# Clinical trial results:
# A Phase 2, Open-label Study of Zanubrutinib (BGB-3111) in Patients with Relapsed or Refractory Marginal Zone Lymphoma

## Summary

| | |
|---|---|
| EudraCT number | 2018-001284-24 |
| Trial protocol | GB FR IT |
| Global end of trial date | 04 May 2022 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 19 May 2023 |
| First version publication date | 19 May 2023 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | BGB-3111-214 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03846427 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | BeiGene, Ltd., c/o BeiGene USA, Inc. |
| Sponsor organisation address | 1840 Gateway Drive, Third Floor, San Mateo, United States, 94404 |
| Public contact | BeiGene Clinical Support, BeiGene, Ltd., 1 877-828-5568, clinicaltrials@beigene.com |
| Scientific contact | BeiGene Clinical Support, BeiGene, Ltd., 1 877-828-5568, clinicaltrials@beigene.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 | 31 May 2022 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 04 May 2022 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the efficacy of zanubrutinib in relapsed or refractory marginal zone lymphoma as measured by overall response rate in accordance with the Lugano Classification determined by independent central review.

Protection of trial subjects:

This trial was designed and monitored in accordance with Sponsor procedures, which comply with the ethical principles of GCP as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki. The IEC/IRB-approved ICF was signed and dated by the subject or the subject's legally authorized representative before his or her participation in the study. A copy of each signed ICF was provided to the subject or the subject's legally authorized representative. All signed and dated ICFs were retained in each patient's study file or in the site file. For any updated or revised ICFs, written informed consent was obtained using the IEC/IRB-approved updated/revised ICFs for continued participation in the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 19 February 2019 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | United Kingdom: 11 |
| Country: Number of subjects enrolled | Czechia: 1 |
| Country: Number of subjects enrolled | France: 5 |
| Country: Number of subjects enrolled | Italy: 11 |
| Country: Number of subjects enrolled | Australia: 14 |
| Country: Number of subjects enrolled | China: 11 |
| Country: Number of subjects enrolled | New Zealand: 7 |
| Country: Number of subjects enrolled | United States: 7 |
| Country: Number of subjects enrolled | Korea, Republic of: 1 |
| Worldwide total number of subjects | 68 |
| EEA total number of subjects | 17 |

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) | 27 |
| From 65 to 84 years | 38 |
| 85 years and over | 3 |

## Subject disposition

### Recruitment

Recruitment details:

This study was conducted at 31 study centers in 9 countries. A total of 38 participants rolled over to BGB-3111-LTE1 (NCT04170283) after study completion.

### Pre-assignment

Screening details:

The study was composed of an initial screening phase (up to 35 days), a single-arm treatment phase, and a follow-up phase.

### Period 1

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

### Arms

| | |
|---|---|
| **Arm title** | Zanubrutinib |

Arm description:

Zanubrutinib 160 mg (two 80-mg capsules) orally twice daily with or without food until progressive disease, intolerable toxicity, or withdrawal of consent

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Zanubrutinib |
| Investigational medicinal product code | |
| Other name | BGB-3111, Brukinsa |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Zanubrutinib 160 mg (two 80-mg capsules) orally twice daily with or without food

| **Number of subjects in period 1** | Zanubrutinib |
|---|---|
| Started | 68 |
| Completed | 51 |
| Not completed | 17 |
| Consent withdrawn by subject | 3 |
| Physician decision | 1 |
| Death | 13 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Overall Study |

Reporting group description: -

| Reporting group values | Overall Study | Total | |
|---|---|---|---|
| Number of subjects | 68 | 68 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | | 0 | |
| Newborns (0-27 days) | | 0 | |
| Infants and toddlers (28 days-23 months) | | 0 | |
| Children (2-11 years) | | 0 | |
| Adolescents (12-17 years) | | 0 | |
| Adults (18-64 years) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 67.9 | | |
| standard deviation | ± 11.41 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 32 | 32 | |
| Male | 36 | 36 | |
| Race/Ethnicity<br>Units: Subjects | | | |
| Asian | 13 | 13 | |
| White | 40 | 40 | |
| Multiple | 2 | 2 | |
| Other | 1 | 1 | |
| Unknown | 1 | 1 | |
| Not Reported | 11 | 11 | |

## End points

### End points reporting groups

| Reporting group title | Zanubrutinib |
|---|---|

Reporting group description:

Zanubrutinib 160 mg (two 80-mg capsules) orally twice daily with or without food until progressive disease, intolerable toxicity, or withdrawal of consent

### Primary: Overall Response Rate (ORR) by Independent Review Committee (IRC) Assessment

| End point title | Overall Response Rate (ORR) by Independent Review Committee (IRC) Assessment[1] |
|---|---|

End point description:

ORR is defined as the percentage of subjects with complete or partial response as the best overall response, as determined by an IRC using the Lugano Classification

| End point type | Primary |
|---|---|

End point timeframe:

Up to approximately 3 years and 2.5 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: Single-arm study: superiority test, P<0.0001; P value was based on the exact binomial test against the null hypothesis of ORR = 30% with alternative of ORR > 30%

| End point values | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 66 | | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 68.2 (55.56 to 79.11) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: ORR by Investigator Assessment

| End point title | ORR by Investigator Assessment |
|---|---|

End point description:

ORR is defined as the percentage of subjects with complete or partial response as the best overall response, as determined by the investigator using the Lugano Classification.

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

End point timeframe:

Up to approximately 3 years and 2.5 months

| End point values | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 66 | | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 75.8 (63.64 to 85.46) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: ORR by IRC Assessment Using Positron Emission Tomography-Computed Tomography (PET-CT)

| End point title | ORR by IRC Assessment Using Positron Emission Tomography-Computed Tomography (PET-CT) |
|---|---|

End point description:

ORR is defined as the percentage of subjects with complete and partial response as the best overall response, as determined by an IRC using PET-CT assessment data for subjects with fluorodeoxyglucose (FDG)-avid disease; analysis set consisted of evaluable subjects with FDG-avid disease at baseline

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

End point timeframe:

Up to approximately 3 years and 2.5 months

| End point values | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 59 | | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 69.5 (56.13 to 80.81) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Progression-free Survival (PFS) by Investigator Assessment

| End point title | Progression-free Survival (PFS) by Investigator Assessment |
|---|---|

End point description:

PFS is defined as the time from first dose until first documentation of progression or death, whichever comes first, as assessed by the investigator using Lugano Classification

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

End point timeframe:

Up to approximately 3 years and 2.5 months

| End point values | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 66[2] | | | |
| Units: Months | | | | |
| median (full range (min-max)) | 9999 (16.5 to 9999) | | | |

Notes:

[2] - 9999 = Not estimable due to insufficient number of subjects with events

### Statistical analyses

No statistical analyses for this end point

## Secondary: PFS Event-Free Rate by Investigator Assessment

| End point title | PFS Event-Free Rate by Investigator Assessment |
|---|---|

End point description:

PFS is defined as the time from first dose until first documentation of progression or death, whichever comes first, as assessed by the investigator using Lugano Classification. The Kaplan-Meier method was used to estimate the percentage of subjects who were event-free for PFS at 24 months with 95% confidence intervals estimated using Greenwood’s formula.

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

End point timeframe:

Up to 3 years and 2.5 months after first participant enrolled; Month 24 reported

| End point values | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 66 | | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 57.9 (44.83 to 68.86) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: PFS by IRC Assessment

| End point title | PFS by IRC Assessment |
|---|---|

End point description:

PFS is defined as the time from first dose until first documentation of progression or death, whichever comes first, as assessed by an IRC using Lugano Classification

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

End point timeframe:

Up to approximately 3 years and 2.5 months

| **End point values** | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 66[3] | | | |
| Units: Months | | | | |
| median (full range (min-max)) | 9999 (27.6 to 9999) | | | |

Notes:

[3] - 9999 = Not estimable due to insufficient number of subjects with events

### Statistical analyses

No statistical analyses for this end point

### Secondary: PFS Event-Free Rate by IRC Assessment

| End point title | PFS Event-Free Rate by IRC Assessment |
|---|---|

End point description:

PFS is defined as the time from first dose until first documentation of progression or death, whichever comes first, as assessed by the IRC using Lugano Classification. The Kaplan-Meier method was used to estimate the percentage of subjects who were event-free for PFS at 24 months with 95% confidence intervals estimated using Greenwood's formula.

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

End point timeframe:

Up to 3 years and 2.5 months after first participant enrolled; Month 24 reported

| **End point values** | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 66 | | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 70.9 (57.20 to 80.95) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Overall Survival (OS)

| End point title | Overall Survival (OS) |
|---|---|

End point description:

OS is defined as the time from first study drug administration to the date of death due to any cause

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

End point timeframe:

Up to approximately 3 years and 2.5 months

| End point values | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 66[4] | | | |
| Units: Months | | | | |
| median (full range (min-max)) | 9999 (9999 to 9999) | | | |

Notes:

[4] - 9999 = Not estimable due to insufficient number of subjects with events

### Statistical analyses

No statistical analyses for this end point

### Secondary: OS Event-Free Rate

| End point title | OS Event-Free Rate |
|---|---|

End point description:

OS is defined as the time from first study drug administration to the date of death due to any cause. The Kaplan-Meier method was used to estimate the percentage of subjects who were event-free for OS at 24 months with 95% confidence intervals estimated using Greenwood's formula.

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

End point timeframe:

Up to 3 years and 2.5 months after first participant enrolled; Month 24 reported

| End point values | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 66 | | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 85.9 (74.7 to 92.4) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of Response (DOR) by Investigator Assessment

| End point title | Duration of Response (DOR) by Investigator Assessment |
|---|---|

End point description:

DOR is defined as the time from the date that response criteria are first met to the date that progressive disease is objectively documented or death, whichever comes first, as assessed by the investigator using Lugano Classification; DOR was summarized for responders only, defined as subjects with a best overall response of partial response or above

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

End point timeframe:

Up to approximately 3 years and 2.5 months

| **End point values** | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 50[5] | | | |
| Units: Months | | | | |
| median (full range (min-max)) | 9999 (22.1 to 9999) | | | |

Notes:

[5] - 9999 = Not estimable due to insufficient number of subjects with events

### Statistical analyses

No statistical analyses for this end point

### Secondary: DOR Event-Free Rate by Investigator Assessment

| End point title | DOR Event-Free Rate by Investigator Assessment |
|---|---|

End point description:

DOR is defined as the time from the date that response criteria are first met to the date that progressive disease is objectively documented or death, whichever comes first, as assessed by the investigator using Lugano Classification. The Kaplan-Meier method was used to estimate the percentage of subjects who were event-free for progression or death at 24 months with 95% confidence intervals estimated using Greenwood's formula; DOR was summarized for responders only, defined as subjects with a best overall response of partial response or above.

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

End point timeframe:

Up to 3 years and 2.5 months after first participant enrolled; Month 24 reported

| **End point values** | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 50 | | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 60.8 (44.8 to 73.6) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: DOR by IRC Assessment

| End point title | DOR by IRC Assessment |
|---|---|

End point description:

DOR is defined as the time from the date that response criteria are first met to the date that progressive disease is objectively documented or death, whichever comes first, as assessed by the IRC using Lugano Classification; DOR was summarized for responders only, defined as subjects with a best overall response of partial response or above.

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

End point timeframe:

Up to approximately 3 years and 2.5 months

| **End point values** | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 45[6] | | | |
| Units: Months | | | | |
| median (full range (min-max)) | 9999 (25.0 to 9999) | | | |

Notes:

[6] - 9999 = Not estimable due to insufficient number of subjects with events

## Statistical analyses

No statistical analyses for this end point

## Secondary: DOR Event-Free Rate by IRC Assessment

| End point title | DOR Event-Free Rate by IRC Assessment |
|---|---|

End point description:

DOR is defined as the time from the date that response criteria are first met to the date that progressive disease is objectively documented or death, whichever comes first, as assessed by the IRC using Lugano Classification. The Kaplan-Meier method was used to estimate the percentage of subjects who were event-free for progression or death at 24 months with 95% confidence intervals estimated using Greenwood's formula; DOR was summarized for responders only, defined as subjects with a best overall response of partial response or above.

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

End point timeframe:

At Month 24

| **End point values** | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 45 | | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 72.9 (54.4 to 84.9) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Treatment Failure (TTF)

| End point title | Time to Treatment Failure (TTF) |
|---|---|

End point description:

TTF is defined as the time from study treatment start to the date of discontinuation of study drug due to any reason

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

End point timeframe:

Up to approximately 3 years and 2.5 months

| End point values | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 66[7] | | | |
| Units: Months | | | | |
| median (full range (min-max)) | 27.8 (14.7 to 9999) | | | |

Notes:

[7] - 9999 = Not estimable due to insufficient number of subjects with events

### Statistical analyses

No statistical analyses for this end point

## Secondary: TTF Event-Free Rate

| End point title | TTF Event-Free Rate |
|---|---|

End point description:

TTF is defined as the time from study treatment start to the date of discontinuation of study drug due to any reason. The Kaplan-Meier method was used to estimate the percentage of subjects who were event-free for TTF at 24 months with 95% confidence intervals estimated using Greenwood’s formula.

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

End point timeframe:

Up to 3 years and 2.5 months after first participant enrolled; Month 24 reported

| End point values | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 66 | | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 53.0 (40.4 to 64.2) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Next Line of Therapy

| End point title | Time to Next Line of Therapy |
|---|---|

End point description:

Time to next line of therapy is defined as the time from study treatment start to the start of the first subsequent therapy for MZL

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

End point timeframe:

Up to approximately 3 years and 2.5 months

| End point values | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 66[8] | | | |
| Units: Months | | | | |
| median (full range (min-max)) | 9999 (9999 to 9999) | | | |

Notes:

[8] - 9999 = Not estimable due to insufficient number of subjects with events

### Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Next Line of Therapy Event-Free Rate

| End point title | Time to Next Line of Therapy Event-Free Rate |
|---|---|

End point description:

Time to next line of therapy is defined as the time from study treatment start to the start of the first subsequent therapy for MZL. The Kaplan-Meier method was used to estimate the percentage of subjects who were event-free for time to next line of therapy at 24 months with 95% confidence intervals estimated using Greenwood’s formula.

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

End point timeframe:

Up to 3 years and 2.5 months after first participant enrolled; Month 24 reported

| End point values | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 66 | | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 74.5 (61.7 to 83.6) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Response (TTR) by Investigator Assessment

| End point title | Time to Response (TTR) by Investigator Assessment |
|---|---|

End point description:

TTR is defined as the time from study treatment start to date of the earliest qualifying response (partial response or better) as assessed by the investigator using Lugano Classification; TTR was summarized for responders only, defined as subjects with a best overall response of partial response or above

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

End point timeframe:

Up to approximately 3 years and 2.5 months

| End point values | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 50 | | | |
| Units: Months | | | | |
| median (full range (min-max)) | 2.79 (1.7 to 16.6) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: TTR by IRC Assessment

| End point title | TTR by IRC Assessment |
|---|---|

End point description:

TTR is defined as the time from study treatment start to date of the earliest qualifying response (partial response or better), as assessed by the IRC using Lugano Classification; TTR was summarized for responders only, defined as subjects with a best overall response of partial response or above

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

End point timeframe:

Up to approximately 3 years and 2.5 months

| End point values | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 45 | | | |
| Units: Months | | | | |
| median (full range (min-max)) | 2.79 (1.7 to 11.1) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in EuroQol 5-dimension 5-level (EQ-5D-5L) Visual Analogue Score (VAS)

| End point title | Change From Baseline in EuroQol 5-dimension 5-level (EQ-5D-5L) Visual Analogue Score (VAS) |
|---|---|

End point description:

Mean change from baseline in EQ-5D-5L VAS. The EQ-5D-5L measures health outcomes using a VAS to record a subject's self-rated health on a scale from 0 to 100, where 100 is 'the best health you can imagine' and 0 is 'the worst health you can imagine.' Positive change from baseline indicates improved health.

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

End point timeframe:

Baseline to Cycle 30 (28 days per cycle)

| **End point values** | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 66 | | | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 3, n = 57 | 1.0 (± 18.18) | | | |
| Cycle 6, n = 50 | 2.2 (± 15.78) | | | |
| Cycle 9, n = 47 | 0.2 (± 16.28) | | | |
| Cycle 12, n = 42 | 2.8 (± 16.15) | | | |
| Cycle 18, n = 33 | 5.6 (± 17.68) | | | |
| Cycle 24, n = 35 | 5.8 (± 15.24) | | | |
| Cycle 30, n = 28 | 1.6 (± 18.15) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) Global Health Status

| End point title | Change From Baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) Global Health Status |
|---|---|

End point description:

Mean change from baseline in EORTC QLQ-C30 Global Health Status/Quality of Life score. The EORTC QLQ-C30 v3.0 is a questionnaire that assesses quality of life of cancer patients and includes global health status and quality of life questions related to their overall health in which subjects respond based on a 7-point scale, where 1 is very poor and 7 is excellent. Answers are converted to a score of 0 to 100, with a positive score from baseline indicating improved health.

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

End point timeframe:

Baseline to Cycle 30 (28 days per cycle)

| End point values | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 66 | | | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 3, n = 58 | 7.471 (± 19.5396) | | | |
| Cycle 6, n = 49 | 7.823 (± 15.8121) | | | |
| Cycle 9, n = 48 | 5.382 (± 20.0833) | | | |
| Cycle 12, n = 42 | 7.143 (± 17.3216) | | | |
| Cycle 18, n = 32 | 10.677 (± 18.4811) | | | |
| Cycle 24, n = 35 | 9.286 (± 19.2561) | | | |
| Cycle 30, n = 28 | 6.250 (± 20.4910) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Adverse Events

| End point title | Number of Subjects With Adverse Events |
|---|---|

End point description:

Number of subjects with treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs), including laboratory tests, physical exams, and vital signs

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

End point timeframe:

From first dose to 30 days after last dose of study drug (Up to approximately 3 years and 2.5 months)

| End point values | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 68 | | | |
| Units: Subjects | | | | |
| At least one TEAE | 68 | | | |
| At least one SAE | 30 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Area Under the Curve From Time 0 to 6 Hours (AUC0-6)

| End point title | Area Under the Curve From Time 0 to 6 Hours (AUC0-6) |
|---|---|

End point description:

Analysis set included all subjects who had at least 1 postdose zanubrutinib plasma concentration

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

End point timeframe:

Predose (within 30 min prior to dose) and 0.5, 1, 2, 3, 4, and 6 hours postdose on Cycle 1 Day 1 (28 days per cycle)

| **End point values** | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 9 | | | |
| Units: Hour*ng/mL | | | | |
| arithmetic mean (standard deviation) | 868.0 (± 304.3) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Apparent Oral Clearance (CL/F) of Zanubrutinib

| End point title | Apparent Oral Clearance (CL/F) of Zanubrutinib |
|---|---|

End point description:

Analysis set included all subjects who had at least 1 postdose zanubrutinib plasma concentration

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

End point timeframe:

Predose (within 30 min prior to dose) and 0.5, 1, 2, 3, 4, and 6 hours postdose on Cycle 1 Day 1 (28 days per cycle)

| **End point values** | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: Liters/hour | | | | |
| arithmetic mean (standard deviation) | 215.3 (± 114.8) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Maximum Observed Concentration (Cmax)

| End point title | Maximum Observed Concentration (Cmax) |
|---|---|

End point description:

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

End point timeframe:

Predose (within 30 min prior to dose) and 0.5, 1, 2, 3, 4, and 6 hours postdose on Cycle 1 Day 1 (28 days per cycle)

| **End point values** | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: nanograms/milliliter | | | | |
| arithmetic mean (standard deviation) | 315.5 (± 120.2) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Elimination Half Life (t1/2)

| End point title | Elimination Half Life (t1/2) |
|---|---|

End point description:

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

End point timeframe:

Predose (within 30 min prior to dose) and 0.5, 1, 2, 3, 4, and 6 hours postdose on Cycle 1 Day 1 (28 days per cycle)

| **End point values** | Zanubrutinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 9 | | | |
| Units: Hours | | | | |
| median (full range (min-max)) | 1.2 (0.8 to 2.7) | | | |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose to 30 days after last dose of study drug (Up to approximately 3 years and 2.5 months)

Adverse event reporting additional description:

Defined as an adverse event that had an onset date or worsening in severity from baseline on or after the date of first dose of study drug up to 30 days after study drug discontinuation or initiation of new anticancer therapy, whichever occurred first.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 24.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Zanubrutinib |

Reporting group description:

Zanubrutinib

| Serious adverse events | Zanubrutinib | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 30 / 68 (44.12%) | | |
| number of deaths (all causes) | 13 | | |
| number of deaths resulting from adverse events | 5 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Bladder cancer recurrent | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Papillary thyroid cancer | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Prostate cancer | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| 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 | 3 / 68 (4.41%) | | |
| occurrences causally related to treatment / all | 1 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Organising pneumonia | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Platelet count decreased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 2 / 68 (2.94%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Humerus fracture | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pelvic fracture | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acetabulum fracture | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Atrial flutter | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|---|---|---|
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Coronary artery stenosis | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Vertebrobasilar insufficiency | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebellar infarction | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sciatica | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Syncope | | | |
| subjects affected / exposed | 2 / 68 (2.94%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Pancytopenia | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|---|---|---|---|
| Anaemia | | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal disorders | | | | |
| Gastrointestinal haemorrhage | | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Faecaloma | | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dysphagia | | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colitis | | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Abdominal pain upper | | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Small intestinal obstruction | | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Large intestinal obstruction | | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrooesophageal reflux disease | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Bile duct stone | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Influenza | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 4 / 68 (5.88%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 2 | | |

| | | | |
|---|---|---|---|
| Bronchitis | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 3 / 68 (4.41%) | | |
| occurrences causally related to treatment / all | 1 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Septic encephalopathy | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tuberculosis | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 68 (1.47%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 3 %

| **Non-serious adverse events** | Zanubrutinib | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 61 / 68 (89.71%) | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 3 / 68 (4.41%) | | |
| occurrences (all) | 5 | | |
| General disorders and administration site conditions | | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 3 / 68 (4.41%) | | |
| occurrences (all) | 4 | | |
| Pyrexia | | | |
| subjects affected / exposed | 8 / 68 (11.76%) | | |
| occurrences (all) | 13 | | |
| Fatigue | | | |
| subjects affected / exposed | 6 / 68 (8.82%) | | |
| occurrences (all) | 9 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 7 / 68 (10.29%) | | |
| occurrences (all) | 8 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 3 / 68 (4.41%) | | |
| occurrences (all) | 3 | | |

| | | | |
|---|---|---|---|
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)<br><br>Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all) | 3 / 68 (4.41%)<br>5<br><br>3 / 68 (4.41%)<br>3 | | |
| Psychiatric disorders<br>Anxiety<br>subjects affected / exposed<br>occurrences (all) | 3 / 68 (4.41%)<br>3 | | |
| Investigations<br>White blood cell count decreased<br>subjects affected / exposed<br>occurrences (all)<br><br>Weight decreased<br>subjects affected / exposed<br>occurrences (all)<br><br>Platelet count decreased<br>subjects affected / exposed<br>occurrences (all)<br><br>Neutrophil count decreased<br>subjects affected / exposed<br>occurrences (all)<br><br>Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 3 / 68 (4.41%)<br>8<br><br>3 / 68 (4.41%)<br>4<br><br>4 / 68 (5.88%)<br>10<br><br>5 / 68 (7.35%)<br>6<br><br>3 / 68 (4.41%)<br>10 | | |
| Injury, poisoning and procedural complications<br>Contusion<br>subjects affected / exposed<br>occurrences (all)<br><br>Fall<br>subjects affected / exposed<br>occurrences (all) | 16 / 68 (23.53%)<br>22<br><br>3 / 68 (4.41%)<br>3 | | |
| Nervous system disorders<br>Dizziness | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 5 / 68 (7.35%) | | |
| occurrences (all) | 5 | | |
| Lethargy | | | |
| subjects affected / exposed | 4 / 68 (5.88%) | | |
| occurrences (all) | 5 | | |
| Paraesthesia | | | |
| subjects affected / exposed | 3 / 68 (4.41%) | | |
| occurrences (all) | 3 | | |
| Sciatica | | | |
| subjects affected / exposed | 3 / 68 (4.41%) | | |
| occurrences (all) | 4 | | |
| Blood and lymphatic system disorders | | | |
| Neutropenia | | | |
| subjects affected / exposed | 6 / 68 (8.82%) | | |
| occurrences (all) | 11 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 7 / 68 (10.29%) | | |
| occurrences (all) | 10 | | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 68 (4.41%) | | |
| occurrences (all) | 4 | | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 3 / 68 (4.41%) | | |
| occurrences (all) | 4 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 15 / 68 (22.06%) | | |
| occurrences (all) | 26 | | |
| Constipation | | | |
| subjects affected / exposed | 12 / 68 (17.65%) | | |
| occurrences (all) | 15 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 8 / 68 (11.76%) | | |
| occurrences (all) | 11 | | |
| Vomiting | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 68 (5.88%) | | |
| occurrences (all) | 4 | | |
| Toothache | | | |
| subjects affected / exposed | 3 / 68 (4.41%) | | |
| occurrences (all) | 3 | | |
| Nausea | | | |
| subjects affected / exposed | 7 / 68 (10.29%) | | |
| occurrences (all) | 9 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 3 / 68 (4.41%) | | |
| occurrences (all) | 3 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 4 / 68 (5.88%) | | |
| occurrences (all) | 4 | | |
| Dysphagia | | | |
| subjects affected / exposed | 3 / 68 (4.41%) | | |
| occurrences (all) | 4 | | |
| Skin and subcutaneous tissue disorders | | | |
| Petechiae | | | |
| subjects affected / exposed | 3 / 68 (4.41%) | | |
| occurrences (all) | 3 | | |
| Rash | | | |
| subjects affected / exposed | 3 / 68 (4.41%) | | |
| occurrences (all) | 3 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 10 / 68 (14.71%) | | |
| occurrences (all) | 11 | | |
| Back pain | | | |
| subjects affected / exposed | 8 / 68 (11.76%) | | |
| occurrences (all) | 11 | | |
| Myalgia | | | |
| subjects affected / exposed | 3 / 68 (4.41%) | | |
| occurrences (all) | 3 | | |
| Pain in extremity | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 68 (4.41%) | | |
| occurrences (all) | 4 | | |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 6 / 68 (8.82%) | | |
| occurrences (all) | 6 | | |
| Oral herpes | | | |
| subjects affected / exposed | 3 / 68 (4.41%) | | |
| occurrences (all) | 3 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 4 / 68 (5.88%) | | |
| occurrences (all) | 6 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 9 / 68 (13.24%) | | |
| occurrences (all) | 10 | | |
| Tonsillitis | | | |
| subjects affected / exposed | 4 / 68 (5.88%) | | |
| occurrences (all) | 5 | | |
| Metabolism and nutrition disorders | | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 5 / 68 (7.35%) | | |
| occurrences (all) | 7 | | |
| Hyperuricaemia | | | |
| subjects affected / exposed | 3 / 68 (4.41%) | | |
| occurrences (all) | 3 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 29 August 2018 | • For CT, PET, and disease-related constitutional symptom assessments, the first assessment was moved from Week 8 to Week 12.<br>• Updated inclusion criteria to 1) ensure that subjects with WM were not included in this study; 2) ensure that all subjects had either available archival tumor tissue or underwent a tumor biopsy; and 3) update definition of measurable disease to align with the Lugano classification criteria.<br>• Updated to collect 12-lead ECG data only at screening and as clinically indicated.<br>• Updated to provide guidance on the risk of opportunistic infections, including Pneumocystis jiroveci pneumonia. |
| 20 September 2019 | • Updated to correct errors and clarify content where needed.<br>• Increased the number of study centers to approximately 60.<br>• Updated inclusion criteria to 1) list specific MZL symptoms dictating the need for systemic therapy; 2) remove an incorrect statement; and 3) update contraception information for female subjects of childbearing potential for consistency across BeiGene protocols and clarity.<br>• Added to exclusion criteria: In France only, subjects whose ejection fraction is < 45% should not enter the study. |
| 03 June 2020 | • Extended the time window of the primary efficacy analysis to 12 months (after the last subject received the first dose of study drug). |

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/34526366