 51 (33.33%)	
occurrences (all)	19	42	
Thrombocytopenia			
subjects affected / exposed	2 / 51 (3.92%)	3 / 51 (5.88%)	
occurrences (all)	3	5	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	6 / 51 (11.76%)	1 / 51 (1.96%)	
occurrences (all)	12	1	
Fatigue			
subjects affected / exposed	7 / 51 (13.73%)	5 / 51 (9.80%)	
occurrences (all)	11	6	
Pyrexia			
subjects affected / exposed	9 / 51 (17.65%)	9 / 51 (17.65%)	
occurrences (all)	22	11	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 51 (7.84%)	2 / 51 (3.92%)	
occurrences (all)	4	3	
Constipation			
subjects affected / exposed	6 / 51 (11.76%)	3 / 51 (5.88%)	
occurrences (all)	9	3	
Diarrhoea			
subjects affected / exposed	17 / 51 (33.33%)	10 / 51 (19.61%)	
occurrences (all)	33	16	
Nausea			
subjects affected / exposed	7 / 51 (13.73%)	8 / 51 (15.69%)	
occurrences (all)	10	12	
Stomatitis			
subjects affected / exposed	3 / 51 (5.88%)	4 / 51 (7.84%)	
occurrences (all)	4	4	
Vomiting			

subjects affected / exposed	5 / 51 (9.80%)	1 / 51 (1.96%)	
occurrences (all)	31	1	
Dyspepsia			
subjects affected / exposed	5 / 51 (9.80%)	3 / 51 (5.88%)	
occurrences (all)	7	3	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 51 (5.88%)	3 / 51 (5.88%)	
occurrences (all)	6	3	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	4 / 51 (7.84%)	4 / 51 (7.84%)	
occurrences (all)	10	4	
Rash			
subjects affected / exposed	4 / 51 (7.84%)	6 / 51 (11.76%)	
occurrences (all)	4	7	
Rash maculo-papular			
subjects affected / exposed	2 / 51 (3.92%)	3 / 51 (5.88%)	
occurrences (all)	2	3	
Urticaria			
subjects affected / exposed	4 / 51 (7.84%)	2 / 51 (3.92%)	
occurrences (all)	6	2	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	3 / 51 (5.88%)	0 / 51 (0.00%)	
occurrences (all)	4	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 51 (9.80%)	0 / 51 (0.00%)	
occurrences (all)	5	0	
Pain in extremity			
subjects affected / exposed	4 / 51 (7.84%)	4 / 51 (7.84%)	
occurrences (all)	4	4	
Spinal pain			
subjects affected / exposed	0 / 51 (0.00%)	3 / 51 (5.88%)	
occurrences (all)	0	3	

Infections and infestations			
COVID-19			
subjects affected / exposed	8 / 51 (15.69%)	10 / 51 (19.61%)	
occurrences (all)	9	11	
Pneumonia			
subjects affected / exposed	2 / 51 (3.92%)	5 / 51 (9.80%)	
occurrences (all)	4	5	
Upper respiratory tract infection			
subjects affected / exposed	4 / 51 (7.84%)	3 / 51 (5.88%)	
occurrences (all)	4	4	
Urinary tract infection			
subjects affected / exposed	5 / 51 (9.80%)	2 / 51 (3.92%)	
occurrences (all)	6	2	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 51 (7.84%)	2 / 51 (3.92%)	
occurrences (all)	5	2	
Hyperglycaemia			
subjects affected / exposed	0 / 51 (0.00%)	3 / 51 (5.88%)	
occurrences (all)	0	3	
Hyperkalaemia			
subjects affected / exposed	1 / 51 (1.96%)	4 / 51 (7.84%)	
occurrences (all)	1	8	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 January 2020	• Added an optional tumor biopsy at Screening • Added Cycle 1, Day 43 visit, with hematology, concomitant medications, focused physical examination, vitals, adverse events, drug diary, and self-admin of drug • Clarified that only cases of overdose that cause a serious adverse event are required to be reported within 24 hours, and that Investigator will determine if and when dosing should resume • Modified inclusion/exclusion criteria
18 May 2021	• Removed Long-Term and Survival Follow Up visits, and revised study end date to be 2 years after last participant randomized • Removed all Progressive Disease/Biomarker sampling after Cycle 2

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported