



Clinical trial results:

A Phase 2 Study to Assess the Efficacy and Safety of Idelalisib in Subjects with Indolent B-Cell Non-Hodgkin Lymphomas Refractory to Rituximab and Alkylating Agents

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2010-022155-33 |
| Trial protocol | DE GB IT |
| Global end of trial date | 16 May 2018 |

Results information

| | |
|--------------------------------|---|
| Result version number | v2 (current) |
| This version publication date | 30 June 2019 |
| First version publication date | 30 May 2019 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set Update to study start date, primary completion date, time frames for some endpoints, and death (all causes) data. |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 101-09 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01282424 |
| 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 | 16 May 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 02 May 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 16 May 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the overall response rate and to evaluate the efficacy and safety of idelalisib (IDELA; GS-1101) in participants with previously treated indolent Non-Hodgkin Lymphoma (iNHL) that was refractory both to rituximab and to alkylating-agent-containing chemotherapy.

Eligible participants initiated oral therapy with idelalisib at a starting dose of 150 mg taken twice per day. Treatment with idelalisib continued in compliant participants as long as the study was still ongoing and the participants appear to be benefiting from treatment with acceptable safety.

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 | 18 March 2011 |
| 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? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Poland: 8 |
| Country: Number of subjects enrolled | United Kingdom: 8 |
| Country: Number of subjects enrolled | France: 10 |
| Country: Number of subjects enrolled | Germany: 10 |
| Country: Number of subjects enrolled | Italy: 6 |
| Country: Number of subjects enrolled | United States: 83 |
| Worldwide total number of subjects | 125 |
| EEA total number of subjects | 42 |

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) | 69 |
| From 65 to 84 years | 54 |
| 85 years and over | 2 |

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at a total of 54 study sites in North America and Europe. The first participant was screened on 04 March 2011. The last participant observation was on 16 May 2018.

Pre-assignment

Screening details:

125 participants were enrolled and treated and comprise the Intent-to-Treat (ITT) Analysis Set.

Period 1

| | |
|------------------------------|-----------------------------------|
| Period 1 title | Treatment Period (TP) (81 months) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------|------------|
| Arm title | Idelalisib |
|------------------|------------|

Arm description:

Idelalisib 150 mg tablet administered orally twice daily until tumor progression or development of unacceptable toxicity.

| | |
|--|-------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Idelalisib |
| Investigational medicinal product code | GS-1101 |
| Other name | IDELA, formerly CAL-101 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Idelalisib 150 mg administered twice daily until tumor progression or development of unacceptable toxicity.

| Number of subjects in period 1 | Idelalisib |
|--------------------------------|-------------------|
| Started | 125 |
| Completed: Disease Progression | 70 ^[1] |
| Completed: Death | 9 ^[2] |
| Completed | 79 |
| Not completed | 46 |
| Withdrew Consent | 6 |
| Adverse Event | 30 |
| Investigator Request | 7 |
| Other (Unknown) | 3 |

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: 70 participants with disease progression is a subcategory for the number of participants

who completed the TP overall.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: 9 participants who died during the study is a subcategory for the number of participants who completed the TP overall.

Period 2

| | |
|------------------------------|--------------------------------------|
| Period 2 title | Long-term Follow-up Period (5 years) |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|-----------|------------|
| Arm title | Idelalisib |
|-----------|------------|

Arm description:

Idelalisib 150 mg tablet administered orally twice daily until tumor progression or development of unacceptable toxicity.

| | |
|--|-------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Idelalisib |
| Investigational medicinal product code | GS-1101 |
| Other name | IDELA, formerly CAL-101 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Idelalisib 150 mg administered twice daily until tumor progression or development of unacceptable toxicity.

| Number of subjects in period 2 ^[3] | Idelalisib |
|--|------------|
| Started | 54 |
| Completed | 20 |
| Not completed | 64 |
| Withdrew Consent | 2 |
| Other (Unknown) | 21 |
| Death | 40 |
| Lost to follow-up | 1 |
| Joined | 30 |
| Discontinued TP but joined Long-term Follow-up | 30 |

Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: 54 of 79 participants who completed the TP entered the Long-term Follow up Period. 30 additional participants who discontinued the TP also joined the Long-term Follow-up Period. Therefore, a total of 84 participants entered the Long-term Follow up Period.

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Idelalisib |
|-----------------------|------------|

Reporting group description:

Idelalisib 150 mg tablet administered orally twice daily until tumor progression or development of unacceptable toxicity.

| Reporting group values | Idelalisib | Total | |
|--|------------|-------|--|
| Number of subjects | 125 | 125 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 62 | | |
| standard deviation | ± 11.4 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 45 | 45 | |
| Male | 80 | 80 | |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| Ethnicity: Hispanic or Latino | 6 | 6 | |
| Ethnicity: Not Hispanic or Latino | 117 | 117 | |
| Ethnicity: Missing | 2 | 2 | |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| Race: White/Caucasian | 110 | 110 | |
| Race: Black or African American | 2 | 2 | |
| Race: Asian | 3 | 3 | |
| Race: American Indian or Alaska Native | 1 | 1 | |
| Race: Other | 8 | 8 | |
| Race: Missing | 1 | 1 | |
| Karnofsky Performance Status | | | |
| Karnofsky performance status classified participants according to their functional impairment. Scores ranged from 0-100, the lower the score, the worse the survival for most serious illnesses. | | | |
| Units: Subjects | | | |
| Score = 60 | 2 | 2 | |
| Score = 70 | 6 | 6 | |
| Score = 80 | 27 | 27 | |
| Score = 90 | 44 | 44 | |
| Score = 100 | 46 | 46 | |
| Baseline Disease History | | | |
| LPL/WM: Lymphoplasmacytic lymphoma/Waldenström macroglobulinemia | | | |
| Units: Subjects | | | |
| Follicular lymphoma | 72 | 72 | |
| Small lymphocytic lymphoma | 28 | 28 | |

| | | | |
|------------------------|----|----|--|
| LPL/WM | 10 | 10 | |
| Marginal zone lymphoma | 15 | 15 | |

End points

End points reporting groups

| | |
|---|------------|
| Reporting group title | Idelalisib |
| Reporting group description: Idelalisib 150 mg tablet administered orally twice daily until tumor progression or development of unacceptable toxicity. | |
| Reporting group title | Idelalisib |
| Reporting group description: Idelalisib 150 mg tablet administered orally twice daily until tumor progression or development of unacceptable toxicity. | |

Primary: Overall Response Rate

| | |
|---|--------------------------------------|
| End point title | Overall Response Rate ^[1] |
| End point description: Overall response rate (ORR) was assessed based on the International Working Group Revised Response Criteria for Malignant Lymphoma (Cheson, 2007), and was defined as the percentage of participants achieving a complete response (CR) or partial response (PR; or minor response [MR] for participants with WM) as assessed by the study independent review committee (IRC). CR was defined as the complete resolution of all disease-related radiological abnormalities and the disappearance of all signs and symptoms related to the disease. PR was defined as a $\geq 50\%$ reduction in the sum of the products of the longest perpendicular diameters of all index lesions, with no new lesions. For WM only, response was defined as a reduction in immunoglobulin M (IgM) of $\geq 50\%$ decrease for PR, and $\geq 25\%$ decrease for MR; no increase from baseline in the sum of the products of the longest perpendicular diameters of all index lesions, with no new lesions or signs and symptoms of active disease (Owen, 2013) | |
| End point type | Primary |
| End point timeframe: Start of Treatment to End of Treatment (up to 81 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: The statistical analysis of this primary endpoint is provided in the attachment. | |

| | | | | |
|-----------------------------------|---------------------|--|--|--|
| End point values | Idelalisib | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 125 ^[2] | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 57.6 (48.4 to 66.4) | | | |

Notes:

[2] - ITT Analysis Set included enrolled participants who received at least one dose of study drug.

| | |
|-----------------------------------|---|
| Attachments (see zip file) | Statistical Analysis/101-09_Primary_Endpoint_StatsAnalysis. |
|-----------------------------------|---|

