Clinical trial results:
A Phase 2, Open-Label, 2-Cohort Study of INCB050465, a PI3K Inhibitor, in Subjects With Relapsed or Refractory Marginal Zone Lymphoma With or Without Prior Exposure to a BTK Inhibitor

Summary

EudraCT number	2017-000970-12
Trial protocol	GB ES DE BE DK FR PL IT
Global end of trial date	29 May 2024

Results information

Result version number	v1 (current)
This version publication date	05 June 2025
First version publication date	05 June 2025

Trial information

Trial identification

Sponsor protocol code	INCB 50465-204 (CITADEL-204)

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Incyte Corporation
Sponsor organisation address	1801 Augustine Cutoff Drive, Wilmington, United States, 19803
Public contact	Study Director, Incyte Corporation, 1 8554633463, medinfo@incyte.com
Scientific contact	Study Director, Incyte Corporation, 1 8554633463, medinfo@incyte.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	29 May 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 May 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study was conducted to assess the efficacy of INCB050465 in terms of objective response rate (ORR) in participants with marginal zone lymphoma that is relapsed or refractory after at least 1 systemic treatment regimen.

Protection of trial subjects:

This study was performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and conducted in adherence to the study Protocol, Good Clinical Practices as defined in Title 21 of the United States Code of Federal Regulations Parts 11, 50, 54, 56, and 312, as well as International Council on Harmonisation Good Clinical Practice consolidated guidelines (E6) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 December 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Israel: 12
Country: Number of subjects enrolled	Italy: 25
Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	United States: 41
Worldwide total number of subjects	110
EEA total number of subjects	53

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	28
From 65 to 84 years	73
85 years and over	9

Subject disposition

Recruitment

Recruitment details:

This study enrolled participants at 46 study centers in the United States, Italy, Israel, France, Spain, Poland, Belgium, Great Britain, and Germany.

Pre-assignment

Screening details:

110 participants with relapsed or refractory marginal zone lymphoma were enrolled based on previous treatment with ibrutinib as Cohort 1 (exposed to ibrutinib before enrollment) and Cohort 2 (not exposed to Bruton's tyrosine kinase [BTK] inhibitor before enrollment). Participants were further allocated to Treatments A and B in each Cohort.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Treatment A (Exposed to Ibrutinib)

Arm description:

Participants received parsaclisib 20 milligrams (mg), orally, once daily (QD) for 8 weeks followed by 20 mg once weekly (QW), for up to 52 weeks. Participants who were exposed to ibrutinib before enrollment were included in this group.

Arm type	Experimental
Investigational medicinal product name	parsaclisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 mg, 2.5 mg, 5 mg, and 20 mg tablets taken orally

Arm title	Cohort 1: Treatment B (Exposed to Ibrutinib)

Arm description:

Participants received parsaclisib 20 mg, orally, QD for 8 weeks followed by 2.5 mg QD, for up to 52 weeks. Participants who were exposed to ibrutinib before enrollment were included in this group.

Arm type	Experimental
Investigational medicinal product name	parsaclisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 mg, 2.5 mg, 5 mg, and 20 mg tablets taken orally

Arm title	Cohort 2: Treatment A (BTK Inhibitor Naïve)

Arm description:

Participants received parsaclisib 20 mg, orally, QD for 8 weeks followed by 20 mg QW, for up to 52 weeks. Participants who were not exposed to Bruton's Tyrosine Kinase (BTK) inhibitor before enrollment were included in this group

Arm type	Experimental

Investigational medicinal product name	parsaclisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 mg, 2.5 mg, 5 mg, and 20 mg tablets taken orally

Arm title	Cohort 2: Treatment B (BTK Inhibitor Naïve)

Arm description:

Participants received parsaclisib 20 mg, orally, QD for 8 weeks followed by 2.5 mg QD, for up to 52 weeks. Participants who were not exposed to BTK inhibitor before enrollment were included in this group.

Arm type	Experimental
Investigational medicinal product name	parsaclisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 mg, 2.5 mg, 5 mg, and 20 mg tablets taken orally

Number of subjects in period 1	Cohort 1: Treatment A (Exposed to Ibrutinib)	Cohort 1: Treatment B (Exposed to Ibrutinib)	Cohort 2: Treatment A (BTK Inhibitor Naïve)
Started	4	6	28
Completed	0	2	13
Not completed	4	4	15
Adverse event, serious fatal	3	2	6
Changed Physicians	-	-	-
Exclusion Criteria Met	-	-	1
Withdrawal by Participant	-	-	2
Site Closed	-	-	-
Histological Criteria Not Met	-	-	-
Participant Transferred to Rollover Study	1	1	5
Removed for Safety	-	-	-
Progression of Chronic Lymphocytic Leukemia	-	-	-
Lost to follow-up	-	1	-
Discharged from the Trust	-	-	1
Multifactorial Cognitive Decline	-	-	-

Number of subjects in period 1	Cohort 2: Treatment B (BTK Inhibitor Naïve)
Started	72

Completed	26
Not completed	46
Adverse event, serious fatal	24
Changed Physicians	1
Exclusion Criteria Met	-
Withdrawal by Participant	6
Site Closed	1
Histological Criteria Not Met	1
Participant Transferred to Rollover Study	6
Removed for Safety	1
Progression of Chronic Lymphocytic Leukemia	1
Lost to follow-up	4
Discharged from the Trust	-
Multifactorial Cognitive Decline	1

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: Treatment A (Exposed to Ibrutinib)
Reporting group description:	
Participants received parsaclisib 20 milligrams (mg), orally, once daily (QD) for 8 weeks followed by 20 mg once weekly (QW), for up to 52 weeks. Participants who were exposed to ibrutinib before enrollment were included in this group.	
Reporting group title	Cohort 1: Treatment B (Exposed to Ibrutinib)
Reporting group description:	
Participants received parsaclisib 20 mg, orally, QD for 8 weeks followed by 2.5 mg QD, for up to 52 weeks. Participants who were exposed to ibrutinib before enrollment were included in this group.	
Reporting group title	Cohort 2: Treatment A (BTK Inhibitor Naïve)
Reporting group description:	
Participants received parsaclisib 20 mg, orally, QD for 8 weeks followed by 20 mg QW, for up to 52 weeks. Participants who were not exposed to Bruton's Tyrosine Kinase (BTK) inhibitor before enrollment were included in this group	
Reporting group title	Cohort 2: Treatment B (BTK Inhibitor Naïve)
Reporting group description:	
Participants received parsaclisib 20 mg, orally, QD for 8 weeks followed by 2.5 mg QD, for up to 52 weeks. Participants who were not exposed to BTK inhibitor before enrollment were included in this group.	

Reporting group values	Cohort 1: Treatment A (Exposed to Ibrutinib)	Cohort 1: Treatment B (Exposed to Ibrutinib)	Cohort 2: Treatment A (BTK Inhibitor Naïve)
Number of subjects	4	6	28
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	8
From 65-84 years	4	6	19
85 years and over	0	0	1
Age Continuous Units: years			
arithmetic mean	73.5	72.2	68.1
full range (min-max)	71 to 76	65 to 78	52 to 86
Sex: Female, Male Units: participants			
Female	2	4	16
Male	2	2	12
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	2	3
Not Hispanic or Latino	3	4	19
Unknown or Not Reported	1	0	6

Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	0
White	3	5	23
More than one race	0	0	0
Unknown or Not Reported	1	0	5

Reporting group values	Cohort 2: Treatment B (BTK Inhibitor Naïve)	Total	
Number of subjects	72	110	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	20	28	
From 65-84 years	44	73	
85 years and over	8	9	
Age Continuous Units: years			
arithmetic mean	69.8		
full range (min-max)	35 to 95	-	
Sex: Female, Male Units: participants			
Female	31	53	
Male	41	57	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	4	9	
Not Hispanic or Latino	57	83	
Unknown or Not Reported	11	18	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	1	1	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	2	
White	60	91	
More than one race	0	0	
Unknown or Not Reported	10	16	

End points

End points reporting groups

Reporting group title	Cohort 1: Treatment A (Exposed to Ibrutinib)
Reporting group description:	
Participants received parsaclisib 20 milligrams (mg), orally, once daily (QD) for 8 weeks followed by 20 mg once weekly (QW), for up to 52 weeks. Participants who were exposed to ibrutinib before enrollment were included in this group.	
Reporting group title	Cohort 1: Treatment B (Exposed to Ibrutinib)
Reporting group description:	
Participants received parsaclisib 20 mg, orally, QD for 8 weeks followed by 2.5 mg QD, for up to 52 weeks. Participants who were exposed to ibrutinib before enrollment were included in this group.	
Reporting group title	Cohort 2: Treatment A (BTK Inhibitor Naïve)
Reporting group description:	
Participants received parsaclisib 20 mg, orally, QD for 8 weeks followed by 20 mg QW, for up to 52 weeks. Participants who were not exposed to Bruton's Tyrosine Kinase (BTK) inhibitor before enrollment were included in this group	
Reporting group title	Cohort 2: Treatment B (BTK Inhibitor Naïve)
Reporting group description:	
Participants received parsaclisib 20 mg, orally, QD for 8 weeks followed by 2.5 mg QD, for up to 52 weeks. Participants who were not exposed to BTK inhibitor before enrollment were included in this group.	

Primary: Objective Response Rate (ORR) Based on Lugano Classification Criteria

End point title	Objective Response Rate (ORR) Based on Lugano Classification Criteria[1]
End point description:	
ORR=percentage of participants with complete response(CR) or partial response(PR) per revised response criteria for lymphomas,determined by independent review committee(IRC).Criteria for CR:1.Target nodes/nodal masses of lymph nodes,extralymphatic sites regressed to≤1.5cm in longest dimension transverse diameter of lesion(LDi);2.Absence of non-measured lesion;3.Organ enlargement regressed to normal;4.No new lesions;5.Normal bone marrow morphology;if indeterminate,immunohistochemistry negative.Criteria for PR:1.Lymph nodes,extralymphatic sites-≥50%decrease in sum of product of perpendicular diameters for multiple lesions(SPD)of up to 6 target measurable nodes,extranodal sites;if lesion is too small to measure on computed tomography(CT),assign 5mm×5mm as default;if no longer visible,0×0mm.Node >5mm×5mm but smaller than normal,use actual measurement.2.Absent/regressed non-measured lesions,no increase.3.Organ enlargement-Spleen regressed by >50%in length beyond normal.4.No new lesions.	
End point type	Primary
End point timeframe:	
Up to approximately 161 weeks	
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: Statistical analysis was not conducted for this endpoint.	

End point values	Cohort 1: Treatment A (Exposed to Ibrutinib)	Cohort 1: Treatment B (Exposed to Ibrutinib)	Cohort 2: Treatment A (BTK Inhibitor Naïve)	Cohort 2: Treatment B (BTK Inhibitor Naïve)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[2]	6[3]	28[4]	72[5]
Units: percentage of participants				
number (confidence interval 95%)	50.0 (6.8 to 93.2)	33.3 (4.3 to 77.7)	57.1 (37.2 to 75.5)	58.3 (46.1 to 69.8)

Notes:

[2] - Full Analysis Set: all participants enrolled in the study who received ≥1 dose of parsaclisib

[3] - Full Analysis Set: all participants enrolled in the study who received ≥1 dose of parsaclisib

[4] - Full Analysis Set: all participants enrolled in the study who received ≥1 dose of parsaclisib

[5] - Full Analysis Set: all participants enrolled in the study who received ≥1 dose of parsaclisib

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Response Rate (CRR) based on Lugano Classification Criteria

End point title	Complete Response Rate (CRR) based on Lugano Classification Criteria

End point description:

CRR is defined as the percentage of participants with a CR as determined by an IRC. The criteria for CR included: 1.Target nodes/nodal masses of lymph nodes and extralymphatic sites must regress to ≤ 1.5 cm in LDi; 2. Absence of non-measured lesion; 3.Organ enlargement regressed to normal; 4.No new lesions; 5.Bone marrow must be normal by morphology; if indeterminate, immunohistochemistry negative.

End point type	Secondary

End point timeframe:

Up to 1305 days

End point values	Cohort 1: Treatment A (Exposed to Ibrutinib)	Cohort 1: Treatment B (Exposed to Ibrutinib)	Cohort 2: Treatment A (BTK Inhibitor Naïve)	Cohort 2: Treatment B (BTK Inhibitor Naïve)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[6]	6[7]	28[8]	72[9]
Units: percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 60.2)	0.0 (0.0 to 45.9)	10.7 (2.3 to 28.2)	4.2 (0.9 to 11.7)

Notes:

[6] - Full Analysis Set: all participants enrolled in the study who received ≥1 dose of parsaclisib

[7] - Full Analysis Set: all participants enrolled in the study who received ≥1 dose of parsaclisib

[8] - Full Analysis Set: all participants enrolled in the study who received ≥1 dose of parsaclisib

[9] - Full Analysis Set: all participants enrolled in the study who received ≥1 dose of parsaclisib

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=time from first documented evidence of CR/PR until disease progression/death from any cause among participants who achieve an objective response as determined by IRC. CR: 1.Target nodes/nodal masses of lymph nodes/extralymphatic sites must regress to ≤1.5 cm in LDi; 2. Absence of non-measured lesion; 3.Organ enlargement regressed to normal; 4.No new lesions; 5.Bone marrow normal by morphology; if indeterminate, immunohistochemistry negative. PR: 1.Lymph nodes and extralymphatic sites- a. ≥50% decrease in SPD of up to 6 target measurable nodes and extranodal sites; b. when a lesion is too small to measure on CT, assign 5 mm×5 mm as the default; c.when no longer visible, 0×0 mm. For a node >5 mm×5 mm but smaller than normal, use actual measurement.

2.Non-measured lesions- Absent/regressed, but no increase. 3. Organ enlargement-Spleen regressed by >50% in length beyond normal. 4.No new lesions. -9999, 9999=not estimable due to the low number of participants with events of response.

End point type	Secondary

End point timeframe:

Up to 1305 days

End point values	Cohort 1: Treatment A (Exposed to Ibrutinib)	Cohort 1: Treatment B (Exposed to Ibrutinib)	Cohort 2: Treatment A (BTK Inhibitor Naïve)	Cohort 2: Treatment B (BTK Inhibitor Naïve)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2[10]	2[11]	17[12]	41[13]
Units: months				
median (confidence interval 95%)	9999 (-9999 to 9999)	9999 (-9999 to 9999)	16.69 (3.71 to 9999)	13.57 (8.05 to 17.74)

Notes:

[10] - Full Analysis Set. Only participants with objective response were analyzed.

[11] - Full Analysis Set. Only participants with objective response were analyzed.

[12] - Full Analysis Set. Only participants with objective response were analyzed.

[13] - Full Analysis Set. Only participants with objective response were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS is defined as the time from the date of the first dose of study treatment until death from any cause. 9999=values were not estimable due to the low number of participants with events.

End point type	Secondary

End point timeframe:

up to 2354 days

End point values	Cohort 1: Treatment A (Exposed to Ibrutinib)	Cohort 1: Treatment B (Exposed to Ibrutinib)	Cohort 2: Treatment A (BTK Inhibitor Naïve)	Cohort 2: Treatment B (BTK Inhibitor Naïve)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[14]	6[15]	28[16]	72[17]
Units: months				
median (confidence interval 95%)	18.94 (7.26 to 9999)	9999 (3.22 to 9999)	9999 (59.60 to 9999)	63.54 (39.72 to 9999)

Notes:

[14] - Full Analysis Set: all participants enrolled in the study who received ≥1 dose of parsaclisib

[15] - Full Analysis Set: all participants enrolled in the study who received ≥1 dose of parsaclisib

[16] - Full Analysis Set: all participants enrolled in the study who received ≥1 dose of parsaclisib

[17] - Full Analysis Set: all participants enrolled in the study who received ≥1 dose of parsaclisib

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 is defined as the time from the date of the first dose of study treatment until the earliest date of disease progression, as determined by radiographic disease assessment provided by an IRC, or death from any cause. -9999, 9999=The median and the lower and upper limits of the 95% CI were not estimable due to the low number of participants with events.

End point type	Secondary

End point timeframe:

Up to 1305 days

End point values	Cohort 1: Treatment A (Exposed to Ibrutinib)	Cohort 1: Treatment B (Exposed to Ibrutinib)	Cohort 2: Treatment A (BTK Inhibitor Naïve)	Cohort 2: Treatment B (BTK Inhibitor Naïve)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[18]	6[19]	28[20]	72[21]
Units: months				
median (confidence interval 95%)	9999 (-9999 to 9999)	9999 (-9999 to 9999)	19.42 (8.77 to 9999)	17.74 (11.53 to 22.34)

Notes:

[18] - Full Analysis Set: all participants enrolled in the study who received ≥1 dose of parsaclisib

[19] - Full Analysis Set: all participants enrolled in the study who received ≥1 dose of parsaclisib

[20] - Full Analysis Set: all participants enrolled in the study who received ≥1 dose of parsaclisib

[21] - Full Analysis Set: all participants enrolled in the study who received ≥1 dose of parsaclisib

Statistical analyses

No statistical analyses for this end point

Secondary: Best Percent Change from Baseline in Target Lesion Size

End point title	Best Percent Change from Baseline in Target Lesion Size

End point description:

Target lesion size is measured by the sum of the product of diameters of all target lesion sizes and is determined by the IRC. The best percent change from Baseline is defined as the largest decrease, or smallest increase (if no decrease available), from Baseline in target lesion sizes on/before new (next-line) anti-lymphoma therapy during the study. Baseline is the last nonmissing measurement obtained before the first administration of study drug. A negative percent change from Baseline indicates improvement.

End point type	Secondary

End point timeframe:

Up to 1305 days

End point values	Cohort 1: Treatment A (Exposed to Ibrutinib)	Cohort 1: Treatment B (Exposed to Ibrutinib)	Cohort 2: Treatment A (BTK Inhibitor Naïve)	Cohort 2: Treatment B (BTK Inhibitor Naïve)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[22]	5[23]	20[24]	51[25]
Units: percent change in lesion size				
arithmetic mean (standard deviation)	-48.83 (± 21.193)	-54.84 (± 21.454)	-71.22 (± 18.566)	-66.76 (± 19.971)

Notes:

[22] - Full Analysis Set. Only participants with available data were analyzed.

[23] - Full Analysis Set. Only participants with available data were analyzed.

[24] - Full Analysis Set. Only participants with available data were analyzed.

[25] - Full Analysis Set. Only participants with available data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

End point title	Percentage of Participants With Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

End point description:

An adverse event (AE) is any untoward medical occurrence associated with use of a drug in humans, whether or not considered drug related, that occurs after a participant provides informed consent. A TEAE is any AE either reported for the first time or worsening of a pre-existing event after first dose of study drug and within 30 days of the last administration of study drug regardless of starting new anti-lymphoma therapy. A SAE is any untoward medical occurrence that results in death, is life-threatening, requires inpatient hospitalization/prolongation of existing hospitalization, results in persistent or significant disability/incapacity, leads to a congenital anomaly/birth defect or is considered to be an important medical event that may not result in death, be immediately life-threatening, or require hospitalization but may be considered serious when, based on appropriate medical judgment, the event may jeopardize the participant or may require medical or surgical intervention.

End point type	Secondary

End point timeframe:

From first dose of study drug up to 1980 days

End point values	Cohort 1: Treatment A (Exposed to Ibrutinib)	Cohort 1: Treatment B (Exposed to Ibrutinib)	Cohort 2: Treatment A (BTK Inhibitor Naïve)	Cohort 2: Treatment B (BTK Inhibitor Naïve)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[26]	6[27]	28[28]	72[29]
Units: percentage of participants				
number (not applicable)				
TEAEs	100.0	83.3	92.9	97.2
SAEs	50.0	33.3	32.1	63.9

Notes:
[26] - Safety Population: all enrolled participants who received at least 1 dose of parsaclisib
[27] - Safety Population: all enrolled participants who received at least 1 dose of parsaclisib
[28] - Safety Population: all enrolled participants who received at least 1 dose of parsaclisib
[29] - Safety Population: all enrolled participants who received at least 1 dose of parsaclisib

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

up to 2354 days

Adverse event reporting additional description:

Adverse events have been reported for members of the Safety Population, comprised of all enrolled participants who received at least 1 dose of parsaclisib.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22

Reporting groups

Reporting group title	Cohort 1: Treatment (Trt) A (Exposed to Ibrutinib)

Reporting group description:

Participants received parsaclisib 20 milligrams (mg), orally, once daily (QD) for 8 weeks followed by 20 mg once weekly (QW), for up to 52 weeks. Participants who were exposed to ibrutinib before enrollment were included in this group.

Reporting group title	Cohort 2: Trt B (Bruton's Tyrosine Kinase Inhibitor Naïve)

Reporting group description:

Participants received parsaclisib 20 mg tablets, orally, QD for 8 weeks followed by 2.5 mg tablets QD, for up to 52 weeks. Participants who were not exposed to BTK inhibitor before enrollment were included in this group.

Reporting group title	Cohort 2: Trt A (Bruton's Tyrosine Kinase Inhibitor Naïve)

Reporting group description:

Participants received parsaclisib 20 mg tablets, orally, QD for 8 weeks followed by 20 mg tablets QW, for up to 52 weeks. Participants who were not exposed to BTK inhibitor before enrollment were included in this group.

Reporting group title	Cohort 1: Treatment B (Exposed to Ibrutinib)

Reporting group description:

Participants received parsaclisib 20 mg, orally, QD for 8 weeks followed by 2.5 mg QD, for up to 52 weeks. Participants who were exposed to ibrutinib before enrollment were included in this group.

Serious adverse events	Cohort 1: Treatment (Trt) A (Exposed to Ibrutinib)	Cohort 2: Trt B (Bruton's Tyrosine Kinase Inhibitor Naïve)	Cohort 2: Trt A (Bruton's Tyrosine Kinase Inhibitor Naïve)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)	46 / 72 (63.89%)	9 / 28 (32.14%)
number of deaths (all causes)	3	25	6
number of deaths resulting from adverse events	0	8	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bowen's disease			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Breast cancer			

subjects affected / exposed	0 / 4 (0.00%)	0 / 72 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Marginal zone lymphoma recurrent			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Lung neoplasm malignant			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Squamous cell carcinoma			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Peripheral ischaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
General disorders and administration site conditions			

Death			
subjects affected / exposed	0 / 4 (0.00%)	0 / 72 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Fatigue			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
General physical health deterioration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 72 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 72 (2.78%)	0 / 28 (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
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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			
Acute respiratory failure			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Chronic obstructive pulmonary disease			

subjects affected / exposed	0 / 4 (0.00%)	0 / 72 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Pneumonitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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			
Blood calcium increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 72 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecal volume increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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

Splenic rupture			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Atrial fibrillation			
subjects affected / exposed	0 / 4 (0.00%)	3 / 72 (4.17%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 4 (0.00%)	0 / 72 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Sinus tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Nervous system disorders			
Encephalopathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 72 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial pressure increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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

Seizure			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 72 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 72 (2.78%)	0 / 28 (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
Eosinophilia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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 neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	4 / 72 (5.56%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	4 / 5	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Hyperviscosity syndrome			
subjects affected / exposed	1 / 4 (25.00%)	0 / 72 (0.00%)	0 / 28 (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
Microangiopathic haemolytic anaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Eye disorders			
Retinal haemorrhage			
subjects affected / exposed	1 / 4 (25.00%)	0 / 72 (0.00%)	0 / 28 (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

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	2 / 72 (2.78%)	0 / 28 (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
Colitis			
subjects affected / exposed	0 / 4 (0.00%)	6 / 72 (8.33%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	6 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	6 / 72 (8.33%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	5 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Gastritis			
subjects affected / exposed	0 / 4 (0.00%)	2 / 72 (2.78%)	0 / 28 (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
Gastrointestinal angiodysplasia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Intestinal infarction			

subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Hypertransaminasaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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			
Eczema			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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	0 / 4 (0.00%)	2 / 72 (2.78%)	0 / 28 (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
Rash maculo-papular			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Toxic skin eruption			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 4 (0.00%)	2 / 72 (2.78%)	0 / 28 (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

Oliguria			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Renal tubular necrosis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Renal failure			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Musculoskeletal and connective tissue disorders			
Intervertebral disc disorder			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 72 (2.78%)	0 / 28 (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
Bronchitis viral			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
COVID-19			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Appendicitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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

Cytomegalovirus colitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Device related infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Cytomegalovirus infection reactivation			
subjects affected / exposed	0 / 4 (0.00%)	2 / 72 (2.78%)	0 / 28 (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
Cytomegalovirus infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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 viral			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Enterobacter sepsis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Pneumonia pneumococcal			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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			
subjects affected / exposed	1 / 4 (25.00%)	7 / 72 (9.72%)	2 / 28 (7.14%)
occurrences causally related to treatment / all	0 / 1	4 / 8	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	0 / 4 (0.00%)	2 / 72 (2.78%)	0 / 28 (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
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Urosepsis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	2 / 72 (2.78%)	0 / 28 (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
Yersinia infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Hypercalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 72 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			

subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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
Tumour lysis syndrome			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (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

Serious adverse events	Cohort 1: Treatment B (Exposed to Ibrutinib)		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 6 (33.33%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bowen's disease			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Marginal zone lymphoma recurrent			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung neoplasm malignant			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Invasive ductal breast carcinoma			

subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of lung				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Hypotension				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral ischaemia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Death				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Pain				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Systemic inflammatory response syndrome				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory failure				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				

subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood calcium increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Faecal volume increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Splenic rupture			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			

subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus tachycardia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Encephalopathy				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intracranial pressure increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				

Anaemia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eosinophilia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperviscosity syndrome				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Microangiopathic haemolytic anaemia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Retinal haemorrhage				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Diarrhoea				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenitis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterocolitis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal angiodysplasia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal infarction				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertransaminasaemia				

subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rash			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Toxic skin eruption			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Oliguria			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal tubular necrosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal failure			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc disorder			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchitis viral			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cytomegalovirus colitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Cytomegalovirus infection reactivation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cytomegalovirus infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterocolitis viral			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterobacter sepsis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia pneumococcal			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urosepsis			

subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Yersinia infection				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Failure to thrive				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Hypoglycaemia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tumour lysis syndrome				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	Cohort 1: Treatment (Trt) A (Exposed to Ibrutinib)	Cohort 2: Trt B (Bruton's Tyrosine Kinase Inhibitor Naïve)	Cohort 2: Trt A (Bruton's Tyrosine Kinase Inhibitor Naïve)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	67 / 72 (93.06%)	25 / 28 (89.29%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Seborrhoeic keratosis			
subjects affected / exposed	0 / 4 (0.00%)	5 / 72 (6.94%)	0 / 28 (0.00%)
occurrences (all)	0	5	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	6 / 72 (8.33%)	2 / 28 (7.14%)
occurrences (all)	0	6	2
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	4 / 72 (5.56%)	1 / 28 (3.57%)
occurrences (all)	0	4	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	3 / 72 (4.17%)	4 / 28 (14.29%)
occurrences (all)	0	3	6
Chest pain			
subjects affected / exposed	0 / 4 (0.00%)	4 / 72 (5.56%)	0 / 28 (0.00%)
occurrences (all)	0	6	0
Fatigue			
subjects affected / exposed	1 / 4 (25.00%)	11 / 72 (15.28%)	3 / 28 (10.71%)
occurrences (all)	1	11	5
Influenza like illness			
subjects affected / exposed	0 / 4 (0.00%)	3 / 72 (4.17%)	2 / 28 (7.14%)
occurrences (all)	0	4	4
Oedema peripheral			
subjects affected / exposed	0 / 4 (0.00%)	9 / 72 (12.50%)	3 / 28 (10.71%)
occurrences (all)	0	9	3
Peripheral swelling			

subjects affected / exposed	1 / 4 (25.00%)	1 / 72 (1.39%)	1 / 28 (3.57%)
occurrences (all)	1	1	1
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	10 / 72 (13.89%)	4 / 28 (14.29%)
occurrences (all)	0	14	8
Reproductive system and breast disorders			
Vulvovaginal dryness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 72 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 4 (25.00%)	7 / 72 (9.72%)	2 / 28 (7.14%)
occurrences (all)	1	7	2
Cough			
subjects affected / exposed	0 / 4 (0.00%)	22 / 72 (30.56%)	5 / 28 (17.86%)
occurrences (all)	0	24	8
Epistaxis			
subjects affected / exposed	1 / 4 (25.00%)	3 / 72 (4.17%)	2 / 28 (7.14%)
occurrences (all)	3	3	2
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)	3 / 72 (4.17%)	2 / 28 (7.14%)
occurrences (all)	0	4	3
Productive cough			
subjects affected / exposed	0 / 4 (0.00%)	4 / 72 (5.56%)	1 / 28 (3.57%)
occurrences (all)	0	7	1
Pulmonary embolism			
subjects affected / exposed	2 / 4 (50.00%)	1 / 72 (1.39%)	1 / 28 (3.57%)
occurrences (all)	2	1	1
Dyspnoea exertional			
subjects affected / exposed	1 / 4 (25.00%)	1 / 72 (1.39%)	0 / 28 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 4 (25.00%)	1 / 72 (1.39%)	2 / 28 (7.14%)
occurrences (all)	1	1	2
Insomnia			

subjects affected / exposed	0 / 4 (0.00%)	6 / 72 (8.33%)	1 / 28 (3.57%)
occurrences (all)	0	6	1
Investigations			
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 4 (25.00%)	2 / 72 (2.78%)	1 / 28 (3.57%)
occurrences (all)	1	2	1
Blood bilirubin increased			
subjects affected / exposed	0 / 4 (0.00%)	2 / 72 (2.78%)	3 / 28 (10.71%)
occurrences (all)	0	3	3
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 4 (0.00%)	4 / 72 (5.56%)	1 / 28 (3.57%)
occurrences (all)	0	5	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	7 / 72 (9.72%)	2 / 28 (7.14%)
occurrences (all)	0	11	5
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	6 / 72 (8.33%)	2 / 28 (7.14%)
occurrences (all)	0	9	6
Platelet count decreased			
subjects affected / exposed	0 / 4 (0.00%)	4 / 72 (5.56%)	2 / 28 (7.14%)
occurrences (all)	0	11	2
Neutrophil count decreased			
subjects affected / exposed	0 / 4 (0.00%)	4 / 72 (5.56%)	2 / 28 (7.14%)
occurrences (all)	0	9	7
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 4 (25.00%)	3 / 72 (4.17%)	0 / 28 (0.00%)
occurrences (all)	1	3	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 4 (25.00%)	3 / 72 (4.17%)	2 / 28 (7.14%)
occurrences (all)	1	9	3

Chest injury			
subjects affected / exposed	1 / 4 (25.00%)	0 / 72 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 4 (25.00%)	1 / 72 (1.39%)	0 / 28 (0.00%)
occurrences (all)	1	4	0
Ventricular arrhythmia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 72 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)	9 / 72 (12.50%)	2 / 28 (7.14%)
occurrences (all)	0	11	2
Headache			
subjects affected / exposed	0 / 4 (0.00%)	10 / 72 (13.89%)	3 / 28 (10.71%)
occurrences (all)	0	12	3
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	2 / 28 (7.14%)
occurrences (all)	0	1	2
Paraesthesia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	10 / 72 (13.89%)	4 / 28 (14.29%)
occurrences (all)	0	14	5
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	10 / 72 (13.89%)	4 / 28 (14.29%)
occurrences (all)	0	20	5
Thrombocytopenia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 72 (2.78%)	3 / 28 (10.71%)
occurrences (all)	0	2	4
Normochromic normocytic anaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 72 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			

Tinnitus			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	2 / 28 (7.14%)
occurrences (all)	0	1	2
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	1 / 4 (25.00%)	1 / 72 (1.39%)	0 / 28 (0.00%)
occurrences (all)	1	1	0
Vision blurred			
subjects affected / exposed	0 / 4 (0.00%)	4 / 72 (5.56%)	0 / 28 (0.00%)
occurrences (all)	0	4	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 4 (50.00%)	10 / 72 (13.89%)	1 / 28 (3.57%)
occurrences (all)	2	11	1
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	3 / 72 (4.17%)	3 / 28 (10.71%)
occurrences (all)	0	3	3
Dyspepsia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 72 (2.78%)	2 / 28 (7.14%)
occurrences (all)	0	2	3
Dry mouth			
subjects affected / exposed	0 / 4 (0.00%)	3 / 72 (4.17%)	2 / 28 (7.14%)
occurrences (all)	0	3	2
Diarrhoea			
subjects affected / exposed	1 / 4 (25.00%)	37 / 72 (51.39%)	9 / 28 (32.14%)
occurrences (all)	1	66	19
Constipation			
subjects affected / exposed	1 / 4 (25.00%)	11 / 72 (15.28%)	3 / 28 (10.71%)
occurrences (all)	1	12	5
Colitis			
subjects affected / exposed	0 / 4 (0.00%)	5 / 72 (6.94%)	0 / 28 (0.00%)
occurrences (all)	0	6	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 4 (0.00%)	4 / 72 (5.56%)	2 / 28 (7.14%)
occurrences (all)	0	4	2
Nausea			

subjects affected / exposed	1 / 4 (25.00%)	13 / 72 (18.06%)	3 / 28 (10.71%)
occurrences (all)	1	18	3
Stomatitis			
subjects affected / exposed	0 / 4 (0.00%)	5 / 72 (6.94%)	4 / 28 (14.29%)
occurrences (all)	0	5	6
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)	5 / 72 (6.94%)	4 / 28 (14.29%)
occurrences (all)	0	8	5
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 4 (25.00%)	2 / 72 (2.78%)	1 / 28 (3.57%)
occurrences (all)	1	2	1
Actinic keratosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 72 (0.00%)	3 / 28 (10.71%)
occurrences (all)	0	0	4
Ecchymosis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	2 / 28 (7.14%)
occurrences (all)	0	1	2
Dry skin			
subjects affected / exposed	0 / 4 (0.00%)	5 / 72 (6.94%)	2 / 28 (7.14%)
occurrences (all)	0	5	2
Eczema			
subjects affected / exposed	0 / 4 (0.00%)	3 / 72 (4.17%)	3 / 28 (10.71%)
occurrences (all)	0	5	3
Erythema			
subjects affected / exposed	0 / 4 (0.00%)	4 / 72 (5.56%)	0 / 28 (0.00%)
occurrences (all)	0	4	0
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	11 / 72 (15.28%)	5 / 28 (17.86%)
occurrences (all)	0	13	6
Rash			
subjects affected / exposed	1 / 4 (25.00%)	11 / 72 (15.28%)	5 / 28 (17.86%)
occurrences (all)	1	12	8
Rash maculo-papular			
subjects affected / exposed	0 / 4 (0.00%)	5 / 72 (6.94%)	2 / 28 (7.14%)
occurrences (all)	0	6	3

