Clinical trial results:
Dose Optimization Study of Idelalisib in Follicular Lymphoma

Summary

EudraCT number	2015-000366-66
Trial protocol	GB CZ PL ES FR IT
Global end of trial date	27 September 2022

Results information

Result version number	v1
This version publication date	16 July 2023
First version publication date	16 July 2023

Trial information

Trial identification

Sponsor protocol code	GS-US-313-1580

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02536300
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.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	27 September 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 September 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to establish a safe and effective dosing regimen of idelalisib in participants with relapsed or refractory follicular lymphoma (FL) who have no other therapeutic options.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements. This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 January 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Czechia: 8
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Israel: 4
Country: Number of subjects enrolled	Italy: 19
Country: Number of subjects enrolled	Poland: 19
Country: Number of subjects enrolled	Romania: 1
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	United Kingdom: 15
Worldwide total number of subjects	96
EEA total number of subjects	74

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	45
From 65 to 84 years	48
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Australia, Canada, Europe, Israel, and the United Kingdom.

Pre-assignment

Screening details:

145 participants were screened.

Period 1

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

Blinding implementation details:

Double-blind: Prior to protocol amendment 5; Open-label: Participants enrolled as of protocol amendment 5

Arms

Are arms mutually exclusive?	Yes
Arm title	Idelalisib 150 mg BID

Arm description:

Participants received idelalisib 150 mg tablets, orally, twice daily (BID), continuously for up to maximum 33.5 months.

Arm type	Experimental
Investigational medicinal product name	Idelalisib
Investigational medicinal product code	
Other name	Zydelig®, GS-1101, CAL-101
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Administered 150 mg, BID, continuously.

Arm title	Idelalisib 100 mg BID

Arm description:

Participants received idelalisib 100 mg tablets, orally, BID, continuously for up to maximum 63.6 months.

Arm type	Experimental
Investigational medicinal product name	Idelalisib
Investigational medicinal product code	
Other name	Zydelig®, GS-1101, CAL-101
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Administered 100 mg, BID, continuously.

Arm title	Idelalisib 150 mg BID INT

Arm description:

Participants received idelalisib 150 mg tablets, orally, BID for 21 days and 7 days off-treatment (intermittent [INT] dosing schedule) in each 28-day cycle for up to maximum of 24.6 months.

Arm type	Experimental

Investigational medicinal product name	Idelalisib
Investigational medicinal product code	
Other name	Zydelig®, GS-1101, CAL-101
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Administered 150 mg, BID for 21 days and 7 days off-treatment (INT dosing schedule) in each 28-day cycle.

Number of subjects in period 1	Idelalisib 150 mg BID	Idelalisib 100 mg BID	Idelalisib 150 mg BID INT
Started	47	27	22
Completed	0	0	0
Not completed	47	27	22
Consent withdrawn by subject	4	2	-
Protocol violation	-	1	-
Non-compliance With Study Drug	1	-	-
Death	7	-	5
Investigator's Discretion	17	11	2
Progressive Disease	11	7	6
Study Terminated by Sponsor	6	4	7
Non-study Specific Anti-cancer Therapy Initiation	1	2	1
Enrolled but Never Treated	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Idelalisib 150 mg BID
Reporting group description:	
Participants received idelalisib 150 mg tablets, orally, twice daily (BID), continuously for up to maximum 33.5 months.	
Reporting group title	Idelalisib 100 mg BID
Reporting group description:	
Participants received idelalisib 100 mg tablets, orally, BID, continuously for up to maximum 63.6 months.	
Reporting group title	Idelalisib 150 mg BID INT
Reporting group description:	
Participants received idelalisib 150 mg tablets, orally, BID for 21 days and 7 days off-treatment (intermittent [INT] dosing schedule) in each 28-day cycle for up to maximum of 24.6 months.	

Reporting group values	Idelalisib 150 mg BID	Idelalisib 100 mg BID	Idelalisib 150 mg BID INT
Number of subjects	47	27	22
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	65	62	63
standard deviation	± 13.0	± 13.6	± 11.6
Gender categorical			
Units: Subjects			
Female	23	13	9
Male	24	14	13
Race			
Units: Subjects			
White	42	25	19
Asian	1	0	0
Black or African American	0	0	1
Unknown or Not Reported	4	1	2
Other or More Than One Race	0	1	0
Ethnicity			
Units: Subjects			
Hispanic or Latino	1	0	2
Not Hispanic or Latino	42	26	18
Unknown or Not Reported	4	1	2

Reporting group values	Total		
Number of subjects	96		
Age categorical			
Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- 		
Gender categorical Units: Subjects			
Female	45		
Male	51		
Race Units: Subjects			
White	86		
Asian	1		
Black or African American	1		
Unknown or Not Reported	7		
Other or More Than One Race	1		
Ethnicity Units: Subjects			
Hispanic or Latino	3		
Not Hispanic or Latino	86		
Unknown or Not Reported	7		

End points

End points reporting groups

Reporting group title	Idelalisib 150 mg BID
Reporting group description:	
Participants received idelalisib 150 mg tablets, orally, twice daily (BID), continuously for up to maximum 33.5 months.	
Reporting group title	Idelalisib 100 mg BID
Reporting group description:	
Participants received idelalisib 100 mg tablets, orally, BID, continuously for up to maximum 63.6 months.	
Reporting group title	Idelalisib 150 mg BID INT
Reporting group description:	
Participants received idelalisib 150 mg tablets, orally, BID for 21 days and 7 days off-treatment (intermittent [INT] dosing schedule) in each 28-day cycle for up to maximum of 24.6 months.	

Primary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)[1]
End point description:	
ORR=percentage of participants who achieve a partial response (PR)/ complete response (CR).PR criteria: No evidence of new disease,a ≥50% decrease from baseline in sum of products of diameters (SPD) of index lesions,no increase in non-index disease, liver/spleen size and no new liver/spleen enlargement.Persistence of bone marrow involvement in participant who meets other CR criteria based on disappearance of all nodal,extra-nodal masses.CR criteria:No evidence of new disease,regression of all index nodal lesions to normal size (≤1.5 cm in longest dimension (LD) for large nodes and ≤1.0 cm in LD,≤1.0 cm in longest perpendicular dimension (LPD) for small nodes),regression to normal of all nodal non-index disease,disappearance of all detectable extra-nodal index,non-index disease,normal spleen, liver size,no new liver/spleen enlargement,morphologically -ve bone marrow. Intent-to-Treat (ITT) analysis set=all participants who were randomized regardless of whether they received any drug.	
End point type	Primary
End point timeframe:	
Randomization up to end of treatment (maximum duration: 73.5 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: No statistical comparison was planned or performed.	

End point values	Idelalisib 150 mg BID	Idelalisib 100 mg BID	Idelalisib 150 mg BID INT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	27	22	
Units: percentage of participants				
number (confidence interval 95%)	38.3 (24.5 to 53.6)	44.4 (25.5 to 64.7)	40.9 (20.7 to 63.6)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Grade 4 or Higher Treatment-Emergent

Adverse Events (TEAEs)

End point title	Number of Participants With Grade 4 or Higher Treatment-Emergent Adverse Events (TEAEs)[2]

End point description:

TEAEs were defined as 1 or both of any AEs leading to premature discontinuation of study drug, or any AEs with an onset date on or after the study drug start date and no later than the last exposure date after permanent discontinuation of the study drug. TEAEs severity was graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 5.0. Grade 1: Mild; Grade 2: Moderate; Grade 3: Severe; Grade 4: Life-threatening; Grade 5: Fatal. Participants were counted at the highest AE grade experienced. Safety analysis set included all participants who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

First dose date up to 30 days after last dose of study drug (maximum 64.6 months)

Notes:

[2] - 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: No statistical comparison was planned or performed.

End point values	Idelalisib 150 mg BID	Idelalisib 100 mg BID	Idelalisib 150 mg BID INT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	27	21	
Units: participants	15	12	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR) by Week 24

End point title	Overall Response Rate (ORR) by Week 24

End point description:

ORR by Week 24 is defined as the percentage of participants who achieve a PR or CR by Week 24. PR criteria: No evidence of new disease, a 50% decrease from baseline in SPD of index lesions, no increase in non-index disease, no increase in liver/spleen size and no new liver/spleen enlargement. CR criteria: No evidence of new disease, regression of all index nodal lesions to normal size (≤1.5 cm in LD for large nodes and ≤1.0 cm in LD, ≤1.0 cm in LPD for small nodes), regression to normal of all nodal non-index disease, disappearance of all detectable extra-nodal index and non-index disease, normal spleen and liver size, no new liver/spleen enlargement, morphologically negative bone marrow. Participants in the ITT analysis set were analysed.

End point type	Secondary

End point timeframe:

First dose date up to Week 24

End point values	Idelalisib 150 mg BID	Idelalisib 100 mg BID	Idelalisib 150 mg BID INT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	27	22	
Units: percentage of participants				
number (confidence interval 95%)	36.2 (22.7 to 51.5)	33.3 (16.5 to 54.0)	27.3 (10.7 to 50.2)	

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: interval from first documentation of CR/PR to earlier of first documentation of disease progression (PD) by independent review committee (IRC)/death from any cause. PR and CR criteria: Please refer the description of endpoint#2 (ORR). PD: New node of >1.5 cm or >1.0 to ≤1.5 cm in LD, >1.0 cm in LPD, new/unequivocal reappearance of resolved extra-nodal lesion, new non-index disease, increase by 50% in SPD of index lesions, LD of individual node/extra-nodal mass. Participants in the ITT analysis set who achieved CR or PR were analysed. 9999=The upper limit of 95% confidence interval (CI) was not estimable as the values were not reached.

End point type	Secondary

End point timeframe:

From first documentation of CR or PR until PD or death from any cause (maximum duration: 73.5 months)

End point values	Idelalisib 150 mg BID	Idelalisib 100 mg BID	Idelalisib 150 mg BID INT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	12	9	
Units: months				
median (confidence interval 95%)	27.1 (7.7 to 9999)	18.0 (2.7 to 9999)	5.7 (0.3 to 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With any TEAE, Grade 3 or Higher TEAEs, Serious TEAEs, Idelalisib-related TEAEs, TEAEs Leading to Interruption or Discontinuation of Idelalisib

End point title	Number of Participants With any TEAE, Grade 3 or Higher TEAEs, Serious TEAEs, Idelalisib-related TEAEs, TEAEs Leading to Interruption or Discontinuation of Idelalisib

End point description:

TEAEs were defined as 1 or both of any AEs leading to premature discontinuation of study drug, or any AEs with an onset date on or after the study drug start date and no later than the last exposure date after permanent discontinuation of the study drug. TEAEs severity was graded according to the NCI CTCAE version 5.0. Grade 1: Mild; Grade 2: Moderate; Grade 3: Severe; Grade 4: Life-threatening; Grade 5: Fatal. Participants are counted at the highest AE grade experienced. Participants in the safety analysis set were analysed.

End point type	Secondary

End point timeframe:

First dose date up to 30 days after last dose of study drug (maximum 64.6 months)

End point values	Idelalisib 150 mg BID	Idelalisib 100 mg BID	Idelalisib 150 mg BID INT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	27	21	
Units: participants				
Any TEAE	45	26	19	
Grade 3 or Higher TEAEs	41	25	12	
Serious TEAEs	31	19	11	
Idelalisib-related TEAEs	38	25	11	
TEAEs Leading to Interruption of Idelalisib	32	18	6	
TEAEs Leading to Discontinuation of Idelalisib	28	13	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Treatment-Emergent Laboratory Abnormalities

End point title	Number of Participants With Clinically Significant Treatment-Emergent Laboratory Abnormalities

End point description:

Treatment-emergent laboratory abnormality was defined as an increase of at least 1 toxicity grade from baseline at any time postbaseline up to and including the date of last study drug dose plus 30 days. Laboratory abnormalities included hematology and serum chemistry parameters. Clinically significant laboratory abnormalities were graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 for severity as Grade 1 (mild), Grade 2 (moderate), Grade 3 (severe), or Grade 4 (life threatening). The number of participants with any post-baseline abnormal laboratory value in Grade 1-4 categories are reported. Participants in the safety analysis set with available data were analysed.

End point type	Secondary

End point timeframe:

First dose date up to 30 days after last dose of study drug (maximum 64.6 months)

End point values	Idelalisib 150 mg BID	Idelalisib 100 mg BID	Idelalisib 150 mg BID INT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	27	20	
Units: participants				
Hematology: Grade 1	7	5	2	
Hematology: Grade 2	12	7	5	
Hematology: Grade 3	15	11	5	
Hematology: Grade 4	6	3	2	
Serum Chemistry: Grade 1 N=47,27,19	9	5	8	

Serum Chemistry: Grade 2 N=47,27,19	17	8	4	
Serum Chemistry: Grade 3 N=47,27,19	10	11	6	
Serum Chemistry: Grade 4 N=47,27,19	7	3	1	

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 interval (in months) from randomization to the earlier of the first documentation of PD by IRC or death from any cause. PD criteria: New node of >1.5 cm or >1.0 cm to ≤1.5 cm in LD, >1.0 cm in LPD, new/unequivocal reappearance of resolved extra-nodal lesion, new non-index disease, increase by 50% in SPD of index lesions, LD of individual node/extra-nodal mass. Participants in the ITT analysis set were analysed.

End point type	Secondary

End point timeframe:

Randomization up to PD or death from any cause (maximum duration: 73.5 months)

End point values	Idelalisib 150 mg BID	Idelalisib 100 mg BID	Idelalisib 150 mg BID INT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	27	22	
Units: months				
median (confidence interval 95%)	9.8 (5.5 to 28.7)	19.4 (13.9 to 23.3)	8.3 (2.9 to 8.7)	

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 interval (in months) from randomization to death from any cause. Participants in the ITT analysis set were analysed. 9999=The upper limit of 95% CI was not estimable as the values were not reached. 99999=Median and upper limit of 95% CI were not estimable as the values were not reached.

End point type	Secondary

End point timeframe:

Randomization up to death from any cause (maximum duration: 73.5 months)

End point values	Idelalisib 150 mg BID	Idelalisib 100 mg BID	Idelalisib 150 mg BID INT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	27	22	
Units: months				
median (confidence interval 95%)	28.7 (14.0 to 9999)	99999 (23.3 to 99999)	99999 (13.9 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Plasma Concentration of Idelalisib

End point title	Trough Plasma Concentration of Idelalisib

End point description:

Pharmacokinetic (PK) analysis set included participants who received at least 1 dose of study drug and had at least 1 sample with detectable drug concentration. Participants in the PK analysis set with available data were analysed. 9999=Mean and Standard Deviation (SD) were not available as the values were below the level of quantitation.

End point type	Secondary

End point timeframe:

Predose on Day (D) 1, Weeks (Wk) 2, 4, 6, 8, 10, 12, 16, 20, 24, 32, and 48

End point values	Idelalisib 150 mg BID	Idelalisib 100 mg BID	Idelalisib 150 mg BID INT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	44	27	21	
Units: nanograms per millilitre (ng/ml)				
arithmetic mean (standard deviation)				
D 1 N=43,27,21	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	
Wk 2 N=44,25,17	683.68 (± 514.166)	382.94 (± 352.842)	636.35 (± 461.042)	
Wk 4 N=38,23,18	623.64 (± 466.557)	447.78 (± 356.971)	94.14 (± 231.647)	
Wk 6 N=34,23,15	581.20 (± 470.988)	361.90 (± 248.996)	596.80 (± 401.619)	
Wk 8 N=32,21,14	655.16 (± 498.873)	430.33 (± 477.877)	77.66 (± 274.313)	
Wk 10 N=25,22,15	616.05 (± 370.862)	356.12 (± 372.557)	387.40 (± 314.249)	
Wk 12 N=27,21,16	630.56 (± 664.066)	389.21 (± 466.104)	272.44 (± 626.451)	
Wk 16 N=26,20,15	729.23 (± 832.158)	730.29 (± 936.798)	111.67 (± 296.666)	
Wk 20 N=22,19,14	525.91 (± 411.330)	745.58 (± 841.105)	107.34 (± 269.434)	
Wk 24 N=19,17,12	460.74 (± 321.766)	728.76 (± 760.391)	9999 (± 9999)	
Wk 32 N=16,11,11	446.13 (± 450.821)	388.58 (± 351.293)	352.73 (± 875.923)	
Wk 48 N=8,8,5	706.13 (± 580.022)	552.13 (± 571.081)	165.00 (± 368.951)	

Statistical analyses

No statistical analyses for this end point

Secondary: Peak Plasma Concentration of Idelalisib

End point title	Peak Plasma Concentration of Idelalisib

End point description:

Participants in the PK analysis set with available data were analysed.

End point type	Secondary

End point timeframe:

1.5 hours postdose on Day (D) 1, Weeks (Wk) 2, 4, 6, 8, 10, 12, 16, 20, 24, 32, and 48

End point values	Idelalisib 150 mg BID	Idelalisib 100 mg BID	Idelalisib 150 mg BID INT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	43	27	20	
Units: ng/ml				
arithmetic mean (standard deviation)				
D 1	2626.12 (± 1330.290)	1575.81 (± 803.317)	2221.35 (± 1621.291)	
Wk 2 N=42,24,18	2306.12 (± 810.433)	1520.29 (± 675.089)	2186.89 (± 1265.850)	
Wk 4 N=39,23,17	2353.95 (± 930.754)	1528.48 (± 759.936)	2608.12 (± 1009.937)	
Wk 6 N=30,21,15	2433.33 (± 1092.969)	1682.52 (± 939.455)	2341.33 (± 948.133)	
Wk 8 N=29,20,14	2207.59 (± 980.606)	1649.25 (± 940.683)	2786.43 (± 1591.408)	
Wk 10 N=24,19,15	2435.00 (± 1027.469)	1601.11 (± 804.605)	2380.00 (± 1118.679)	
Wk 12 N=24,19,15	2328.13 (± 1141.764)	1658.89 (± 837.159)	2316.20 (± 1391.815)	
Wk 16 N=23,20,12	2634.39 (± 1323.611)	1756.37 (± 826.784)	2372.50 (± 1335.420)	
Wk 20 N=19,17,13	2354.26 (± 1440.587)	1925.29 (± 776.516)	2177.69 (± 1417.505)	
Wk 24 N=15,17,10	2058.47 (± 905.071)	1914.65 (± 1151.998)	1906.30 (± 1099.458)	
Wk 32 N=14,10,10	2009.71 (± 1231.296)	2028.00 (± 593.236)	1825.00 (± 947.892)	
Wk 48 N=8,9,5	2655.13 (± 1348.957)	1448.33 (± 650.798)	1312.00 (± 850.894)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Onset of Adverse Events of Interest (AEIs)

End point title	Time to Onset of Adverse Events of Interest (AEIs)

End point description:

Time to onset of AEIs is defined as the interval (in months) from the start of idelalisib treatment to the first documentation of start of AEI. AEIs included grade ≥ 3 diarrhea/colitis, rash, febrile neutropenia, infection, and any grade of: Pneumonitis, bowel perforation, progressive multifocal leukoencephalopathy (PML), Pneumocystis jirovecii pneumonia (PJP), cytomegalovirus (CMV) infection, and organizing pneumonia.

End point type	Secondary

End point timeframe:

First dose date up to 30 days after last dose of study drug (maximum 64.6 months)

End point values	Idelalisib 150 mg BID	Idelalisib 100 mg BID	Idelalisib 150 mg BID INT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[3]	0[4]	0[5]	
Units: months				
median (inter-quartile range (Q1-Q3))	(to)	(to)	(to)	

Notes:

[3] - AEIs data was not collected for analysis.

[4] - AEIs data was not collected for analysis.

[5] - AEIs data was not collected for analysis.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-Cause Mortality: Enrollment up to last follow up visit (maximum 73.5 months); Adverse Events: First dose date up to 30 days after last dose of study drug (maximum 64.6 months)

Adverse event reporting additional description:

All-Cause Mortality: All enrolled analysis set included all participants who received a study participant identification number after screening and was used for participant enrollment summary and data listings, unless otherwise specified.
Adverse Events: Safety analysis set included all participants who received at least 1 dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25

Reporting groups

Reporting group title	Idelalisib 150 mg BID

Reporting group description:

Participants received idelalisib 150 mg tablets, orally, BID, continuously for up to maximum 33.5 months.

Reporting group title	Idelalisib 150 mg BID INT

Reporting group description:

Participants received idelalisib 150 mg tablets, orally, BID for 21 days and 7 days off-treatment (INT dosing schedule) in each 28-day cycle for up to maximum of 24.6 months.

Reporting group title	Idelalisib 100 mg BID

Reporting group description:

Participants received idelalisib 100 mg tablets, orally, BID, continuously for up to maximum 63.6 months.

Serious adverse events	Idelalisib 150 mg BID	Idelalisib 150 mg BID INT	Idelalisib 100 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	31 / 47 (65.96%)	11 / 21 (52.38%)	19 / 27 (70.37%)
number of deaths (all causes)	20	6	12
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (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
Acute myeloid leukaemia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 21 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Generalised oedema			
subjects affected / exposed	0 / 47 (0.00%)	0 / 21 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 47 (2.13%)	1 / 21 (4.76%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial pain			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (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
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (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
Lung disorder			
subjects affected / exposed	0 / 47 (0.00%)	0 / 21 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			

subjects affected / exposed	0 / 47 (0.00%)	1 / 21 (4.76%)	0 / 27 (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
Pneumonitis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 47 (0.00%)	0 / 21 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
International normalised ratio ~ increased			
subjects affected / exposed	0 / 47 (0.00%)	0 / 21 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical condition abnormal			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (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
Klebsiella test positive			
subjects affected / exposed	0 / 47 (0.00%)	0 / 21 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Pelvic fracture			
subjects affected / exposed	0 / 47 (0.00%)	0 / 21 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 47 (0.00%)	0 / 21 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Atrial flutter			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 47 (2.13%)	1 / 21 (4.76%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	0 / 47 (0.00%)	1 / 21 (4.76%)	0 / 27 (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
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (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
Febrile neutropenia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	2 / 27 (7.41%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	2 / 47 (4.26%)	1 / 21 (4.76%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Visual field defect			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (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			
Diarrhoea			

subjects affected / exposed	7 / 47 (14.89%)	0 / 21 (0.00%)	6 / 27 (22.22%)
occurrences causally related to treatment / all	7 / 7	0 / 0	7 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	3 / 47 (6.38%)	0 / 21 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	2 / 47 (4.26%)	0 / 21 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 47 (2.13%)	1 / 21 (4.76%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stevens-Johnson syndrome			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	0 / 47 (0.00%)	0 / 21 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 47 (0.00%)	0 / 21 (0.00%)	4 / 27 (14.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Haematuria			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (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
Hydronephrosis			
subjects affected / exposed	0 / 47 (0.00%)	1 / 21 (4.76%)	0 / 27 (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 failure			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (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
Renal impairment			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (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
Endocrine disorders			
Hypercalcaemia of malignancy			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteonecrosis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 21 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mobility decreased			
subjects affected / exposed	0 / 47 (0.00%)	0 / 21 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Infections and infestations			
Sepsis			

subjects affected / exposed	0 / 47 (0.00%)	1 / 21 (4.76%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Covid-19 pneumonia			
subjects affected / exposed	1 / 47 (2.13%)	1 / 21 (4.76%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia			
subjects affected / exposed	1 / 47 (2.13%)	1 / 21 (4.76%)	2 / 27 (7.41%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Covid-19			
subjects affected / exposed	1 / 47 (2.13%)	2 / 21 (9.52%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal infection			
subjects affected / exposed	0 / 47 (0.00%)	1 / 21 (4.76%)	0 / 27 (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 haemophilus			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (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
Aspergillus infection			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			

subjects affected / exposed	0 / 47 (0.00%)	0 / 21 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronavirus pneumonia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (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
Neutropenic sepsis			
subjects affected / exposed	0 / 47 (0.00%)	1 / 21 (4.76%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Oesophageal candidiasis			
subjects affected / exposed	0 / 47 (0.00%)	0 / 21 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (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
Suspected COVID-19			
subjects affected / exposed	0 / 47 (0.00%)	0 / 21 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 47 (0.00%)	0 / 21 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	2 / 47 (4.26%)	0 / 21 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 21 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Idelalisib 150 mg BID	Idelalisib 150 mg BID INT	Idelalisib 100 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 47 (93.62%)	16 / 21 (76.19%)	24 / 27 (88.89%)
Investigations			
Weight decreased			
subjects affected / exposed	4 / 47 (8.51%)	0 / 21 (0.00%)	3 / 27 (11.11%)
occurrences (all)	4	0	4
Alanine aminotransferase increased			
subjects affected / exposed	9 / 47 (19.15%)	0 / 21 (0.00%)	5 / 27 (18.52%)
occurrences (all)	11	0	10
Aspartate aminotransferase increased			

subjects affected / exposed	8 / 47 (17.02%)	0 / 21 (0.00%)	6 / 27 (22.22%)
occurrences (all)	10	0	9
Transaminases increased			
subjects affected / exposed	1 / 47 (2.13%)	2 / 21 (9.52%)	0 / 27 (0.00%)
occurrences (all)	1	3	0
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 47 (10.64%)	0 / 21 (0.00%)	2 / 27 (7.41%)
occurrences (all)	5	0	2
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 47 (6.38%)	1 / 21 (4.76%)	2 / 27 (7.41%)
occurrences (all)	3	1	3
Dizziness			
subjects affected / exposed	0 / 47 (0.00%)	2 / 21 (9.52%)	1 / 27 (3.70%)
occurrences (all)	0	2	1
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	6 / 47 (12.77%)	0 / 21 (0.00%)	3 / 27 (11.11%)
occurrences (all)	7	0	5
Neutropenia			
subjects affected / exposed	12 / 47 (25.53%)	4 / 21 (19.05%)	10 / 27 (37.04%)
occurrences (all)	29	9	21
Anaemia			
subjects affected / exposed	10 / 47 (21.28%)	2 / 21 (9.52%)	3 / 27 (11.11%)
occurrences (all)	12	4	4
Febrile neutropenia			
subjects affected / exposed	0 / 47 (0.00%)	0 / 21 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	11 / 47 (23.40%)	3 / 21 (14.29%)	6 / 27 (22.22%)
occurrences (all)	13	6	6
Asthenia			
subjects affected / exposed	4 / 47 (8.51%)	3 / 21 (14.29%)	4 / 27 (14.81%)
occurrences (all)	5	4	6

Oedema peripheral			
subjects affected / exposed	5 / 47 (10.64%)	3 / 21 (14.29%)	2 / 27 (7.41%)
occurrences (all)	5	4	2
Fatigue			
subjects affected / exposed	5 / 47 (10.64%)	2 / 21 (9.52%)	2 / 27 (7.41%)
occurrences (all)	5	2	2
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	19 / 47 (40.43%)	6 / 21 (28.57%)	12 / 27 (44.44%)
occurrences (all)	35	9	39
Abdominal pain			
subjects affected / exposed	5 / 47 (10.64%)	2 / 21 (9.52%)	2 / 27 (7.41%)
occurrences (all)	5	2	2
Colitis			
subjects affected / exposed	3 / 47 (6.38%)	0 / 21 (0.00%)	1 / 27 (3.70%)
occurrences (all)	3	0	1
Nausea			
subjects affected / exposed	5 / 47 (10.64%)	4 / 21 (19.05%)	6 / 27 (22.22%)
occurrences (all)	5	5	7
Constipation			
subjects affected / exposed	6 / 47 (12.77%)	2 / 21 (9.52%)	4 / 27 (14.81%)
occurrences (all)	6	2	6
Vomiting			
subjects affected / exposed	4 / 47 (8.51%)	1 / 21 (4.76%)	5 / 27 (18.52%)
occurrences (all)	4	2	9
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 47 (17.02%)	0 / 21 (0.00%)	4 / 27 (14.81%)
occurrences (all)	8	0	8
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	11 / 47 (23.40%)	6 / 21 (28.57%)	4 / 27 (14.81%)
occurrences (all)	19	9	8
Hyperhidrosis			
subjects affected / exposed	3 / 47 (6.38%)	0 / 21 (0.00%)	0 / 27 (0.00%)
occurrences (all)	4	0	0

Psoriasis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 21 (0.00%)	2 / 27 (7.41%)
occurrences (all)	1	0	2
Rash papular			
subjects affected / exposed	0 / 47 (0.00%)	2 / 21 (9.52%)	0 / 27 (0.00%)
occurrences (all)	0	2	0
Dermatitis allergic			
subjects affected / exposed	1 / 47 (2.13%)	2 / 21 (9.52%)	1 / 27 (3.70%)
occurrences (all)	1	2	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 47 (0.00%)	1 / 21 (4.76%)	2 / 27 (7.41%)
occurrences (all)	0	1	2
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	4 / 47 (8.51%)	1 / 21 (4.76%)	4 / 27 (14.81%)
occurrences (all)	4	1	5
Muscle spasms			
subjects affected / exposed	1 / 47 (2.13%)	3 / 21 (14.29%)	0 / 27 (0.00%)
occurrences (all)	1	3	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	3 / 47 (6.38%)	0 / 21 (0.00%)	4 / 27 (14.81%)
occurrences (all)	4	0	5
Influenza			
subjects affected / exposed	3 / 47 (6.38%)	0 / 21 (0.00%)	0 / 27 (0.00%)
occurrences (all)	3	0	0
Respiratory tract infection			
subjects affected / exposed	3 / 47 (6.38%)	1 / 21 (4.76%)	0 / 27 (0.00%)
occurrences (all)	3	1	0
Urinary tract infection			
subjects affected / exposed	3 / 47 (6.38%)	2 / 21 (9.52%)	4 / 27 (14.81%)
occurrences (all)	3	2	8
Bronchitis			
subjects affected / exposed	2 / 47 (4.26%)	2 / 21 (9.52%)	1 / 27 (3.70%)
occurrences (all)	3	3	1

Oral candidiasis			
subjects affected / exposed	4 / 47 (8.51%)	1 / 21 (4.76%)	0 / 27 (0.00%)
occurrences (all)	4	2	0
Covid-19			
subjects affected / exposed	1 / 47 (2.13%)	2 / 21 (9.52%)	1 / 27 (3.70%)
occurrences (all)	1	2	1
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	3 / 47 (6.38%)	2 / 21 (9.52%)	2 / 27 (7.41%)
occurrences (all)	3	2	2
Decreased appetite			
subjects affected / exposed	5 / 47 (10.64%)	1 / 21 (4.76%)	2 / 27 (7.41%)
occurrences (all)	6	1	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 March 2016	• Updated the safety information and guidelines for toxicity management to be consistent across idelalisib study protocols, changes included mandated prophylaxis for Pneumocystis jirovecii pneumonia (PJP), Cytomegalovirus (CMV) surveillance, and increased monitoring: CMV testing frequency update (once in 4weeks); Toxicity Management updated to 'Recommendations for Evaluation, Intervention, and Drug Discontinuation for Specific Adverse Events or Conditions' • Target population was modified to align with the European Union (EU) licensed indication of idelalisib. Inclusion criteria modified to require that participants be refractory to and disease progression within 6 months from the last dose of at least two lines of prior therapy; Title and all protocol language modified to include only participants with follicular lymphoma; Removed stratification by FL/Small Lymphocytic Lymphoma (SLL) • Clarified and revised inclusion/exclusion criterion requirements: Modified inclusion criteria to align with Grade 3 neutropenia, thrombocytopenia, and anemia; Removed inclusion criteria due to French central ethics committee (CEC) request • Clarified the section Vital Signs to specify which vital signs will be collected and at which visits • Revised text to allow for the 30-Day Follow-up visit to be conducted via phone (instead of a clinic visit) • Updated language added to Appendix Pregnancy Precautions, Definition for Female of Childbearing Potential, and Contraceptive Requirements to align with the EU guidance for Zydelig contraception language in protocol amendments • Updated language added to Appendix Efficacy Assessments, Nodal Index Lesions to align with Cheson criteria
07 June 2016	• Removed screening viral titers • Clarified that around the timing of protocol requires unblinding during study participation
08 September 2016	Alignment with Urgent Safety Measures to define the recommended versus required actions related to dose modifications for adverse events related to idelalisib.
25 September 2017	Organizing pneumonia (OP) emerged as a potential safety signal during Gilead routine signal detection monitoring. This risk was included in the Investigator's Brochure (IB). All idelalisib protocols with ongoing participants were amended to add OP as a potential risk.
13 March 2019	Amended to fulfill a new post marketing requirement (PMR) 2180-10, to verify the clinical benefit of Zydelig, including defined efficacy and safety endpoints and an alternative, non-continuous dosing regimen proposed by Food and Drug Administration (FDA), as follows: • Conduct a trial establishing a safe and effective dosing regimen of idelalisib in patients with relapsed or refractory FL who have no other therapeutic options and require treatment. Include a dosing-regimen arm of 28-day cycles with 21 days on-treatment and 7 days off-treatment • The primary efficacy endpoint should be ORR. There should be sufficient follow-up to provide a credible assessment of DOR. A dosing regimen of idelalisib was considered to be effective in relapsed/refractory FL if the ORR is greater than 50% with a DOR of at least 6 months • The primary safety endpoint should be incidence of grade 4 and 5 TEAE. A dosing regimen of idelalisib was considered safe in this patient population if the rate of grade 4 and 5 TEAE is less than 30% • In addition, enrollment to Arm B was closed. This decision was based on preliminary data suggesting that Arm B appears unlikely to meet the PMR objective of achieving an ORR ≥50%, and there was insufficient exposure to the 100mg twice daily dosing regimen to evaluate intermediate and long term safety

18 March 2021	• Unblinded the remaining blinded participants on the study for data analysis and the study design was made open label and all subsequent participants moved into Arm A and all participants enlisted into newly created Arm C were enrolled in an unblinded manner. However, there were participants remaining on the study who had been originally blinded across Arm A and Arm B • Included appendix Pandemic Risk Assessment and Mitigation Plan, which summarized potential risks associated with participants being unable to attend study visits due to an ongoing pandemic and mitigation plans • Exclusion criteria was updated to clarify that participants who received antiviral prophylaxis specifically for CMV should be excluded. • Include drug reactions with eosinophilia and systemic symptoms (DRESS) and progressive multifocal leukoencephalopathy (PML) as specific adverse events to align with the current version of the IB • Added a section outlining coronavirus disease 2019 (COVID-19) vaccination guidelines whilst a participant is on study drug

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
27 September 2022	Gilead has made the decision to close the study due to enrollment challenges.	-

Notes:

Limitations and caveats

None reported