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

| | |
|--|----------------------|
| End point title | Duration of Response |
| End point description: | |
| Duration of Response (DOR) was defined as the interval from the first documentation of CR or PR (or MR for participants with WM) to the earlier of the first documentation of disease progression as assessed by the study IRC or death from any cause. DOR was analyzed using Kaplan-Meier (KM) estimates. Participants in ITT Analysis Set who achieved a CR or PR (or MR for participants with WM) were analyzed. | |
| End point type | Secondary |
| End point timeframe: | |
| Start of Treatment to End of Treatment (up to 81 months) | |

| | | | | |
|---------------------------------------|--------------------|--|--|--|
| End point values | Idelalisib | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 72 | | | |
| Units: months | | | | |
| median (inter-quartile range (Q1-Q3)) | 12.5 (6.2 to 28.6) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Lymph Node Response Rate

| | |
|--|--------------------------|
| End point title | Lymph Node Response Rate |
| End point description: | |
| Lymph node response (LNR) was defined as the percentage of participants who achieved a $\geq 50\%$ decrease from baseline in the sum of the product of the perpendicular diameters (SPD) of measurable index lesions as assessed by the study IRC. Participants in the ITT Analysis Set were analyzed. | |
| End point type | Secondary |
| End point timeframe: | |
| Start of Treatment to End of Treatment (up to 81 months) | |

| | | | | |
|-----------------------------------|---------------------|--|--|--|
| End point values | Idelalisib | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 125 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 56.8 (47.6 to 65.6) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response

| | |
|-----------------|------------------|
| End point title | Time to Response |
|-----------------|------------------|

End point description:

Time to response (TTR) was defined as the interval from the start of idelalisib treatment to the first documentation of CR or PR (or MR for participants with WM) as assessed by the study IRC. Participants in the ITT Analysis Set who achieved a CR or PR (or MR for participants with WM) were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Start of Treatment to End of Treatment (up to 81 months)

| End point values | Idelalisib | | | |
|---------------------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 72 | | | |
| Units: months | | | | |
| median (inter-quartile range (Q1-Q3)) | 2.0 (1.8 to 4.2) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival

| | |
|-----------------|---------------------------|
| End point title | Progression-Free Survival |
|-----------------|---------------------------|

End point description:

Progression-free survival (PFS) was defined as the interval from the start of idelalisib treatment to the earlier of the first documentation of disease progression as assessed by the study IRC or death from any cause. PFS was analyzed using KM estimates. Participants in the ITT Analysis Set were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Start of Treatment to End of Treatment (up to 81 months)

| End point values | Idelalisib | | | |
|----------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 125 | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 11.1 (8.3 to 14.0) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

| | |
|-----------------|------------------|
| End point title | Overall Survival |
|-----------------|------------------|

End point description:

Overall survival (OS) was defined as the time interval from the start of idelalisib treatment to death from any cause. OS was analyzed using KM estimates. Participants in the ITT Analysis Set were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Start of Treatment to Last Long-Term Follow-Up Visit (up to maximum of 7 years)

| End point values | Idelalisib | | | |
|----------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 125 | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 48.6 (33.9 to 71.7) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Health-Related Quality of Life Using the Functional Assessment of Cancer Therapy: Lymphoma Subscale (FACT-LymS)

| | |
|-----------------|---|
| End point title | Change in Health-Related Quality of Life Using the Functional Assessment of Cancer Therapy: Lymphoma Subscale (FACT-LymS) |
|-----------------|---|

End point description:

Change in health-related quality of life events were reported by participants using the Functional Assessment of Cancer Therapy: Lymphoma Subscale (FACT-LymS) assessment tool. Results are presented as the mean (SD) best change from baseline. The best change from baseline was defined as the highest change score (improvement) after baseline.

The FACT-LymS is on a scale from 0-60, with higher scores associated with a better quality of life. It incorporates values from 15 questions, each rated 0-4, related to study indications. Participants in the ITT Analysis Set with available data were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to End of Treatment (up to 81 months)

| End point values | Idelalisib | | | |
|--------------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 113 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | 10.3 (\pm 17.08) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Karnofsky Performance Status

| | |
|-----------------|--|
| End point title | Change in Karnofsky Performance Status |
|-----------------|--|

End point description:

The change in Karnofsky performance status was reported as the best (highest change score) and worst (lowest change score) change from baseline using the Karnofsky performance criteria. The Karnofsky score classified participants according to their functional impairment. Scores are on a scale from 0-100, the lower the score, the worse the survival for most serious illnesses. Participants in the ITT Analysis Set with available data were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to End of Treatment (up to 81 months)

| End point values | Idelalisib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 122 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Best change | 3.0 (± 8.71) | | | |
| Worst change | -10.7 (± 12.61) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Changes in Plasma Concentrations of Disease-Associated Chemokines and Cytokines

| | |
|-----------------|---|
| End point title | Changes in Plasma Concentrations of Disease-Associated Chemokines and Cytokines |
|-----------------|---|

End point description:

Analysis of the cytokine/chemokine was planned to be performed on a subset of samples from this study along with a subset of samples from other studies. Therefore, data for this endpoint are not reported here because the analysis population includes participants who were not enrolled in this study.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Enrollment to End of Treatment (up to 81 months)

| End point values | Idelalisib | | | |
|--------------------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0 ^[3] | | | |
| Units: pg/mL | | | | |
| arithmetic mean (standard deviation) | () | | | |

Notes:

[3] - Data not reported

Statistical analyses

No statistical analyses for this end point

Secondary: Safety and Tolerability of Idelalisib Assessed as the Number of Participants Experiencing Adverse Events (AEs) or Abnormalities in Vital Signs, Laboratory Tests, or Electrocardiograms

| | |
|-----------------|---|
| End point title | Safety and Tolerability of Idelalisib Assessed as the Number of Participants Experiencing Adverse Events (AEs) or Abnormalities in Vital Signs, Laboratory Tests, or Electrocardiograms |
|-----------------|---|

End point description:

This composite endpoint measured the safety and tolerability profile of idelalisib. "Clinically meaningful" abnormalities in vital signs and electrocardiograms (ECG) were as determined by the investigator. Participants in the ITT Analysis Set were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Start of Treatment to End of Treatment (up to 81 months) plus 30 days

| End point values | Idelalisib | | | |
|--|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 125 | | | |
| Units: participants | | | | |
| Any AE | 123 | | | |
| AE leading to drug discontinuation | 35 | | | |
| Serious AE | 72 | | | |
| Vital signs abnormal – clinically meaningful | 0 | | | |
| ECG abnormal – clinically meaningful | 0 | | | |
| Grade 3 or 4 hemoglobin | 2 | | | |
| Grade 3 or 4 neutrophils | 35 | | | |
| Grade 3 or 4 platelets | 9 | | | |
| Grade 3 or 4 alanine aminotransferase | 16 | | | |
| Grade 3 or 4 aspartate aminotransferase | 11 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Study Drug Exposure

| | |
|-----------------|---------------------|
| End point title | Study Drug Exposure |
|-----------------|---------------------|

End point description:

The average idelalisib exposure was summarized. Participants in the ITT Analysis Set were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Start of Treatment to End of Treatment (up to 81 months)

| End point values | Idelalisib | | | |
|--------------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 125 | | | |
| Units: months | | | | |
| arithmetic mean (standard deviation) | 13.2 (± 15.08) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Idelalisib Plasma Concentration

| | |
|-----------------|---------------------------------|
| End point title | Idelalisib Plasma Concentration |
|-----------------|---------------------------------|

End point description:

Pharmacokinetic (PK) Analysis Set included participants in the ITT Analysis Set who had the necessary baseline and on-study measurements.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Predose and at 1.5 hours (± 5 minutes) postdose on Day 29

| End point values | Idelalisib | | | |
|--------------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 125 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Predose (n = 108) | 471.6 (± 486.53) | | | |
| Postdose (n =106) | 2187.7 (± 1050.76) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Cmax

| | |
|-----------------|--------------------|
| End point title | PK Parameter: Cmax |
|-----------------|--------------------|

End point description:

Cmax at Days 1 and 29 was analyzed. Cmax is defined as the maximum concentration of drug. Participants in the PK Analysis Set with available data were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Predose and at 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, and 12 hours postdose on Days 1 and 29

| End point values | Idelalisib | | | |
|--------------------------------------|-------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cmax at Day 1 | 2647.5 (\pm 1084.99) | | | |
| Cmax at Day 29 | 2258.8 (\pm 809.61) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Tmax

| | |
|-----------------|--------------------|
| End point title | PK Parameter: Tmax |
|-----------------|--------------------|

End point description:

Tmax at Days 1 and 29 was analyzed. Tmax is defined as the time of Cmax (the maximum concentration of drug). Participants in the PK Analysis Set with available data were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Predose and at 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, and 12 hours postdose on Days 1 and 29

| End point values | Idelalisib | | | |
|--|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: hours | | | | |
| arithmetic mean (inter-quartile range (Q1-Q3)) | | | | |
| Tmax at Day 1 | 1.00 (0.99 to 1.04) | | | |

| | | | | |
|----------------|---------------------|--|--|--|
| Tmax at Day 29 | 1.00 (0.95 to 2.00) | | | |
|----------------|---------------------|--|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: AUClast

| | |
|-----------------|-----------------------|
| End point title | PK Parameter: AUClast |
|-----------------|-----------------------|

End point description:

AUClast at Days 1 and 29 was analyzed. AUClast is defined as the concentration of drug from time zero to the last observable concentration. Participants in the PK Analysis Set with available data were analyzed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Predose and at 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, and 12 hours postdose on Days 1 and 29

| End point values | Idelalisib | | | |
|--------------------------------------|----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: hours x ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| AUClast at Day 1 | 9094.76 (± 2960.391) | | | |
| AUClast at Day 29 | 9293.39 (± 3996.826) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: Start of Treatment to End of Treatment (up to 81 months) plus 30 days; All-Cause Mortality: Baseline to Last Long-Term Follow-Up Visit (up to maximum of 7 years)

Adverse event reporting additional description:

ITT Analysis Set included enrolled participants who received at least one dose of study drug.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Idelalisib |
|-----------------------|------------|

Reporting group description:

Idelalisib 150 mg tablet administered orally twice daily until tumor progression or development of unacceptable toxicity.

| Serious adverse events | Idelalisib | | |
|---|-------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 72 / 125 (57.60%) | | |
| number of deaths (all causes) | 64 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Adenocarcinoma | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastric cancer | | | |

| | | | |
|--|-------------------|--|--|
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin cancer | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lymphorrhoea | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 15 / 125 (12.00%) | | |
| occurrences causally related to treatment / all | 0 / 16 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peripheral swelling | | | |
| subjects affected / exposed | 3 / 125 (2.40%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Asthenia | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Chest pain | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 2 | | |
| Death | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Autoimmune disorder | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 3 / 125 (2.40%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonitis | | | |
| subjects affected / exposed | 3 / 125 (2.40%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 1 | | |

| | | | |
|---|-----------------|--|--|
| Pleural effusion | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lung infiltration | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fracture | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Head injury | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hip fracture | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Limb injury | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Cardiac failure | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Cardiomyopathy | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sinus tachycardia | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Cerebral ischaemia | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Paraplegia | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 5 / 125 (4.00%) | | |
| occurrences causally related to treatment / all | 0 / 8 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neutropenia | | | |
| subjects affected / exposed | 3 / 125 (2.40%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Autoimmune haemolytic anaemia | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Splenic infarction | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Visual impairment | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 11 / 125 (8.80%) | | |
| occurrences causally related to treatment / all | 0 / 14 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Colitis | | | |
| subjects affected / exposed | 5 / 125 (4.00%) | | |
| occurrences causally related to treatment / all | 0 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Melaena | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abdominal pain | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Acute abdomen | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Autoimmune colitis | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Enteritis | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Enterocolitis | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal haemorrhage | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haemorrhoids | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Mouth haemorrhage | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nausea | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oesophagitis | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancreatitis | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatic function abnormal | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|--------------------------------------|--|--|
| Dermatitis exfoliative generalised subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 125 (0.80%) 0 / 1 0 / 0 | | |
| Erythema subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 125 (0.80%) 0 / 1 0 / 0 | | |
| Rash subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 125 (0.80%) 0 / 1 0 / 0 | | |
| Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 4 / 125 (3.20%) 0 / 4 0 / 0 | | |
| Hydronephrosis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 125 (0.80%) 0 / 1 0 / 0 | | |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 125 (0.80%) 0 / 1 0 / 0 | | |
| Infections and infestations Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 15 / 125 (12.00%) 0 / 21 0 / 3 | | |
| Cytomegalovirus colitis | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 2 / 125 (1.60%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Device related infection | | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Perirectal abscess | | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumocystis jirovecii pneumonia | | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Sepsis | | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Septic shock | | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Urinary tract infection | | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cellulitis | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis | | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Herpes zoster | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infective exacerbation of chronic obstructive airways disease | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lung infection | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pharyngitis | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia cytomegaloviral | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia necrotising | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia pneumococcal | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia pseudomonal | | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia staphylococcal | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia streptococcal | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sepsis syndrome | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sinusitis | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Soft tissue infection | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Staphylococcal infection | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Toxoplasmosis | | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Varicella zoster virus infection | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Wound infection | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 4 / 125 (3.20%) | | |
| occurrences causally related to treatment / all | 0 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 2 / 125 (1.60%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Failure to thrive | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolic acidosis | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 125 (0.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Idelalisib | | |
|---|--------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 123 / 125 (98.40%) | | |
| Investigations | | | |
| Weight decreased | | | |
| subjects affected / exposed | 19 / 125 (15.20%) | | |
| occurrences (all) | 21 | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 18 / 125 (14.40%) | | |
| occurrences (all) | 22 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 16 / 125 (12.80%) | | |
| occurrences (all) | 20 | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 9 / 125 (7.20%) | | |
| occurrences (all) | 10 | | |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 7 / 125 (5.60%) | | |
| occurrences (all) | 9 | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 9 / 125 (7.20%) | | |
| occurrences (all) | 9 | | |
| Hypotension | | | |
| subjects affected / exposed | 8 / 125 (6.40%) | | |
| occurrences (all) | 11 | | |
| Nervous system disorders | | | |
| Headache | | | |

| | | | |
|--|-------------------|--|--|
| subjects affected / exposed | 17 / 125 (13.60%) | | |
| occurrences (all) | 18 | | |
| Dizziness | | | |
| subjects affected / exposed | 11 / 125 (8.80%) | | |
| occurrences (all) | 14 | | |
| Dysgeusia | | | |
| subjects affected / exposed | 7 / 125 (5.60%) | | |
| occurrences (all) | 7 | | |
| Blood and lymphatic system disorders | | | |
| Neutropenia | | | |
| subjects affected / exposed | 35 / 125 (28.00%) | | |
| occurrences (all) | 69 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 23 / 125 (18.40%) | | |
| occurrences (all) | 28 | | |
| Anaemia | | | |
| subjects affected / exposed | 18 / 125 (14.40%) | | |
| occurrences (all) | 21 | | |
| Leukopenia | | | |
| subjects affected / exposed | 9 / 125 (7.20%) | | |
| occurrences (all) | 11 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 40 / 125 (32.00%) | | |
| occurrences (all) | 48 | | |
| Pyrexia | | | |
| subjects affected / exposed | 34 / 125 (27.20%) | | |
| occurrences (all) | 59 | | |
| Asthenia | | | |
| subjects affected / exposed | 14 / 125 (11.20%) | | |
| occurrences (all) | 14 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 13 / 125 (10.40%) | | |
| occurrences (all) | 13 | | |
| Chills | | | |

| | | | |
|---|-------------------|--|--|
| subjects affected / exposed | 11 / 125 (8.80%) | | |
| occurrences (all) | 13 | | |
| Pain | | | |
| subjects affected / exposed | 9 / 125 (7.20%) | | |
| occurrences (all) | 11 | | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 8 / 125 (6.40%) | | |
| occurrences (all) | 9 | | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 59 / 125 (47.20%) | | |
| occurrences (all) | 95 | | |
| Nausea | | | |
| subjects affected / exposed | 38 / 125 (30.40%) | | |
| occurrences (all) | 50 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 21 / 125 (16.80%) | | |
| occurrences (all) | 22 | | |
| Vomiting | | | |
| subjects affected / exposed | 20 / 125 (16.00%) | | |
| occurrences (all) | 22 | | |
| Constipation | | | |
| subjects affected / exposed | 11 / 125 (8.80%) | | |
| occurrences (all) | 14 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 10 / 125 (8.00%) | | |
| occurrences (all) | 10 | | |
| Stomatitis | | | |
| subjects affected / exposed | 8 / 125 (6.40%) | | |
| occurrences (all) | 8 | | |
| Dysphagia | | | |
| subjects affected / exposed | 7 / 125 (5.60%) | | |
| occurrences (all) | 7 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|--|-------------------------|--|--|
| Cough subjects affected / exposed occurrences (all) | 40 / 125 (32.00%) 55 | | |
| Dyspnoea subjects affected / exposed occurrences (all) | 22 / 125 (17.60%) 26 | | |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 11 / 125 (8.80%) 12 | | |
| Pleural effusion subjects affected / exposed occurrences (all) | 7 / 125 (5.60%) 7 | | |
| Skin and subcutaneous tissue disorders | | | |
| Night sweats subjects affected / exposed occurrences (all) | 18 / 125 (14.40%) 25 | | |
| Rash subjects affected / exposed occurrences (all) | 18 / 125 (14.40%) 19 | | |
| Dry skin subjects affected / exposed occurrences (all) | 9 / 125 (7.20%) 9 | | |
| Pruritus subjects affected / exposed occurrences (all) | 9 / 125 (7.20%) 12 | | |
| Psychiatric disorders | | | |
| Insomnia subjects affected / exposed occurrences (all) | 12 / 125 (9.60%) 12 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain subjects affected / exposed occurrences (all) | 13 / 125 (10.40%) 13 | | |
| Arthralgia subjects affected / exposed occurrences (all) | 8 / 125 (6.40%) 10 | | |

| | | | |
|---|---------------------------------|--|--|
| <p>Infections and infestations</p> <p>Upper respiratory tract infection subjects affected / exposed occurrences (all)</p> | <p>23 / 125 (18.40%) 33</p> | | |
| <p>Pneumonia subjects affected / exposed occurrences (all)</p> | <p>8 / 125 (6.40%) 10</p> | | |
| <p>Urinary tract infection subjects affected / exposed occurrences (all)</p> | <p>8 / 125 (6.40%) 10</p> | | |
| <p>Bronchitis subjects affected / exposed occurrences (all)</p> | <p>7 / 125 (5.60%) 8</p> | | |
| <p>Herpes zoster subjects affected / exposed occurrences (all)</p> | <p>7 / 125 (5.60%) 7</p> | | |
| <p>Metabolism and nutrition disorders</p> <p>Decreased appetite subjects affected / exposed occurrences (all)</p> | <p>23 / 125 (18.40%) 28</p> | | |
| <p>Hypokalaemia subjects affected / exposed occurrences (all)</p> | <p>15 / 125 (12.00%) 19</p> | | |
| <p>Hyperglycaemia subjects affected / exposed occurrences (all)</p> | <p>11 / 125 (8.80%) 15</p> | | |
| <p>Dehydration subjects affected / exposed occurrences (all)</p> | <p>10 / 125 (8.00%) 12</p> | | |
| <p>Hypocalcaemia subjects affected / exposed occurrences (all)</p> | <p>7 / 125 (5.60%) 10</p> | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 22 December 2010 | <ul style="list-style-type: none">• Clarified inclusion criteria for participants with Grade 3 FL to enroll only participants with Grades 1, 2, or 3a FL (not Grade 3b), ie, only participants with indolent FL.• Amended storage and stability to allow brief excursions of IDELA down to 5°C.• Clarified the response definition in the event that PET scans were obtained for participants with a PR |
| 24 January 2011 | <ul style="list-style-type: none">• Amended inclusion criteria to ensure all participants were of legal age (≥ 18 years of age) at the time of entry into the study.• Removed the statement that idelalisib would be shipped at controlled room temperature, as this was not required. |
| 23 April 2012 | <ul style="list-style-type: none">• Updated toxicology section to include findings available from 13-week toxicology studies.• Included a new section to provide new reproductive toxicity findings received from a definitive embryo-fetal development toxicity study.• Provided clarification regarding the inclusion of participants with SLL to state that the allogeneic lymphocyte cytotoxicity must be $\leq 5 \times 10^9/L$ at the time of diagnosis and at the time of study entry. This clarification was made to ensure that participants with CLL were excluded.• Clarified the inclusion criteria regarding presence of radiographically measurable lymphadenopathy description and included a requirement for the length of longest perpendicular diameter. This provided enhanced clarity regarding the definition of measurable disease for study inclusion.• Revised inclusion criteria to ensure resolution of all acute toxicities to Grade ≤ 1 before the initiation of study treatment (exception of alopecia, neurotoxicity, and bone marrow parameters with resolution to Grade ≤ 2).• Removed the treatment stratification enrollment limit for participants who had received prior bendamustine.• Further defined the criteria for lesion selection and tumor response. This aligned the protocol with central imaging methods.• Provided time window surrounding the collection of PK samples to minimize deviations.• Added the requirement for collection and consideration for overall response of IgM serum monoclonal protein levels assessed by serum protein electrophoresis (SPEP) for participants with WM.• Included the provision "as allowed by local law" in the event of potential transition of participants from study treatment to commercial supply, should study drug become approved in the country in which the participant lives.• Changed the Stage 1 ORR analysis to be based on investigator response assessment instead of IRC assessment. |
| 23 May 2013 | <ul style="list-style-type: none">• Established storage of biological samples (with participant's informed consent) for future studies.• Clarified that final efficacy analysis occurs ≥ 24 weeks after the last participant enrolls.• Aligned the clinical response section with the criteria for the IRC.• Removed stratification analysis.• Revised dose modifications to no longer include reductions below 100 mg BID (based on PK data and exposure-response analysis for safety and efficacy).• Updated the pregnancy risk language, based on current animal studies data. |

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|-------------------|---|
| 18 July 2013 | <ul style="list-style-type: none"> Modified the definition of SAE to exclude untoward medical occurrences which resulted in death due to disease progression. Modified the definition of SAE to include CLL progression or death due to CLL progression only if assessed that study drug caused or contributed to the disease progression. |
| 28 October 2014 | <ul style="list-style-type: none"> Updated the general information on idelalisib to reflect approval status in the United States and European Union Align the following information with Investigator's Brochure Edition 11 <ul style="list-style-type: none"> -Guidance to investigators for evaluation, intervention, and drug interruption/discontinuation for specific adverse events (AEs) -Information regarding the interaction of idelalisib with CYP3A inhibitors, inducers, and substrates |
| 25 March 2016 | <ul style="list-style-type: none"> Updated the safety information and guidelines for toxicity management to be consistent across idelalisib study protocols. These changes included mandated prophylaxis for <i>Pneumocystis jirovecii</i> pneumonia (PJP), cytomegalovirus (CMV) surveillance, and increased monitoring. Removed references to 75 mg tablets, as this dose strength was no longer formulated |
| 22 August 2016 | <ul style="list-style-type: none"> Updated the recommended and required guidelines for toxicity management to be consistent across idelalisib study protocols Updated the recommended and required guidelines for toxicity management to be consistent across idelalisib study protocols |
| 13 October 2016 | <ul style="list-style-type: none"> In order to provide clear guidance for idelalisib administration in the event of pneumonitis, the language around actions to be taken was revised. |
| 23 November 2016 | <ul style="list-style-type: none"> It was a France-only version which included additional information, per the request of the health authority, concerning discontinuation of idelalisib following an event of Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) and management of co-administered medications. |
| 05 September 2017 | <ul style="list-style-type: none"> Organizing pneumonia emerged as a potential safety signal during Gilead routine signal detection monitoring. This risk was added to the protocol. |
| 06 October 2017 | <ul style="list-style-type: none"> Organizing pneumonia emerged as a potential safety signal during Gilead routine signal detection monitoring. This risk was added to the protocol. It was a France-only version, which included information, per the request of the health authority, concerning discontinuation of idelalisib following an event of SJS or TEN and management of co-administered medications. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/24450858>