Rash pruritic			
subjects affected / exposed	0 / 4 (0.00%)	4 / 72 (5.56%)	1 / 28 (3.57%)
occurrences (all)	0	4	1
Urticaria			
subjects affected / exposed	0 / 4 (0.00%)	3 / 72 (4.17%)	2 / 28 (7.14%)
occurrences (all)	0	3	2
Rosacea			
subjects affected / exposed	1 / 4 (25.00%)	1 / 72 (1.39%)	0 / 28 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 4 (0.00%)	4 / 72 (5.56%)	1 / 28 (3.57%)
occurrences (all)	0	4	1
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	9 / 72 (12.50%)	4 / 28 (14.29%)
occurrences (all)	0	11	4
Muscle spasms			
subjects affected / exposed	0 / 4 (0.00%)	4 / 72 (5.56%)	2 / 28 (7.14%)
occurrences (all)	0	4	4
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)	4 / 72 (5.56%)	2 / 28 (7.14%)
occurrences (all)	0	4	3
Neck pain			
subjects affected / exposed	0 / 4 (0.00%)	2 / 72 (2.78%)	1 / 28 (3.57%)
occurrences (all)	0	2	1
Muscular weakness			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 4 (25.00%)	4 / 72 (5.56%)	4 / 28 (14.29%)
occurrences (all)	2	4	4
Conjunctivitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	2 / 28 (7.14%)
occurrences (all)	0	1	2
Herpes zoster			

subjects affected / exposed	0 / 4 (0.00%)	3 / 72 (4.17%)	1 / 28 (3.57%)
occurrences (all)	0	3	1
Infected bite			
subjects affected / exposed	0 / 4 (0.00%)	0 / 72 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Nasopharyngitis			
subjects affected / exposed	1 / 4 (25.00%)	3 / 72 (4.17%)	4 / 28 (14.29%)
occurrences (all)	1	3	4
Sinusitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	2 / 28 (7.14%)
occurrences (all)	0	1	3
Upper respiratory tract infection			
subjects affected / exposed	1 / 4 (25.00%)	11 / 72 (15.28%)	0 / 28 (0.00%)
occurrences (all)	2	13	0
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	6 / 72 (8.33%)	3 / 28 (10.71%)
occurrences (all)	0	9	3
Rhinitis			
subjects affected / exposed	1 / 4 (25.00%)	1 / 72 (1.39%)	0 / 28 (0.00%)
occurrences (all)	1	1	0
Oral herpes			
subjects affected / exposed	1 / 4 (25.00%)	3 / 72 (4.17%)	0 / 28 (0.00%)
occurrences (all)	1	4	0
Oral candidiasis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 72 (1.39%)	0 / 28 (0.00%)
occurrences (all)	0	2	0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	4 / 72 (5.56%)	0 / 28 (0.00%)
occurrences (all)	0	4	0
Decreased appetite			
subjects affected / exposed	1 / 4 (25.00%)	11 / 72 (15.28%)	2 / 28 (7.14%)
occurrences (all)	1	12	3
Hyperglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	4 / 72 (5.56%)	0 / 28 (0.00%)
occurrences (all)	0	5	0

Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	6 / 72 (8.33%)	1 / 28 (3.57%)
occurrences (all)	0	8	1
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)	4 / 72 (5.56%)	0 / 28 (0.00%)
occurrences (all)	0	11	0
Hypoglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 72 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 1: Treatment B (Exposed to Ibrutinib)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Seborrhoeic keratosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Influenza like illness			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Peripheral swelling			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Reproductive system and breast disorders			
Vulvovaginal dryness			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	3		
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Productive cough			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pulmonary embolism			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dyspnoea exertional			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Investigations			
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood bilirubin increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Neutrophil count decreased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all) Chest injury subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0		
Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all) Ventricular arrhythmia subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Syncope subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 1 / 6 (16.67%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all)	 0 / 6 (0.00%) 0 1 / 6 (16.67%) 1		

Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Normochromic normocytic anaemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Eye disorders Conjunctival haemorrhage subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Vision blurred subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Dyspepsia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Dry mouth subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Diarrhoea subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 3		
Constipation subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Colitis			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Actinic keratosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Ecchymosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Eczema			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		

Rash subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Rash pruritic subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Urticaria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Rosacea subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Musculoskeletal and connective tissue disorders			
Arthritis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Arthralgia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Muscle spasms subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Myalgia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Neck pain subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Muscular weakness subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Infections and infestations			

COVID-19 subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0			
Conjunctivitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0			
Herpes zoster subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1			
Infected bite subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0			
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1			
Sinusitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0			
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0			
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1			
Rhinitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0			
Oral herpes subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0			
Oral candidiasis subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1			
Metabolism and nutrition disorders Dehydration				

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Decreased appetite			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Hyperkalaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypoglycaemia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 July 2018	The primary purpose of this amendment was to modify the dose reduction schedules.
07 December 2018	The primary purpose of this amendment was to close enrollment in Cohort 1 and to increase the number of participants enrolled in Cohort 2 to better understand the safety and efficacy of INCB050465 administered at one of the 2 treatment regimens.
20 December 2019	The primary purpose of this amendment was to provide additional guidance on dose modification in the event of diarrhea and colitis and to define the end of the study, including the option to receive continued treatment with INCB050465 in a rollover protocol.
07 September 2022	The primary purpose of this amendment was to describe risks associated with COVID-19.
24 January 2024	The primary purpose of this amendment was to institute hematology testing every 2 weeks for the first 8 weeks of dosing and revise the exclusion criterion for liver disease.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported