Clinical trial results:
A Phase 2 Study of LY2606368 in Patients with Extensive Stage Disease Small Cell Lung Cancer

Summary

EudraCT number	2015-005069-21
Trial protocol	NL DE GR GB ES
Global end of trial date	28 February 2019

Results information

Result version number	v1 (current)
This version publication date	24 February 2020
First version publication date	24 February 2020

Trial information

Trial identification

Sponsor protocol code	I4D-MC-JTJH

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02735980
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, United States, 46285
Public contact	Available Mon-Fri 9AM -5 PM EST, Eli Lilly and Company, 877 CTLilly,
Scientific contact	Available Mon-Fri 9 AM -5 PM EST, Eli Lilly and Company, 877 285-4559,

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	28 February 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 February 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Cohort 1: To estimate the Overall Response Rate (ORR) when a dose of 105 mg/m2 LY2606368 every 14 days is administered to patients with ED-SCLC that have platinum-sensitive disease.

Cohort 2: To estimate the ORR when a dose of 105 mg/m2 LY2606368 every 14 days is administered in patients with Extensive-stage Disease Small Cell Lung Cancer (ED-SCLC) that have platinum resistant/refractory disease.

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	11 May 2016
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: 8
Country: Number of subjects enrolled	Turkey: 21
Country: Number of subjects enrolled	United States: 45
Country: Number of subjects enrolled	Ukraine: 2
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	France: 12
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Greece: 4
Worldwide total number of subjects	133
EEA total number of subjects	57

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)	83
From 65 to 84 years	49
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

No text entered

Pre-assignment

Screening details:

No text entered

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	105 mg/m^2 Prexasertib (Platinum Sensitive Disease)

Arm description:

Intravenous (IV) prexasertib (LY2606368)administered on day 1 of every 14 day cycle

Arm type	Experimental
Investigational medicinal product name	Prexasertib
Investigational medicinal product code	
Other name	LY2606368
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

105 mg/m^2 Intravenous (IV) prexasertib administered of every 14 days with extensive stage disease small cell lung cancer (ED-SCLC) who had platinum-sensitive disease (has prior platinum based therapy with subsequent progression greater or less than 90 days after last dose of platinum based therapy).

Arm title	105 mg/m^2 Prexasertib (Platinum Resistant Disease)

Arm description:

105 mg/m^2 IV prexasertib administered of every 14 days with extensive stage disease small cell lung cancer (ED-SCLC) who had resistant/refractory disease (did not have an objective response to platinum-based therapy or had progression greater than 90 days after the last dose of platinum).

Arm type	Experimental
Investigational medicinal product name	Prexasertib
Investigational medicinal product code	
Other name	LY2606368
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

105 mg/m^2 IV prexasertib administered of every 14 days with extensive stage disease small cell lung cancer (ED-SCLC) who had resistant/refractory disease (did not have an objective response to platinum-based therapy or had progression greater than 90 days after the last dose of platinum).

Arm title	40 mg/m2 Prexasertib Exploratory Addendum

Arm description:

40 mg/m2 IV prexasertib (LY2606368) administered on Days 1, 2 and 3 of a 14-day cycle

Arm type	Experimental

Investigational medicinal product name	Prexasertib
Investigational medicinal product code	
Other name	LY2606368
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 mg/m^2 IV prexasertib Day 1, 2, and Day 3 of a 14 day cycle in participants with ED-SCLC platinum sensitive disease.

Number of subjects in period 1	105 mg/m^2 Prexasertib (Platinum Sensitive Disease)	105 mg/m^2 Prexasertib (Platinum Resistant Disease)	40 mg/m2 Prexasertib Exploratory Addendum
Started	58	60	15
Received at least 1 dose of study drug	56	60	15
Completed	48	49	14
Not completed	10	11	1
Physician decision	3	1	-
Consent withdrawn by subject	1	2	-
death	5	4	-
screen failure	1	-	-
Adverse event, non-fatal	-	4	1

Baseline characteristics

Reporting groups	
Reporting group title	105 mg/m^2 Prexasertib (Platinum Sensitive Disease)
Reporting group description:	
Intravenous (IV) prexasertib (LY2606368)administered on day 1 of every 14 day cycle	
Reporting group title	105 mg/m^2 Prexasertib (Platinum Resistant Disease)
Reporting group description:	
105 mg/m^2 IV prexasertib administered of every 14 days with extensive stage disease small cell lung cancer (ED-SCLC) who had resistant/refractory disease (did not have an objective response to platinum-based therapy or had progression greater than 90 days after the last dose of platinum).	
Reporting group title	40 mg/m2 Prexasertib Exploratory Addendum
Reporting group description:	
40 mg/m2 IV prexasertib (LY2606368) administered on Days 1, 2 and 3 of a 14-day cycle	

Reporting group values	105 mg/m^2 Prexasertib (Platinum Sensitive Disease)	105 mg/m^2 Prexasertib (Platinum Resistant Disease)	40 mg/m2 Prexasertib Exploratory Addendum
Number of subjects	58	60	15
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	64.17	61.45	61.67
standard deviation	± 9.21	± 7.20	± 7.33
Gender categorical Units: Subjects			
Female	23	10	4
Male	35	50	11
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	52	53	15
Unknown or not reported	6	7	0

Reporting group values	Total		
Number of subjects	133		

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			
standard deviation	-		
Gender categorical Units: Subjects			
Female	37		
Male	96		
Ethnicity Units: Subjects			
Hispanic or Latino	0		
Not Hispanic or Latino	120		
Unknown or not reported	13		

Subject analysis sets

Subject analysis set title	PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All randomized participants who received at least 1 dose of study drug and had evaluable PK parameters. Cohort 1 and Cohort 2 received the same dose and were combined per protocol.

Reporting group values	PK population		
Number of subjects	99		
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 standard deviation	 ±		
Gender categorical Units: Subjects			
Female Male			
Ethnicity Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or not reported	0 99 0		

End points

End points reporting groups

Reporting group title	105 mg/m^2 Prexasertib (Platinum Sensitive Disease)
Reporting group description:	
Intravenous (IV) prexasertib (LY2606368)administered on day 1 of every 14 day cycle	
Reporting group title	105 mg/m^2 Prexasertib (Platinum Resistant Disease)
Reporting group description:	
105 mg/m^2 IV prexasertib administered of every 14 days with extensive stage disease small cell lung cancer (ED-SCLC) who had resistant/refractory disease (did not have an objective response to platinum-based therapy or had progression greater than 90 days after the last dose of platinum).	
Reporting group title	40 mg/m2 Prexasertib Exploratory Addendum
Reporting group description:	
40 mg/m2 IV prexasertib (LY2606368) administered on Days 1, 2 and 3 of a 14-day cycle	
Subject analysis set title	PK population
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All randomized participants who received at least 1 dose of study drug and had evaluable PK parameters. Cohort 1 and Cohort 2 received the same dose and were combined per protocol.	

Primary: Percentage of Participants With Complete Response (CR) or Partial Response (PR) (Objective Response Rate [ORR])

End point title	Percentage of Participants With Complete Response (CR) or Partial Response (PR) (Objective Response Rate [ORR])[1]
End point description:	
ORR was the percentage of participants achieving a best overall response (BOR) of complete response (CR) or partial response (PR) as per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. CR defined as the disappearance of all target and non-target lesions and no appearance of new lesions. PR defined as at least a 30% decrease in the sum of the longest diameters (LD) of target lesions (taking as reference the baseline sum LD), no progression of non-target lesions, and no appearance of new lesions	
End point type	Primary
End point timeframe:	
Baseline to 10 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

End point values	105 mg/m^2 Prexasertib (Platinum Sensitive Disease)	105 mg/m^2 Prexasertib (Platinum Resistant Disease)	40 mg/m2 Prexasertib Exploratory Addendum	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	58[2]	60[3]	15[4]	
Units: participants				
number (confidence interval 95%)	5.2 (0.7 to 9.6)	0 (0.0 to 3.7)	0 (0.0 to 14.8)	

Notes:

[2] - All randomized participants who received at least 1 dose of study drug.

[3] - All randomized participants who received at least 1 dose of study drug.

[4] - All randomized participants who received at least 1 dose of study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics(PK): Maximum Concentration (Cmax) of Prexasertib Cohort 1 and Cohort 2

End point title	Pharmacokinetics(PK): Maximum Concentration (Cmax) of Prexasertib Cohort 1 and Cohort 2

End point description:

Pharmacokinetics(PK): Maximum Concentration of Prexasertib. The same dose was administered to Cohort 1 and Cohort 2 and were combined for analysis.
All randomized participants who received at least 1 dose of study drug and had evaluable PK parameters. Cohort 1 and Cohort 2 received the same dose and were combined per protocol.

End point type	Secondary

End point timeframe:

Cycle 1,3, 5, and 7: Day 1, Day 2 and Day 3- Prior to start of infusion, end of infusion plus 10 minutes, Day 8: anytime

End point values	PK population			
Subject group type	Subject analysis set			
Number of subjects analysed	99[5]			
Units: nanogram per milliliter				
geometric mean (geometric coefficient of variation)				
Cycle 1	722 (± 64)			
Cycle 3	735 (± 71)			
Cycle 5	732 (± 69)			
Cycle 7	1230 (± 22)			

Notes:

[5] - Cohort 1 and 2 were combined, Cycle 3, 5 and 7 had 53, 16 and 5 participants respectively.

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics(PK): Maximum Concentration of Prexasertib Cohort 3 (40 mg/m^2, Protocol Addenda)

End point title	Pharmacokinetics(PK): Maximum Concentration of Prexasertib Cohort 3 (40 mg/m^2, Protocol Addenda)[6]

End point description:

Pharmacokinetics(PK): Maximum Concentration of Prexasertib

End point type	Secondary

End point timeframe:

Cycle 1: Day 3 prior to infusion and within 10 minutes of end of infusion

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis performed

End point values	40 mg/m2 Prexasertib Exploratory Addendum			
Subject group type	Reporting group			
Number of subjects analysed	15[7]			
Units: nanograms per milliliter				
geometric mean (geometric coefficient of variation)	227 (± 68)			

Notes:

[7] - Al randomized participants with at least 1 dose of study drug and evaluable parameters.

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate: Percentage of Participants With a Best Overall Response of CR, PR, or Stable Disease (SD)

End point title	Disease Control Rate: Percentage of Participants With a Best Overall Response of CR, PR, or Stable Disease (SD)

End point description:

Disease Control Rate is the time from the date measurement criteria for Complete Response (CR), Partial Response (PR) or Stable Disease (SD) divided by the total number of participants enrolled in the corresponding cohort.

End point type	Secondary

End point timeframe:

Baseline through Disease Progression or Death from Any Cause to 28 months

End point values	105 mg/m^2 Prexasertib (Platinum Sensitive Disease)	105 mg/m^2 Prexasertib (Platinum Resistant Disease)	40 mg/m2 Prexasertib Exploratory Addendum	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56[8]	60[9]	15[10]	
Units: participants				
number (confidence interval 95%)	31 (12.6 to 31.4)	20.0 (6.6 to 20.6)	40.0 (10.2 to 48.4)	

Notes:

[8] - All randomized participants who received at least 1 dose of study drug.

[9] - All randomized participants who received at least 1 dose of study drug.

[10] - All randomized participants who received at least 1 dose of study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)

End point description:

PFS defined as the from randomization date to the first evidence of disease progression as defined by RECIST v1.1 or death from any cause. Progressive Disease (PD) was at least a 20% increase in the sum of the diameters of target lesions, with reference being the smallest sum on study and an absolute

increase of at least 5 mm, or unequivocal progression of non-target lesions, or 1 or more new lesions. If a participant does not have a complete baseline disease assessment, then the PFS time was censored at the date of first dose, regardless of whether or not objectively determined disease progression or death has been observed for the participant. If a participant was not known to have died or have objective progression as of the data inclusion cutoff date for the analysis, the PFS time was censored at the last adequate tumor assessment date.

End point type	Secondary

End point timeframe:

Baseline to Disease Progression or Death or to 9 months

End point values	105 mg/m^2 Prexasertib (Platinum Sensitive Disease)	105 mg/m^2 Prexasertib (Platinum Resistant Disease)	40 mg/m2 Prexasertib Exploratory Addendum	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	58[11]	60[12]	15[13]	
Units: participants				
median (confidence interval 95%)	31 (12.6 to 31.4)	20.0 (6.6 to 20.6)	40.0 (10.2 to 48.4)	

Notes:

[11] - All randomized participants who received at least 1 dose of study drug.

[12] - All randomized participants who received at least 1 dose of study drug.

[13] - All randomized participants who received at least 1 dose of study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)

End point description:

PFS defined as the from randomization date to the first evidence of disease progression as defined by RECIST v1.1 or death from any cause. Progressive Disease (PD) was at least a 20% increase in the sum of the diameters of target lesions, with reference being the smallest sum on study and an absolute increase of at least 5 mm, or unequivocal progression of non-target lesions, or 1 or more new lesions. If a participant does not have a complete baseline disease assessment, then the PFS time was censored at the date of first dose, regardless of whether or not objectively determined disease progression or death has been observed for the participant. If a participant was not known to have died or have objective progression as of the data inclusion cutoff date for the analysis, the PFS time was censored at the last adequate tumor assessment date.

End point type	Secondary

End point timeframe:

Baseline to Disease Progression or Death (up to 9 months)

End point values	105 mg/m^2 Prexasertib (Platinum Sensitive Disease)	105 mg/m^2 Prexasertib (Platinum Resistant Disease)	40 mg/m2 Prexasertib Exploratory Addendum	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	58[14]	60[15]	15[16]	
Units: participants				
median (confidence interval 95%)	1.41 (1.31 to 1.64)	1.36 (1.25 to 1.45)	1.58 (1.38 to 3.12)	

Notes:

[14] - All randomized participants who received at least 1 dose of study drug.

[15] - All randomized participants who received at least 1 dose of study drug.

[16] - All randomized participants who received at least 1 dose of study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS defined as from randomization date to the date of death due to any cause. For each participant who is not known to have died as of the data-inclusion cutoff date for overall survival analysis, OS time was censored on the last date the participant is known to be alive.

End point type	Secondary

End point timeframe:

Baseline to 9 months

End point values	105 mg/m^2 Prexasertib (Platinum Sensitive Disease)	105 mg/m^2 Prexasertib (Platinum Resistant Disease)	40 mg/m2 Prexasertib Exploratory Addendum	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	58[17]	60[18]	15[19]	
Units: months				
median (confidence interval 95%)	5.42 (3.75 to 8.51)	3.15 (2.27 to 5.52)	7.26 (2.00 to 9.49)	

Notes:

[17] - All randomized participants.

[18] - All randomized participants

[19] - All randomized participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Lung Cancer Symptom Scale Score (LCSS)

End point title	Change From Baseline in Lung Cancer Symptom Scale Score (LCSS)[20]

End point description:

LCSS is a 9-item questionnaire, six measuring major symptoms for lung malignancies (appetite, fatigue,

cough, dyspnea, hemoptysis and pain), and 3 summation items related to total symptomatic distress, activity status and overall quality of life. Participant responses were measured using visual analogue scales (VAS) with 100-mm lines. The LCSS total score was defined as the mean of the 9 items of the scale, each scored between 0 (for best outcome) to 100 (for worst outcome).

End point type	Secondary

End point timeframe:

All randomized participants in Cohort 1 and 2.

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis performed

End point values	105 mg/m^2 Prexasertib (Platinum Sensitive Disease)	105 mg/m^2 Prexasertib (Platinum Resistant Disease)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58[21]	60[22]		
Units: units on a scale				
arithmetic mean (standard deviation)	-2.8 (± 12.3)	-4.0 (± 10.2)		

Notes:

[21] - All participants in Cohort 1 and Cohort 2.

[22] - All participants in Cohort 1 and Cohort 2.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the Average Symptom Burden Index (ASBI)

End point title	Change From Baseline on the Average Symptom Burden Index (ASBI)[23]

End point description:

ABSI was the mean score for the six major lung cancer symptoms (appetite, fatigue, cough, dyspnea, hemoptysis and pain), each scored between 0 (for best outcome) to 100 (for worst outcome).

End point type	Secondary

End point timeframe:

Baseline to 9 months

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis performed

End point values	105 mg/m^2 Prexasertib (Platinum Sensitive Disease)	105 mg/m^2 Prexasertib (Platinum Resistant Disease)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58[24]	60[25]		
Units: units on a scale				
geometric mean (standard deviation)	-3.0 (± 11.9)	-4.4 (± 11.1)		

Notes:
[24] - All randomized participants in Cohort 1 and 2.
[25] - All randomized participants in Cohort 1 and 2.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
10 months	
Adverse event reporting additional description:	
I4D-MC-JTJH	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	Prexasertib (Platinum Sensitive Disease)
Reporting group description: -	
Reporting group title	Prexasertib (Platinum Resistant Disease)
Reporting group description: -	
Reporting group title	Prexasertib Exploratory Addendum (Platinum Sensitive Disease)
Reporting group description: -	

Serious adverse events	Prexasertib (Platinum Sensitive Disease)	Prexasertib (Platinum Resistant Disease)	Prexasertib Exploratory Addendum (Platinum Sensitive Disease)
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 56 (37.50%)	16 / 60 (26.67%)	6 / 15 (40.00%)
number of deaths (all causes)	4	4	2
number of deaths resulting from adverse events	2	1	1
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 15 (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
hypotension			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	1 / 60 (1.67%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
orthostatic hypotension			
alternative dictionary used:			

MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 15 (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
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 56 (3.57%)	0 / 60 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
multiple organ dysfunction syndrome			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 15 (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
pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	1 / 60 (1.67%)	0 / 15 (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
Respiratory, thoracic and mediastinal disorders			
acute respiratory failure			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 15 (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
atelectasis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 15 (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
dyspnoea			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 56 (0.00%)	4 / 60 (6.67%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
epistaxis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	1 / 60 (1.67%)	0 / 15 (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
haemoptysis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	2 / 60 (3.33%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumothorax			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	0 / 60 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
productive cough			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 15 (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
pulmonary embolism			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	1 / 60 (1.67%)	0 / 15 (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
respiratory failure			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 15 (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

Psychiatric disorders			
confusional state			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	1 / 60 (1.67%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
mental status changes			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 56 (3.57%)	0 / 60 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
blood bilirubin increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	1 / 60 (1.67%)	0 / 15 (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
blood creatinine increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	1 / 60 (1.67%)	0 / 15 (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
electrocardiogram qt prolonged			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 15 (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
neutrophil count decreased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	1 / 60 (1.67%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
platelet count decreased			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 56 (0.00%)	4 / 60 (6.67%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	7 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
white blood cell count decreased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	1 / 60 (1.67%)	0 / 15 (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
Injury, poisoning and procedural complications			
subdural haematoma			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	0 / 60 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac disorders			
pericardial effusion			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nervous system disorders			
cauda equina syndrome			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	1 / 60 (1.67%)	0 / 15 (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
encephalopathy			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 15 (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
lethargy			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 15 (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
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	2 / 60 (3.33%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
febrile neutropenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	8 / 56 (14.29%)	1 / 60 (1.67%)	2 / 15 (13.33%)
occurrences causally related to treatment / all	9 / 9	1 / 1	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
leukopenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 15 (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
neutropenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	1 / 60 (1.67%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	1 / 1	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
thrombocytopenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 56 (3.57%)	1 / 60 (1.67%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
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 / 56 (0.00%)	1 / 60 (1.67%)	1 / 15 (6.67%)
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 / 56 (0.00%)	1 / 60 (1.67%)	0 / 15 (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
colitis ischaemic			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
diarrhoea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	1 / 60 (1.67%)	0 / 15 (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
stomatitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 15 (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
vomiting			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	1 / 60 (1.67%)	0 / 15 (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
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 56 (0.00%)	1 / 60 (1.67%)	0 / 15 (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
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	1 / 60 (1.67%)	0 / 15 (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
muscular weakness			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	0 / 60 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 56 (3.57%)	1 / 60 (1.67%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
device related infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	1 / 60 (1.67%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
escherichia bacteraemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 15 (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
parainfluenzae virus infection			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 15 (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
pneumonia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	5 / 56 (8.93%)	0 / 60 (0.00%)	2 / 15 (13.33%)
occurrences causally related to treatment / all	2 / 9	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
pneumonia haemophilus			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 15 (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
sepsis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 56 (5.36%)	1 / 60 (1.67%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	2 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	1 / 1	0 / 0
urinary tract infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 56 (3.57%)	0 / 60 (0.00%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dehydration			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	1 / 56 (1.79%)	1 / 60 (1.67%)	0 / 15 (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

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

Non-serious adverse events	Prexasertib (Platinum Sensitive Disease)	Prexasertib (Platinum Resistant Disease)	Prexasertib Exploratory Addendum (Platinum Sensitive Disease)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	56 / 56 (100.00%)	59 / 60 (98.33%)	15 / 15 (100.00%)
Vascular disorders			
hypotension			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	1 / 60 (1.67%)	1 / 15 (6.67%)
occurrences (all)	1	1	1
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	8 / 56 (14.29%)	5 / 60 (8.33%)	2 / 15 (13.33%)
occurrences (all)	9	7	9
catheter site pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
fatigue			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	16 / 56 (28.57%)	18 / 60 (30.00%)	6 / 15 (40.00%)
occurrences (all)	25	25	8
influenza like illness			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	0 / 60 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	0	2
non-cardiac chest pain			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	7 / 56 (12.50%)	5 / 60 (8.33%)	0 / 15 (0.00%)
occurrences (all)	8	5	0
oedema peripheral			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 56 (7.14%)	1 / 60 (1.67%)	1 / 15 (6.67%)
occurrences (all)	5	1	1
pyrexia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 56 (7.14%)	5 / 60 (8.33%)	3 / 15 (20.00%)
occurrences (all)	4	7	3
Respiratory, thoracic and mediastinal disorders			
bronchial haemorrhage			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	0 / 60 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
cough			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	16 / 56 (28.57%)	9 / 60 (15.00%)	0 / 15 (0.00%)
occurrences (all)	21	9	0
dyspnoea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	11 / 56 (19.64%)	13 / 60 (21.67%)	2 / 15 (13.33%)
occurrences (all)	13	14	2
productive cough			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	4 / 60 (6.67%)	0 / 15 (0.00%)
occurrences (all)	1	4	0
Psychiatric disorders			
confusional state			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	1 / 60 (1.67%)	1 / 15 (6.67%)
occurrences (all)	1	1	1
depression			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	1 / 56 (1.79%)	1 / 60 (1.67%)	1 / 15 (6.67%)
occurrences (all)	1	1	1
insomnia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 56 (3.57%)	3 / 60 (5.00%)	1 / 15 (6.67%)
occurrences (all)	3	3	1
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 56 (3.57%)	4 / 60 (6.67%)	2 / 15 (13.33%)
occurrences (all)	3	8	2
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 56 (5.36%)	5 / 60 (8.33%)	2 / 15 (13.33%)
occurrences (all)	3	5	2
blood cholesterol increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	0 / 60 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
blood creatinine increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	4 / 60 (6.67%)	0 / 15 (0.00%)
occurrences (all)	4	5	0
blood uric acid increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	0 / 60 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
electrocardiogram qt prolonged			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	0 / 60 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
gamma-glutamyltransferase increased			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	2 / 56 (3.57%)	5 / 60 (8.33%)	0 / 15 (0.00%)
occurrences (all)	5	6	0
lipase increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	0 / 60 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
lymphocyte count decreased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	7 / 56 (12.50%)	6 / 60 (10.00%)	3 / 15 (20.00%)
occurrences (all)	18	16	5
neutrophil count decreased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	23 / 56 (41.07%)	26 / 60 (43.33%)	7 / 15 (46.67%)
occurrences (all)	62	68	38
platelet count decreased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	18 / 56 (32.14%)	23 / 60 (38.33%)	9 / 15 (60.00%)
occurrences (all)	49	44	36
weight decreased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	5 / 56 (8.93%)	3 / 60 (5.00%)	1 / 15 (6.67%)
occurrences (all)	5	6	1
white blood cell count decreased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	14 / 56 (25.00%)	18 / 60 (30.00%)	5 / 15 (33.33%)
occurrences (all)	34	59	9
Cardiac disorders			
acute myocardial infarction			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	0 / 60 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	3 / 56 (5.36%)	1 / 60 (1.67%)	2 / 15 (13.33%)
occurrences (all)	5	1	2
encephalopathy			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
headache			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 56 (5.36%)	5 / 60 (8.33%)	1 / 15 (6.67%)
occurrences (all)	3	6	2
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	28 / 56 (50.00%)	20 / 60 (33.33%)	9 / 15 (60.00%)
occurrences (all)	46	36	30
febrile neutropenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	5 / 56 (8.93%)	0 / 60 (0.00%)	1 / 15 (6.67%)
occurrences (all)	5	0	1
leukopenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 56 (5.36%)	6 / 60 (10.00%)	0 / 15 (0.00%)
occurrences (all)	4	11	0
neutropenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	18 / 56 (32.14%)	18 / 60 (30.00%)	4 / 15 (26.67%)
occurrences (all)	30	39	11
thrombocytopenia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	13 / 56 (23.21%)	9 / 60 (15.00%)	4 / 15 (26.67%)
occurrences (all)	27	27	11
Eye disorders			
eye haematoma			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 56 (0.00%)	0 / 60 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	2 / 60 (3.33%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
constipation			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	7 / 56 (12.50%)	6 / 60 (10.00%)	1 / 15 (6.67%)
occurrences (all)	9	6	1
diarrhoea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	10 / 56 (17.86%)	5 / 60 (8.33%)	3 / 15 (20.00%)
occurrences (all)	14	12	3
nausea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	15 / 56 (26.79%)	12 / 60 (20.00%)	3 / 15 (20.00%)
occurrences (all)	17	16	3
stomatitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 56 (5.36%)	2 / 60 (3.33%)	3 / 15 (20.00%)
occurrences (all)	4	2	3
vomiting			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	8 / 56 (14.29%)	7 / 60 (11.67%)	3 / 15 (20.00%)
occurrences (all)	11	11	3
Skin and subcutaneous tissue disorders			
pruritus			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	1 / 60 (1.67%)	1 / 15 (6.67%)
occurrences (all)	1	1	1
Musculoskeletal and connective tissue disorders			

arthralgia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	3 / 60 (5.00%)	2 / 15 (13.33%)
occurrences (all)	1	3	3
back pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	7 / 56 (12.50%)	5 / 60 (8.33%)	0 / 15 (0.00%)
occurrences (all)	7	6	0
bone pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 56 (5.36%)	1 / 60 (1.67%)	0 / 15 (0.00%)
occurrences (all)	5	2	0
muscular weakness			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	3 / 60 (5.00%)	2 / 15 (13.33%)
occurrences (all)	0	3	2
myalgia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	1 / 60 (1.67%)	1 / 15 (6.67%)
occurrences (all)	1	1	2
pain in extremity			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 56 (5.36%)	4 / 60 (6.67%)	0 / 15 (0.00%)
occurrences (all)	4	5	0
Infections and infestations			
oral candidiasis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 56 (3.57%)	0 / 60 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	1
oral herpes			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	0 / 60 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
pharyngitis			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
rhinitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 56 (0.00%)	0 / 60 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
tooth infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 56 (1.79%)	0 / 60 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
urinary tract infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 56 (5.36%)	2 / 60 (3.33%)	1 / 15 (6.67%)
occurrences (all)	3	2	1
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	13 / 56 (23.21%)	14 / 60 (23.33%)	6 / 15 (40.00%)
occurrences (all)	18	20	7
dehydration			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	6 / 56 (10.71%)	2 / 60 (3.33%)	1 / 15 (6.67%)
occurrences (all)	7	3	2
hyperuricaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 56 (5.36%)	2 / 60 (3.33%)	0 / 15 (0.00%)
occurrences (all)	4	3	0
hypokalaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 56 (7.14%)	3 / 60 (5.00%)	2 / 15 (13.33%)
occurrences (all)	4	7	2
hypomagnesaemia			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	3 / 56 (5.36%)	2 / 60 (3.33%)	0 / 15 (0.00%)
occurrences (all)	3	2	0
hyponatraemia alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 56 (7.14%)	2 / 60 (3.33%)	1 / 15 (6.67%)
occurrences (all)	5	2	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported