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	v3 (current)
This version publication date	02 September 2022
First version publication date	14 June 2020
Version creation reason	• Correction of full data set DCR

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 Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	61.3	62.3	59.5
standard deviation	± 9.4	± 9.4	± 8.6
Gender categorical Units: Subjects			
Female	53	46	41
Male	0	0	0
Ethnicity (NIH/OMB) 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) 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 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 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 Units: years			
arithmetic mean	59.0		
standard deviation	± 13.4	-	
Gender categorical Units: Subjects			
Female	29	169	
Male	0	0	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	4	
Not Hispanic or Latino	28	155	
Unknown or Not Reported	1	10	
Race (NIH/OMB) 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 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. 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: Per SAP no inferential data planned 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			

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 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 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 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 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 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 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 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			

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			

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 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			
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 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 lower				
alternative dictionary used: MedDRA 22.0				
subjects affected / exposed	1 / 29 (3.45%)			
occurrences (all)	1			
abdominal pain				
alternative dictionary used: MedDRA 22.0				
subjects affected / exposed	10 / 29 (34.48%)			
occurrences (all)	14			
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. 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