# Clinical trial results:
# A Phase 2 Study of Prexasertib in Platinum-Resistant or Refractory Recurrent Ovarian Cancer

## Summary

| | |
|---|---|
| EudraCT number | 2017-004009-42 |
| Trial protocol | GB ES BE IT |
| Global end of trial date | 03 October 2020 |

**Results information**

| | |
|---|---|
| Result version number | v2 |
| This version publication date | 14 October 2021 |
| First version publication date | 14 June 2020 |
| Version creation reason | • New data added to full data set<br>LPV results needs to be submitted. |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | I4D-MC-JTJN |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03414047 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Trial Number: 16712 |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Eli Lilly and Company |
| Sponsor organisation address | Lilly Corporate Center, Indianapolis, IN, United States, 46285 |
| Public contact | Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly, |
| Scientific contact | Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559, |

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 | 03 October 2020 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 03 October 2020 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the efficacy and safety of prexasertib in women with platinum-resistant or refractory recurrent ovarian cancer.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 10 April 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Korea, Republic of: 13 |
| Country: Number of subjects enrolled | Belgium: 8 |
| Country: Number of subjects enrolled | United States: 32 |
| Country: Number of subjects enrolled | United Kingdom: 20 |
| Country: Number of subjects enrolled | Italy: 23 |
| Country: Number of subjects enrolled | Israel: 20 |
| Country: Number of subjects enrolled | Australia: 34 |
| Country: Number of subjects enrolled | Spain: 19 |
| Worldwide total number of subjects | 169 |
| EEA total number of subjects | 50 |

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) | 169 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Completers included participants who died from any cause and participants who were alive and on study (either on study treatment or in long term follow-up) at study conclusion.

### Pre-assignment

Screening details:

Only 169 participants were assigned to one of the 4 cohorts in this study. Data is not available for 3 participants who discontinued before the start of the treatment.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Prexasertib Cohort 1 |

Arm description:

Participants received 105 milligram per square meter (mg/m²) prexasertib as an approximately 60 (+10) minute IV infusion on Day 1 and 15 of a 28-day cycle. Participants were with platinum-resistant disease, breast cancer susceptibility gene (BRCA) negative and have received ≥3 lines of prior therapy.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Prexasertib |
| Investigational medicinal product code | |
| Other name | LY2606368 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received 105 mg/m² prexasertib as an IV infusion.

| | |
|---|---|
| **Arm title** | Prexasertib Cohort 2 |

Arm description:

Participants received 105 mg/m² prexasertib as an approximately 60 (+10) minute IV infusion on Day 1 and 15 of a 28-day cycle. Participants were with platinum-resistant disease, BRCA negative and have received <3 lines of prior therapy.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Prexasertib |
| Investigational medicinal product code | |
| Other name | LY2606368 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received 105 mg/m² prexasertib as an IV infusion.

| | |
|---|---|
| **Arm title** | Prexasertib Cohort 3 |

Arm description:

Participants received 105 mg/m² prexasertib as an approximately 60 (+10) minute IV infusion on Day 1 and 15 of a 28-day cycle. Participants were with platinum-resistant disease, BRCA positive and received a prior poly ADP ribose polymerase (PARP) inhibitor.

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | Prexasertib |
| Investigational medicinal product code | |
| Other name | LY2606368 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received 105 mg/m² prexasertib as an IV infusion.

| **Arm title** | Prexasertib Cohort 4 |
|---|---|

Arm description:

Participants received 105 mg/m² prexasertib as an approximately 60 (+10) minute IV infusion on Day 1 and 15 of a 28-day cycle. Participants were with platinum refractory disease, BRCA positive or negative, no restriction on number of lines of prior therapy.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Prexasertib |
| Investigational medicinal product code | |
| Other name | LY2606368 |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received 105 mg/m² prexasertib as an IV infusion.

| **Number of subjects in period 1** | Prexasertib Cohort 1 | Prexasertib Cohort 2 | Prexasertib Cohort 3 |
|---|---|---|---|
| Started | 53 | 46 | 41 |
| Received at least one dose of study drug | 53 | 46 | 41 |
| Completed | 51 | 46 | 38 |
| Not completed | 2 | 0 | 3 |
| Consent withdrawn by subject | 1 | - | 2 |
| Physician decision | 1 | - | - |
| Adverse event, non-fatal | - | - | 1 |

| **Number of subjects in period 1** | Prexasertib Cohort 4 |
|---|---|
| Started | 29 |
| Received at least one dose of study drug | 29 |
| Completed | 27 |
| Not completed | 2 |
| Consent withdrawn by subject | - |
| Physician decision | 1 |
| Adverse event, non-fatal | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Prexasertib Cohort 1 |
| Reporting group description: | |
| Participants received 105 milligram per square meter (mg/m²) prexasertib as an approximately 60 (+10) minute IV infusion on Day 1 and 15 of a 28-day cycle. Participants were with platinum-resistant disease, breast cancer susceptibility gene (BRCA) negative and have received ≥3 lines of prior therapy. | |
| Reporting group title | Prexasertib Cohort 2 |
| Reporting group description: | |
| Participants received 105 mg/m² prexasertib as an approximately 60 (+10) minute IV infusion on Day 1 and 15 of a 28-day cycle. Participants were with platinum-resistant disease, BRCA negative and have received <3 lines of prior therapy. | |
| Reporting group title | Prexasertib Cohort 3 |
| Reporting group description: | |
| Participants received 105 mg/m² prexasertib as an approximately 60 (+10) minute IV infusion on Day 1 and 15 of a 28-day cycle. Participants were with platinum-resistant disease, BRCA positive and received a prior poly ADP ribose polymerase (PARP) inhibitor. | |
| Reporting group title | Prexasertib Cohort 4 |
| Reporting group description: | |
| Participants received 105 mg/m² prexasertib as an approximately 60 (+10) minute IV infusion on Day 1 and 15 of a 28-day cycle. Participants were with platinum refractory disease, BRCA positive or negative, no restriction on number of lines of prior therapy. | |

| Reporting group values | Prexasertib Cohort 1 | Prexasertib Cohort 2 | Prexasertib Cohort 3 |
|---|---|---|---|
| Number of subjects | 53 | 46 | 41 |
| Age categorical<br>Units: Subjects | | | |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 61.3 | 62.3 | 59.5 |
| standard deviation | ± 9.4 | ± 9.4 | ± 8.6 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 53 | 46 | 41 |
| Male | 0 | 0 | 0 |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 1 | 3 | 0 |
| Not Hispanic or Latino | 48 | 40 | 39 |
| Unknown or Not Reported | 4 | 3 | 2 |

| | | | |
|---|---|---|---|
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 6 | 8 | 4 |
| Native Hawaiian or Other Pacific Islander | 1 | 1 | 0 |
| Black or African American | 0 | 1 | 0 |
| White | 46 | 36 | 37 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Region of Enrollment<br>Units: Subjects | | | |
| South Korea | 4 | 5 | 2 |
| Belgium | 4 | 1 | 3 |
| United States | 6 | 13 | 3 |
| United Kingdom | 6 | 9 | 4 |
| Italy | 4 | 4 | 8 |
| Israel | 6 | 3 | 7 |
| Australia | 14 | 7 | 10 |
| Spain | 9 | 4 | 4 |

| **Reporting group values** | Prexasertib Cohort 4 | Total | |
|---|---|---|---|
| Number of subjects | 29 | 169 | |
| 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 | 59.0 | | |
| standard deviation | ± 13.4 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 29 | 169 | |
| Male | 0 | 0 | |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 0 | 4 | |
| Not Hispanic or Latino | 28 | 155 | |
| Unknown or Not Reported | 1 | 10 | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |

| | | | |
|---|---|---|---|
| Asian | 3 | 21 | |
| Native Hawaiian or Other Pacific Islander | 0 | 2 | |
| Black or African American | 1 | 2 | |
| White | 25 | 144 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 0 | 0 | |
| Region of Enrollment<br>Units: Subjects | | | |
| South Korea | 2 | 13 | |
| Belgium | 0 | 8 | |
| United States | 10 | 32 | |
| United Kingdom | 1 | 20 | |
| Italy | 7 | 23 | |
| Israel | 4 | 20 | |
| Australia | 3 | 34 | |
| Spain | 2 | 19 | |

## End points

### End points reporting groups

| Reporting group title | Prexasertib Cohort 1 |
|---|---|
| Reporting group description: | |
| Participants received 105 milligram per square meter (mg/m²) prexasertib as an approximately 60 (+10) minute IV infusion on Day 1 and 15 of a 28-day cycle. Participants were with platinum-resistant disease, breast cancer susceptibility gene (BRCA) negative and have received ≥3 lines of prior therapy. | |
| Reporting group title | Prexasertib Cohort 2 |
| Reporting group description: | |
| Participants received 105 mg/m² prexasertib as an approximately 60 (+10) minute IV infusion on Day 1 and 15 of a 28-day cycle. Participants were with platinum-resistant disease, BRCA negative and have received <3 lines of prior therapy. | |
| Reporting group title | Prexasertib Cohort 3 |
| Reporting group description: | |
| Participants received 105 mg/m² prexasertib as an approximately 60 (+10) minute IV infusion on Day 1 and 15 of a 28-day cycle. Participants were with platinum-resistant disease, BRCA positive and received a prior poly ADP ribose polymerase (PARP) inhibitor. | |
| Reporting group title | Prexasertib Cohort 4 |
| Reporting group description: | |
| Participants received 105 mg/m² prexasertib as an approximately 60 (+10) minute IV infusion on Day 1 and 15 of a 28-day cycle. Participants were with platinum refractory disease, BRCA positive or negative, no restriction on number of lines of prior therapy. | |
| Subject analysis set title | Prexasertib |
| Subject analysis set type | Per protocol |
| Subject analysis set description: | |
| Participants received 105 mg/m² prexasertib as an approximately 60 (+10) minute IV infusion on Day 1 and 15 of a 28-day cycle. (Participants combined from all the Cohorts 1 to 4) | |

### Primary: Percentage of Participants Who Achieve Complete Response (CR) or Partial Response (PR): Overall Response Rate (ORR)

| End point title | Percentage of Participants Who Achieve Complete Response (CR) or Partial Response (PR): Overall Response Rate (ORR)[1] |
|---|---|
| End point description: | |
| Overall response rate is the best response of complete response (CR) or partial response (PR) as classified by the independent central review according to the Response Evaluation Criteria In Solid Tumors (RECIST v1.1). CR is a disappearance of all target and non-target lesions and normalization of tumor marker level. PR is an at least 30% decrease in the sum of the diameters of target lesions (taking as reference the baseline sum diameter) without progression of non-target lesions or appearance of new lesions. Overall response rate is calculated as a total number of participants with CR or PR divided by the total number of participants per cohort with at least 1 measurable lesion, multiplied by 100.<br>Analysis Population Description (APD): All randomized participants who received at least one dose of study drug. | |
| End point type | Primary |
| End point timeframe: | |
| Baseline through Disease Progression (Up to 6 months) | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis performed for this outcome.

| End point values | Prexasertib Cohort 1 | Prexasertib Cohort 2 | Prexasertib Cohort 3 | Prexasertib Cohort 4 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 53 | 46 | 41 | 29 |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 11.3 (4.3 to 23.0) | 13.0 (4.9 to 26.3) | 12.2 (4.1 to 26.2) | 6.9 (0.8 to 22.8) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics (PK): Maximum Plasma Concentration (Cmax) of Prexasertib

| End point title | Pharmacokinetics (PK): Maximum Plasma Concentration (Cmax) of Prexasertib |
|---|---|

End point description:

Pharmacokinetics(PK): Maximum Plasma Concentration of Prexasertib. The same dose was administered to Cohort 1, 2, 3 and 4 and were combined for analysis.

APD: All randomized participants who received at least one dose of study drug and had evaluable PK data. Cohort 1, 2, 3 and 4 received the same dose and were combined per protocol.

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

End point timeframe:

Cycle 1, Cycle 2, Cycle 4, Cycle 6 (Day 1 (End of prexasertib infusion (+15 min), 1-2 hours following end of prexasertib infusion), Cycle 2, day 1(Prior to start of prexasertib infusion)

| End point values | Prexasertib | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 151 | | | |
| Units: nanograms per milliliter(ng/mL) | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Cycle 1 | 668 (± 50) | | | |
| Cycle 2 | 718 (± 62) | | | |
| Cycle 4 | 678 (± 61) | | | |
| Cycle 6 | 672 (± 42) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Disease Control Rate (DCR): Percentage of Participants with a Best Overall Response of CR, PR, or Stable Disease (SD) for at Least 4 Months

| End point title | Disease Control Rate (DCR): Percentage of Participants with a Best Overall Response of CR, PR, or Stable Disease (SD) for at |
|---|---|

| | |
|---|---|
| | Least 4 Months |

End point description:

DCR is defined as the number of participants who achieve a best overall response of CR, PR or SD for ≥4 months as determined by per RECIST version 1.1. CR is the disappearance of all target and non-target lesions; PR is a ≥30% decrease in sum of longest diameter of target lesions without new lesion and progression of non-target lesion; SD is neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease. Disease control rate is calculated as a total number of participants with CR or PR or SD divided by the total number of participants treated, then multiplied by 100.

APD: All randomized participants who received at least one dose of study drug.

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

End point timeframe:

Baseline through Disease Progression (up to 6 months)

| **End point values** | Prexasertib Cohort 1 | Prexasertib Cohort 2 | Prexasertib Cohort 3 | Prexasertib Cohort 4 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 53 | 46 | 41 | 29 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 45.3 (31.6 to 59.6) | 32.6 (19.5 to 48.0) | 31.7 (18.1 to 48.1) | 31.0 (15.3 to 50.8) |

## 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 is defined as the time from the date measurement criteria for CR or PR (whichever is first recorded) are first met until the first date that disease is recurrent or objective progression is observed, per RECIST 1.1, or the date of death from any cause in the absence of objectively determined disease progression or recurrence. Participants known to be alive and without disease progression will be censored at the time of the last adequate tumor assessment.

APD: All randomized participants who received at least one dose of study drug and had CR or PR responses. Number of participants censored Cohort 1 = 0, Cohort 2 = 1, Cohort 3 = 0 and Cohort 4 = 0.

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

End point timeframe:

Date of CR or PR to Date of Disease Progression or Death Due to Any Cause (up to 26 months)

| End point values | Prexasertib Cohort 1 | Prexasertib Cohort 2 | Prexasertib Cohort 3 | Prexasertib Cohort 4 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6[2] | 5[3] | 5 | 2[4] |
| Units: Months | | | | |
| median (confidence interval 95%) | 8.57 (5.55 to 99999) | 3.84 (2.79 to 99999) | 5.55 (3.65 to 9.36) | 5.31 (5.06 to 99999) |

Notes:

[2] - 99999-The upper 95% confidence interval was not achieved due to high censoring rate.

[3] - 99999-The upper 95% confidence interval was not achieved due to high censoring rate.

[4] - 99999-The upper 95% confidence interval was not achieved due to high censoring rate.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with at Least a 50% Reduction in CA-125 Levels from Baseline

| End point title | Percentage of Participants with at Least a 50% Reduction in CA-125 Levels from Baseline |
|---|---|

End point description:

CA-125 response is defined as ≥50% reduction in CA-125 levels from a pretreatment sample. The response must be confirmed and maintained for ≥28 days according to GCIG criteria. Participants must have a pretreatment sample that is ≥2 times the upper limit of the reference range and obtained within 2 weeks before starting the treatment.

APD: All randomized participants who received at least one dose of study drug.

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

End point timeframe:

Baseline, 4 Weeks

| End point values | Prexasertib Cohort 1 | Prexasertib Cohort 2 | Prexasertib Cohort 3 | Prexasertib Cohort 4 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 53 | 46 | 41 | 29 |
| Units: Percentage of participants | | | | |
| number (not applicable) | 39.6 | 34.8 | 17.1 | 37.9 |

### 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) is defined as the time from the date of enrollment until the first occurrence of documented disease progression per RECIST 1.1, or death from any cause in the absence of progressive disease (PD). Participants known to be alive and without disease progression will be censored at the time of the last adequate tumor assessment.

APD: All randomized participants who received at least one dose of study drug. Number of participants censored Cohort 1 = 6, Cohort 2 = 4, Cohort 3 = 4 and Cohort 4 = 4.

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

End point timeframe:

Baseline to Disease Progression or Death from any Cause (Up to 26 months)

| **End point values** | Prexasertib Cohort 1 | Prexasertib Cohort 2 | Prexasertib Cohort 3 | Prexasertib Cohort 4 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 47 | 42 | 37 | 25 |
| Units: Months | | | | |
| median (confidence interval 95%) | 3.91 (3.68 to 5.68) | 3.71 (3.12 to 4.70) | 3.58 (1.87 to 3.91) | 3.71 (1.77 to 4.70) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Overall Survival

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

End point description:

Overall survival (OS) is defined as the time from the date of enrollment until death from any cause. If the participant is alive, lost to follow-up or withdrawn from study at the time of data analysis, OS data will be censored on the last date the participant is known to be alive.

APD: All randomized participants who received at least one dose of study drug and had overall survival data. Number of participants censored Cohort 1 = 18, Cohort 2 = 12, Cohort 3 = 12 and Cohort 4 = 4.

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

End point timeframe:

Baseline to Date of Death from Any Cause (Up to 15 months)

| **End point values** | Prexasertib Cohort 1 | Prexasertib Cohort 2 | Prexasertib Cohort 3 | Prexasertib Cohort 4 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 35 | 34 | 29 | 25 |
| Units: Months | | | | |
| median (confidence interval 95%) | 13.04 (7.46 to 19.25) | 14.32 (11.76 to 16.46) | 11.14 (7.23 to 16.43) | 8.18 (6.18 to 11.93) |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| Baseline, upto 26 Months | |
| Adverse event reporting additional description: | |
| All randomized participants who received at least one dose. | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 22.0 |

| Reporting groups | |
|---|---|
| Reporting group title | Prexasertib Cohort 1 |
| Reporting group description: - | |
| Reporting group title | Prexasertib Cohort 2 |
| Reporting group description: - | |
| Reporting group title | Prexasertib Cohort 3 |
| Reporting group description: - | |
| Reporting group title | Prexasertib Cohort 4 |
| Reporting group description: - | |

| Serious adverse events | Prexasertib Cohort 1 | Prexasertib Cohort 2 | Prexasertib Cohort 3 |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 23 / 53 (43.40%) | 17 / 46 (36.96%) | 19 / 41 (46.34%) |
| number of deaths (all causes) | 2 | 1 | 1 |
| number of deaths resulting from adverse events | 1 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| acute myeloid leukaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| hypertension | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| peripheral artery thrombosis | | | |

| | | | |
|---|---|---|---|
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 46 (2.17%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| asthenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| chills | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| death | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| generalised oedema | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hyperpyrexia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| non-cardiac chest pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| obstruction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| peripheral swelling | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 46 (2.17%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pyrexia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 5 / 46 (10.87%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 5 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| dyspnoea | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 53 (3.77%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hypoxia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 46 (2.17%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pleuritic pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pulmonary embolism | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Product issues | | | |
| device dislocation | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 46 (2.17%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| blood creatinine increased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| neutrophil count decreased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 46 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 11 / 11 | 0 / 0 | 6 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| platelet count decreased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 46 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 6 / 6 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| troponin increased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| white blood cell count increased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| fall | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 46 (2.17%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| gastrointestinal stoma complication | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 46 (2.17%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| spinal compression fracture | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| atrioventricular block | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| myocardial infarction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pericardial effusion | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| sinus tachycardia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| **Nervous system disorders** | | | |
| encephalopathy | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| **Blood and lymphatic system disorders** | | | |
| anaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 2 / 46 (4.35%) | 2 / 41 (4.88%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| febrile neutropenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 5 / 53 (9.43%) | 3 / 46 (6.52%) | 5 / 41 (12.20%) |
| occurrences causally related to treatment / all | 5 / 5 | 4 / 4 | 5 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| leukopenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| neutropenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 53 (7.55%) | 3 / 46 (6.52%) | 4 / 41 (9.76%) |
| occurrences causally related to treatment / all | 4 / 4 | 3 / 3 | 4 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| thrombocytopenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 53 (5.66%) | 0 / 46 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 5 / 5 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| abdominal pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 46 (2.17%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ascites | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 46 (2.17%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| colitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| constipation | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 53 (0.00%) | 2 / 46 (4.35%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| diarrhoea | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 2 / 46 (4.35%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| duodenal obstruction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 46 (2.17%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| gastritis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| gastrointestinal obstruction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| gastrooesophageal reflux disease | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 46 (2.17%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| intestinal obstruction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 46 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |

| | | | |
|---|---|---|---|
| large intestinal obstruction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 46 (2.17%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| large intestine perforation | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 53 (3.77%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| nausea | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 1 / 46 (2.17%) | 2 / 41 (4.88%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| obstruction gastric | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| small intestinal obstruction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 3 / 46 (6.52%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| vomiting | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 4 / 46 (8.70%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 2 / 2 | 3 / 4 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| biliary dilatation | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| acute kidney injury | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pollakiuria | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| urinary tract obstruction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| back pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| diverticulitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 46 (2.17%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| escherichia urinary tract infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 46 (2.17%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| gastroenteritis viral | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| localised infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| neutropenic sepsis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 2 / 46 (4.35%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| pneumonia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 1 / 46 (2.17%) | 2 / 41 (4.88%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| sepsis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 53 (3.77%) | 1 / 46 (2.17%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 1 | 0 / 0 |
| septic shock | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| soft tissue infection<br>alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| staphylococcal bacteraemia<br>alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| tonsillitis<br>alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| urinary tract infection<br>alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 3 / 46 (6.52%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| urosepsis<br>alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| viral infection<br>alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| wound infection<br>alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| decreased appetite | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 1 / 46 (2.17%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| dehydration | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 53 (3.77%) | 2 / 46 (4.35%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| hypoalbuminaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Prexasertib Cohort 4 | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 15 / 29 (51.72%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| acute myeloid leukaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| hypertension | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| peripheral artery thrombosis | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| General disorders and administration site conditions | | | | |
| asthenia | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| chills | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| death | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| generalised oedema | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| hyperpyrexia | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| non-cardiac chest pain | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| obstruction | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| peripheral swelling | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| pyrexia | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory, thoracic and mediastinal disorders | | | | |
| dyspnoea | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| hypoxia | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| pleuritic pain | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| pulmonary embolism | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Product issues | | | | |
| device dislocation | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Investigations | | | | |
| blood creatinine increased | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| neutrophil count decreased | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| platelet count decreased | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| troponin increased | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| white blood cell count increased | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Injury, poisoning and procedural complications | | | | |
| fall | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| gastrointestinal stoma complication | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| spinal compression fracture | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac disorders | | | | |
| atrioventricular block | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 1 / 29 (3.45%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| myocardial infarction | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| pericardial effusion | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| sinus tachycardia | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nervous system disorders | | | | |
| encephalopathy | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Blood and lymphatic system disorders | | | | |
| anaemia | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| febrile neutropenia | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 4 / 29 (13.79%) | | | |
| occurrences causally related to treatment / all | 4 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| leukopenia | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| neutropenia | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | | |
| occurrences causally related to treatment / all | 2 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| thrombocytopenia | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal disorders | | | | |
| abdominal pain | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| ascites | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| colitis | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| constipation | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| diarrhoea | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| duodenal obstruction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| gastritis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| gastrointestinal obstruction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| gastrooesophageal reflux disease | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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|---|---|---|---|---|
| intestinal obstruction | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| large intestinal obstruction | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| large intestine perforation | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| nausea | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| obstruction gastric | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| small intestinal obstruction | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| vomiting | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 29 (10.34%) | | |
| occurrences causally related to treatment / all | 1 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| biliary dilatation | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| acute kidney injury | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| pollakiuria | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| urinary tract obstruction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| back pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| diverticulitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| escherichia urinary tract infection | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| gastroenteritis viral | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| localised infection | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| neutropenic sepsis | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| pneumonia | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | | |
| occurrences causally related to treatment / all | 2 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| sepsis | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | | |
| occurrences causally related to treatment / all | 1 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | | |
|---|---|---|---|---|
| septic shock | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| soft tissue infection | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| staphylococcal bacteraemia | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| tonsillitis | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| urinary tract infection | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| urosepsis | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| viral infection | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| wound infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| decreased appetite | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| dehydration | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| hypoalbuminaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | |
| 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** | Prexasertib Cohort 1 | Prexasertib Cohort 2 | Prexasertib Cohort 3 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 53 / 53 (100.00%) | 44 / 46 (95.65%) | 39 / 41 (95.12%) |
| Vascular disorders | | | |
| flushing | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 53 (1.89%) | 1 / 46 (2.17%) | 2 / 41 (4.88%) |
| occurrences (all) | 1 | 1 | 3 |
| hot flush | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 46 (2.17%) | 3 / 41 (7.32%) |
| occurrences (all) | 0 | 4 | 3 |
| hypertension | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 5 / 53 (9.43%) | 2 / 46 (4.35%) | 3 / 41 (7.32%) |
| occurrences (all) | 5 | 2 | 4 |
| General disorders and administration site conditions | | | |
| asthenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 8 / 53 (15.09%) | 8 / 46 (17.39%) | 10 / 41 (24.39%) |
| occurrences (all) | 19 | 16 | 38 |
| catheter site pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 46 (2.17%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 1 | 1 |
| fatigue | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 21 / 53 (39.62%) | 19 / 46 (41.30%) | 12 / 41 (29.27%) |
| occurrences (all) | 84 | 37 | 17 |
| mucosal inflammation | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 5 / 53 (9.43%) | 1 / 46 (2.17%) | 3 / 41 (7.32%) |
| occurrences (all) | 8 | 1 | 5 |
| non-cardiac chest pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 46 (2.17%) | 3 / 41 (7.32%) |
| occurrences (all) | 0 | 1 | 6 |
| oedema peripheral | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 53 (7.55%) | 3 / 46 (6.52%) | 3 / 41 (7.32%) |
| occurrences (all) | 5 | 3 | 3 |
| pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 53 (7.55%) | 2 / 46 (4.35%) | 5 / 41 (12.20%) |
| occurrences (all) | 4 | 3 | 6 |
| pyrexia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 13 / 53 (24.53%) | 5 / 46 (10.87%) | 7 / 41 (17.07%) |
| occurrences (all) | 17 | 6 | 16 |
| Reproductive system and breast disorders | | | |
| pelvic pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 53 (5.66%) | 0 / 46 (0.00%) | 3 / 41 (7.32%) |
| occurrences (all) | 5 | 0 | 3 |
| Respiratory, thoracic and mediastinal disorders | | | |
| cough | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 5 / 53 (9.43%) | 2 / 46 (4.35%) | 4 / 41 (9.76%) |
| occurrences (all) | 8 | 2 | 4 |
| dyspnoea | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 6 / 53 (11.32%) | 7 / 46 (15.22%) | 4 / 41 (9.76%) |
| occurrences (all) | 10 | 8 | 5 |
| oropharyngeal pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 5 / 53 (9.43%) | 2 / 46 (4.35%) | 3 / 41 (7.32%) |
| occurrences (all) | 6 | 2 | 3 |
| Psychiatric disorders | | | |
| anxiety | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 53 (3.77%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| insomnia | | | |
| alternative dictionary used: | | | |

| | | | |
|---|---|---|---|
| MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 3 / 46 (6.52%) | 2 / 41 (4.88%) |
| occurrences (all) | 0 | 3 | 2 |
| Investigations | | | |
| alanine aminotransferase increased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 3 / 46 (6.52%) | 3 / 41 (7.32%) |
| occurrences (all) | 1 | 3 | 4 |
| aspartate aminotransferase increased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 53 (3.77%) | 3 / 46 (6.52%) | 1 / 41 (2.44%) |
| occurrences (all) | 3 | 3 | 1 |
| blood alkaline phosphatase increased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 53 (3.77%) | 3 / 46 (6.52%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| blood creatinine increased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 53 (5.66%) | 2 / 46 (4.35%) | 3 / 41 (7.32%) |
| occurrences (all) | 4 | 2 | 5 |
| neutrophil count decreased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 53 (3.77%) | 9 / 46 (19.57%) | 5 / 41 (12.20%) |
| occurrences (all) | 11 | 13 | 9 |
| platelet count decreased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 8 / 53 (15.09%) | 7 / 46 (15.22%) | 7 / 41 (17.07%) |
| occurrences (all) | 37 | 17 | 28 |
| weight decreased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 53 (3.77%) | 3 / 46 (6.52%) | 1 / 41 (2.44%) |
| occurrences (all) | 2 | 4 | 1 |
| white blood cell count decreased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 53 (1.89%) | 3 / 46 (6.52%) | 1 / 41 (2.44%) |
| occurrences (all) | 1 | 7 | 1 |
| Injury, poisoning and procedural complications | | | |
| fall | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| infusion related reaction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 5 / 53 (9.43%) | 6 / 46 (13.04%) | 4 / 41 (9.76%) |
| occurrences (all) | 5 | 9 | 5 |
| Nervous system disorders | | | |
| dizziness | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 5 / 46 (10.87%) | 1 / 41 (2.44%) |
| occurrences (all) | 1 | 8 | 1 |
| headache | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 8 / 53 (15.09%) | 10 / 46 (21.74%) | 3 / 41 (7.32%) |
| occurrences (all) | 9 | 21 | 7 |
| neuropathy peripheral | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 53 (3.77%) | 3 / 46 (6.52%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 4 | 0 |
| Blood and lymphatic system disorders | | | |
| anaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 20 / 53 (37.74%) | 17 / 46 (36.96%) | 15 / 41 (36.59%) |
| occurrences (all) | 64 | 38 | 40 |
| febrile neutropenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 0 / 46 (0.00%) | 2 / 41 (4.88%) |
| occurrences (all) | 1 | 0 | 2 |
| leukopenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 53 (7.55%) | 1 / 46 (2.17%) | 6 / 41 (14.63%) |
| occurrences (all) | 7 | 2 | 10 |
| neutropenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 19 / 53 (35.85%) | 10 / 46 (21.74%) | 11 / 41 (26.83%) |
| occurrences (all) | 40 | 26 | 24 |
| thrombocytopenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 17 / 53 (32.08%) | 14 / 46 (30.43%) | 14 / 41 (34.15%) |
| occurrences (all) | 83 | 36 | 34 |
| Gastrointestinal disorders | | | |
| abdominal discomfort | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 53 (5.66%) | 2 / 46 (4.35%) | 0 / 41 (0.00%) |
| occurrences (all) | 3 | 3 | 0 |
| abdominal distension | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 53 (7.55%) | 3 / 46 (6.52%) | 2 / 41 (4.88%) |
| occurrences (all) | 4 | 3 | 2 |
| abdominal pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 14 / 53 (26.42%) | 18 / 46 (39.13%) | 11 / 41 (26.83%) |
| occurrences (all) | 18 | 40 | 15 |
| abdominal pain lower | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 2 / 46 (4.35%) | 3 / 41 (7.32%) |
| occurrences (all) | 1 | 4 | 3 |
| abdominal pain upper | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 53 (5.66%) | 4 / 46 (8.70%) | 2 / 41 (4.88%) |
| occurrences (all) | 3 | 6 | 2 |
| ascites | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 53 (1.89%) | 5 / 46 (10.87%) | 2 / 41 (4.88%) |
| occurrences (all) | 1 | 11 | 3 |
| constipation | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 13 / 53 (24.53%) | 12 / 46 (26.09%) | 8 / 41 (19.51%) |
| occurrences (all) | 19 | 15 | 13 |
| diarrhoea | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 19 / 53 (35.85%) | 15 / 46 (32.61%) | 7 / 41 (17.07%) |
| occurrences (all) | 57 | 19 | 11 |
| dry mouth | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 3 / 46 (6.52%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| dyspepsia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 53 (5.66%) | 2 / 46 (4.35%) | 4 / 41 (9.76%) |
| occurrences (all) | 3 | 4 | 4 |
| mouth ulceration | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 53 (5.66%) | 1 / 46 (2.17%) | 1 / 41 (2.44%) |
| occurrences (all) | 5 | 1 | 1 |
| nausea | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 19 / 53 (35.85%) | 24 / 46 (52.17%) | 15 / 41 (36.59%) |
| occurrences (all) | 54 | 56 | 33 |
| small intestinal obstruction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 53 (5.66%) | 2 / 46 (4.35%) | 1 / 41 (2.44%) |
| occurrences (all) | 4 | 2 | 2 |
| vomiting | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 21 / 53 (39.62%) | 13 / 46 (28.26%) | 11 / 41 (26.83%) |
| occurrences (all) | 29 | 20 | 36 |

| | | | |
|---|---|---|---|
| Skin and subcutaneous tissue disorders | | | |
| erythema | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| pruritus | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 5 / 53 (9.43%) | 3 / 46 (6.52%) | 2 / 41 (4.88%) |
| occurrences (all) | 5 | 3 | 3 |
| rash | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 53 (5.66%) | 5 / 46 (10.87%) | 6 / 41 (14.63%) |
| occurrences (all) | 3 | 9 | 7 |
| Renal and urinary disorders | | | |
| pollakiuria | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 46 (2.17%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| arthralgia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 8 / 53 (15.09%) | 5 / 46 (10.87%) | 2 / 41 (4.88%) |
| occurrences (all) | 11 | 6 | 2 |
| back pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 11 / 53 (20.75%) | 8 / 46 (17.39%) | 6 / 41 (14.63%) |
| occurrences (all) | 13 | 14 | 7 |
| bone pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 53 (5.66%) | 0 / 46 (0.00%) | 3 / 41 (7.32%) |
| occurrences (all) | 4 | 0 | 4 |
| groin pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 46 (2.17%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|---|---|---|
| muscle spasms | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 53 (5.66%) | 2 / 46 (4.35%) | 2 / 41 (4.88%) |
| occurrences (all) | 13 | 2 | 3 |
| muscular weakness | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 5 / 46 (10.87%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| myalgia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 3 / 46 (6.52%) | 1 / 41 (2.44%) |
| occurrences (all) | 2 | 4 | 1 |
| Infections and infestations | | | |
| cellulitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 53 (5.66%) | 0 / 46 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| nasopharyngitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 53 (1.89%) | 3 / 46 (6.52%) | 3 / 41 (7.32%) |
| occurrences (all) | 1 | 3 | 3 |
| upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 7 / 53 (13.21%) | 2 / 46 (4.35%) | 0 / 41 (0.00%) |
| occurrences (all) | 9 | 2 | 0 |
| urinary tract infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 53 (7.55%) | 3 / 46 (6.52%) | 0 / 41 (0.00%) |
| occurrences (all) | 9 | 5 | 0 |
| viral infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 53 (5.66%) | 0 / 46 (0.00%) | 2 / 41 (4.88%) |
| occurrences (all) | 3 | 0 | 4 |
| Metabolism and nutrition disorders | | | |

| | | | |
|---|---|---|---|
| decreased appetite | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 12 / 53 (22.64%) | 12 / 46 (26.09%) | 9 / 41 (21.95%) |
| occurrences (all) | 14 | 21 | 12 |
| dehydration | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 1 / 46 (2.17%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| hypoalbuminaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 53 (0.00%) | 3 / 46 (6.52%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 3 | 2 |
| hypokalaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 53 (5.66%) | 2 / 46 (4.35%) | 5 / 41 (12.20%) |
| occurrences (all) | 4 | 11 | 10 |
| hypomagnesaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 53 (3.77%) | 3 / 46 (6.52%) | 2 / 41 (4.88%) |
| occurrences (all) | 3 | 12 | 4 |
| hyponatraemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 53 (7.55%) | 3 / 46 (6.52%) | 3 / 41 (7.32%) |
| occurrences (all) | 6 | 3 | 6 |

| **Non-serious adverse events** | Prexasertib Cohort 4 | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 28 / 29 (96.55%) | | |
| Vascular disorders | | | |
| flushing | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | |
| occurrences (all) | 2 | | |
| hot flush | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences (all) | 0 | | |
| hypertension | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | |
| occurrences (all) | 1 | | |
| General disorders and administration site conditions | | | |
| asthenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 29 (13.79%) | | |
| occurrences (all) | 13 | | |
| catheter site pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | |
| occurrences (all) | 2 | | |
| fatigue | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 12 / 29 (41.38%) | | |
| occurrences (all) | 20 | | |
| mucosal inflammation | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | |
| occurrences (all) | 1 | | |
| non-cardiac chest pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | |
| occurrences (all) | 1 | | |
| oedema peripheral | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | |
| occurrences (all) | 1 | | |
| pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 29 (10.34%) | | |
| occurrences (all) | 3 | | |
| pyrexia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 8 / 29 (27.59%) | | |
| occurrences (all) | 9 | | |
| Reproductive system and breast disorders | | | |
| pelvic pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| cough | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | |
| occurrences (all) | 1 | | |
| dyspnoea | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 29 (13.79%) | | |
| occurrences (all) | 4 | | |
| oropharyngeal pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences (all) | 0 | | |
| Psychiatric disorders | | | |
| anxiety | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | |
| occurrences (all) | 3 | | |
| insomnia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 29 (13.79%) | | |
| occurrences (all) | 4 | | |
| Investigations | | | |

| | | | |
|---|---|---|---|
| alanine aminotransferase increased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | |
| occurrences (all) | 3 | | |
| aspartate aminotransferase increased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | |
| occurrences (all) | 3 | | |
| blood alkaline phosphatase increased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | |
| occurrences (all) | 1 | | |
| blood creatinine increased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences (all) | 0 | | |
| neutrophil count decreased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | |
| occurrences (all) | 1 | | |
| platelet count decreased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 29 (10.34%) | | |
| occurrences (all) | 4 | | |
| weight decreased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | |
| occurrences (all) | 2 | | |
| white blood cell count decreased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|---|---|---|
| fall | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | |
| occurrences (all) | 2 | | |
| infusion related reaction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | |
| occurrences (all) | 2 | | |
| Nervous system disorders | | | |
| dizziness | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 29 (13.79%) | | |
| occurrences (all) | 4 | | |
| headache | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | |
| occurrences (all) | 1 | | |
| neuropathy peripheral | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood and lymphatic system disorders | | | |
| anaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 12 / 29 (41.38%) | | |
| occurrences (all) | 26 | | |
| febrile neutropenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 29 (10.34%) | | |
| occurrences (all) | 3 | | |
| leukopenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 29 (13.79%) | | |
| occurrences (all) | 7 | | |
| neutropenia | | | |

| | | | | |
|---|---|---|---|---|
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 10 / 29 (34.48%) | | | |
| occurrences (all) | 15 | | | |
| thrombocytopenia | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 7 / 29 (24.14%) | | | |
| occurrences (all) | 18 | | | |
| Gastrointestinal disorders | | | | |
| abdominal discomfort | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | | |
| occurrences (all) | 3 | | | |
| abdominal distension | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 5 / 29 (17.24%) | | | |
| occurrences (all) | 7 | | | |
| abdominal pain | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 10 / 29 (34.48%) | | | |
| occurrences (all) | 14 | | | |
| abdominal pain lower | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | | |
| occurrences (all) | 1 | | | |
| abdominal pain upper | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 4 / 29 (13.79%) | | | |
| occurrences (all) | 4 | | | |
| ascites | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | | |
| occurrences (all) | 3 | | | |
| constipation | | | | |
| alternative dictionary used: MedDRA 22.0 | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 5 / 29 (17.24%) | | |
| occurrences (all) | 5 | | |
| diarrhoea | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 8 / 29 (27.59%) | | |
| occurrences (all) | 20 | | |
| dry mouth | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences (all) | 0 | | |
| dyspepsia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences (all) | 0 | | |
| mouth ulceration | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences (all) | 0 | | |
| nausea | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 16 / 29 (55.17%) | | |
| occurrences (all) | 25 | | |
| small intestinal obstruction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 29 (13.79%) | | |
| occurrences (all) | 5 | | |
| vomiting | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 14 / 29 (48.28%) | | |
| occurrences (all) | 25 | | |
| Skin and subcutaneous tissue disorders | | | |
| erythema | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 29 (6.90%) | | |
| occurrences (all) | 2 | | |
| pruritus | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | |
| occurrences (all) | 1 | | |
| rash | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | |
| occurrences (all) | 2 | | |
| Renal and urinary disorders | | | |
| pollakiuria | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | |
| occurrences (all) | 2 | | |
| Musculoskeletal and connective tissue disorders | | | |
| arthralgia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences (all) | 0 | | |
| back pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 6 / 29 (20.69%) | | |
| occurrences (all) | 7 | | |
| bone pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 29 (10.34%) | | |
| occurrences (all) | 3 | | |
| groin pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | |
| occurrences (all) | 3 | | |
| muscle spasms | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 29 (3.45%) | | |
| occurrences (all) | 1 | | |
| muscular weakness | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | |
| occurrences (all) | 1 | | |
| myalgia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences (all) | 0 | | |
| Infections and infestations | | | |
| cellulitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences (all) | 0 | | |
| nasopharyngitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | |
| occurrences (all) | 1 | | |
| upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | |
| occurrences (all) | 1 | | |
| urinary tract infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 29 (13.79%) | | |
| occurrences (all) | 4 | | |
| viral infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences (all) | 0 | | |
| Metabolism and nutrition disorders | | | |
| decreased appetite | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 7 / 29 (24.14%) | | |
| occurrences (all) | 8 | | |
| dehydration | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | |
| occurrences (all) | 2 | | |
| hypoalbuminaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences (all) | 0 | | |
| hypokalaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | | |
| occurrences (all) | 1 | | |
| hypomagnesaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | | |
| occurrences (all) | 2 | | |
| hyponatraemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | | |
| occurrences (all) | 0 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 28 June 2018 | 1) A criterion explicitly excluding patients that have known factors that may increase the risk of infection while on study drug treatment was added.<br>2) A statement indicating that strong P-gp and BRCP inhibitors should be used with caution was added. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported