



Clinical trial results:

A Phase 2 Study of MLN8237, a Novel Aurora A Kinase Inhibitor, in the Treatment of Patients with Platinum-Refractory or Platinum-Resistant Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Carcinoma Summary

EudraCT number	2008-006979-72
Trial protocol	FR PL
Global end of trial date	27 January 2011

Results information

Result version number	v1 (current)
This version publication date	21 January 2018
First version publication date	30 December 2016
Summary attachment (see zip file)	Summary Results (C14006-RDS-2011-12-21.pdf)

Trial information

Trial identification

Sponsor protocol code	C14006
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00853307
WHO universal trial number (UTN)	U1111-1187-6616

Notes:

Sponsors

Sponsor organisation name	Takeda Oncology
Sponsor organisation address	40 Landsdowne Street, Cambridge, MA, United States, 02139
Public contact	Medical Director, Clinical Science, Takeda Oncology, +1 844-662-8532, GlobalOncologyMedinfo@takeda.com
Scientific contact	Medical Director, Clinical Science, Takeda Oncology, +1 844-662-8532, GlobalOncologyMedinfo@takeda.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 January 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 January 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to estimate the objective antitumor response rate of alisertib using the Response Evaluation Criteria in Solid Tumors (RECIST criteria) or CA 125 criteria(1) in participants with platinum-refractory or platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal carcinoma.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 March 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	United States: 23
Worldwide total number of subjects	31
EEA total number of subjects	8

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)	21

From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 17 investigative sites in France, Poland and the United States from 23 March 2009 to 27 January 2011.

Pre-assignment

Screening details:

Participants with a diagnosis of Platinum-refractory and Platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal carcinoma received 50 mg alisertib twice daily for 7 days in 21-day cycles.

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	Alisertib 50 mg (Platinum-Refractory)

Arm description:

Alisertib 50 mg, capsules, orally, twice daily for 7 days, followed by 14-day washout period in 21-day cycles until disease progression or unacceptable treatment-related toxicity (Up to 26 Cycles). Platinum-refractory disease is characterized by a lack of response, progression, or recurrence of disease during a course of platinum-based therapy.

Arm type	Experimental
Investigational medicinal product name	Alisertib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants with Platinum-Refractory received Alisertib 50 mg, capsules, orally, twice daily for 7 days, followed by 14-day washout period in 21-day cycles until disease progression or unacceptable treatment-related toxicity (Up to 26 Cycles).

Arm title	Alisertib 50 mg (Platinum-Resistant)
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Arm description:

Alisertib 50 mg, capsules, orally, twice daily for 7 days, followed by 14-day washout period in 21-day cycles until disease progression or unacceptable treatment-related toxicity (Up to 26 Cycles). Platinum-resistant disease is characterized by progression or recurrence of malignant disease within 6 months after completion of a platinum-based regimen.

Arm type	Experimental
Investigational medicinal product name	Alisertib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants with Platinum-Resistant received Alisertib 50 mg, capsules, orally, twice daily for 7 days, followed by 14-day washout period in 21-day cycles until disease progression or unacceptable treatment-related toxicity (Up to 26 Cycles).

Number of subjects in period 1	Alisertib 50 mg (Platinum- Refractory)	Alisertib 50 mg (Platinum-Resistant)
Started	6	25
Completed	4	20
Not completed	2	5
Consent withdrawn by subject	1	2
Adverse event, non-fatal	1	2
Reason Not Specified	-	1

Baseline characteristics

Reporting groups

Reporting group title	Alisertib 50 mg (Platinum-Refractory)
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Reporting group description:

Alisertib 50 mg, capsules, orally, twice daily for 7 days, followed by 14-day washout period in 21-day cycles until disease progression or unacceptable treatment-related toxicity (Up to 26 Cycles). Platinum-refractory disease is characterized by a lack of response, progression, or recurrence of disease during a course of platinum-based therapy.

Reporting group title	Alisertib 50 mg (Platinum-Resistant)
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Reporting group description:

Alisertib 50 mg, capsules, orally, twice daily for 7 days, followed by 14-day washout period in 21-day cycles until disease progression or unacceptable treatment-related toxicity (Up to 26 Cycles). Platinum-resistant disease is characterized by progression or recurrence of malignant disease within 6 months after completion of a platinum-based regimen.

Reporting group values	Alisertib 50 mg (Platinum-Refractory)	Alisertib 50 mg (Platinum-Resistant)	Total
Number of subjects	6	25	31
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	25	31
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	58.3	56.6	
standard deviation	± 15.38	± 14.19	-
Gender, Male/Female Units: Subjects			
Female	6	25	31
Male	0	0	0
Primary diagnosis Units: Subjects			
Epithelial Ovarian	5	20	25
Fallopian Tube	0	1	1
Primary Peritoneal Carcinoma	1	4	5
Eastern Cooperative Oncology Group (ECOG) Performance Status			
ECOG performance is defined as: 0=Normal activity (fully active, able to carry on all predisease performance without restriction); 1=Symptoms but ambulatory (restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature); 2=In bed <50% of the time (ambulatory and capable of all self-care, but unable to carry out any work activities); 3=In bed >50% of the time (capable of only limited self-care); 4=100% bedridden (completely disabled, cannot carry on any selfcare, totally confined to bed or chair).			

Units: Subjects			
ECOG Performance Status = 0	2	18	20
ECOG Performance Status = 1	4	7	11
Race/Ethnicity, Customized			
Units: Subjects			
White	6	24	30
Asian	0	1	1
Race/Ethnicity, Customized			
Units: Subjects			
Hispanic or Latino	1	1	2
Not Hispanic or Latino	3	22	25
Not Reported	2	2	4
Study Specific Characteristic Years Since Initial Diagnosis			
Units: years			
arithmetic mean	1.59	2.26	
standard deviation	± 0.736	± 1.448	-
Study Specific Characteristic Height			
Units: centimeter (cm)			
arithmetic mean	162.0	160.9	
standard deviation	± 4.83	± 7.76	-
Study Specific Characteristic Weight			
Units: kilogram (kg)			
arithmetic mean	65.16	68.22	
standard deviation	± 9.638	± 17.227	-
Study Specific Characteristic Body Surface Area (BSA)			
Body Surface Area = square root [height (cm)*weight (kg) / 3600].			
Units: meter (m)^2			
arithmetic mean	1.72	1.72	
standard deviation	± 0.167	± 0.223	-

End points

End points reporting groups

Reporting group title	Alisertib 50 mg (Platinum-Refractory)
Reporting group description: Alisertib 50 mg, capsules, orally, twice daily for 7 days, followed by 14-day washout period in 21-day cycles until disease progression or unacceptable treatment-related toxicity (Up to 26 Cycles). Platinum-refractory disease is characterized by a lack of response, progression, or recurrence of disease during a course of platinum-based therapy.	
Reporting group title	Alisertib 50 mg (Platinum-Resistant)
Reporting group description: Alisertib 50 mg, capsules, orally, twice daily for 7 days, followed by 14-day washout period in 21-day cycles until disease progression or unacceptable treatment-related toxicity (Up to 26 Cycles). Platinum-resistant disease is characterized by progression or recurrence of malignant disease within 6 months after completion of a platinum-based regimen.	

Primary: Combined Best Overall Response Rate (ORR) Based on Investigator Assessment

End point title	Combined Best Overall Response Rate (ORR) Based on Investigator Assessment ^[1]
End point description: Combined ORR:percentage of participants with Complete Response(CR)+Partial Response(PR) as assessed by the investigator according to RECIST criteria 1.1 or response by Cancer antigen(CA) 125 criteria.According to RECIST,CR:disappearance of all target lesions;PR:30% decrease in the sum of the longest diameter of target lesions.CA 125 response criteria is defined as either:50% decrease from 2 initially elevated samples;sample demonstrating the 50% decrease must have been confirmed by a fourth sample 28 days later(a total of 4 samples required)or serial decrease of >75% over 3 samples;the third sample was to be obtained 28 days after the second (a total of 3 samples required).Response-evaluable population:all participants who have measurable neoplastic disease according to RECIST criteria OR participants with CA 125 level >40 units/milliliter(mL) and clinical evidence of neoplastic disease and received at least 1 dose of alisertib and have at least 1 post-baseline	
End point type	Primary
End point timeframe: Every 2 cycles up to 12 months until progressive disease (PD); Participants who discontinue study drug before PD: Follow-Up (FU)-every 12 weeks up to 12 months until PD/other cancer therapy; CA 125 Day 1 of cycle, End of Treatment and FU (Up to 22 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 analyses are reported for this endpoint.	

End point values	Alisertib 50 mg (Platinum-Refractory)	Alisertib 50 mg (Platinum-Resistant)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	25		
Units: percentage of participants	0	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)
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End point description:

PFS is defined as the time in days from the date of first study drug administration to the date of first documented Progressive Disease (PD) or death. PD is defined as 20% increase in the sum of the longest diameter of target lesions. CA 125 progression for participants with normal CA 125 levels is defined as a CA 125 level > 2 times the upper limit of normal and for participants with elevated values during the trial, is defined as a CA 125 level greater than 2 times the nadir value of CA 125. For a participant who has not progressed and has not died, PFS is censored at the last response assessment that is stable disease (SD) or better. Response-evaluable population is defined as all participants who have measurable neoplastic disease according to RECIST criteria OR participants with CA 125 level > 40 units/mL and clinical evidence of neoplastic disease and received at least 1 dose of alisertib and have at least 1 post-baseline response assessment.

End point type	Secondary
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End point timeframe:

Every 2 cycles up to 12 months until PD; Participants who discontinue study drug before PD: FU - every 12 weeks up to 12 months until PD/other cancer therapy; CA 125 Day 1 of cycle, End of Treatment and FU (Up to 22 Months)

End point values	Alisertib 50 mg (Platinum- Refractory)	Alisertib 50 mg (Platinum- Resistant)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	25		
Units: days				
median (confidence interval 95%)	36.5 (23.0 to 120.0)	77.0 (43.0 to 122.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration Of Response (DOR)

End point title	Duration Of Response (DOR)
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End point description:

DOR is defined as the time from the date of first documentation of a confirmed response to the date of first documented PD. PD is defined as 20% increase in the sum of the longest diameter of target lesions. Enrollment was closed after 31 participants were enrolled based on interim analysis results, which did not show the level of response needed to justify further investigation.

End point type	Secondary
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End point timeframe:

Every 2 cycles up to 12 months until PD; Participants who discontinue study drug before PD: FU - every 12 weeks up to 12 months until PD/other cancer therapy; CA 125 Day 1 of cycle, End of Treatment and FU (Up to 22 Months)

End point values	Alisertib 50 mg (Platinum- Refractory)	Alisertib 50 mg (Platinum- Resistant)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[2]	0 ^[3]		
Units: days				
median (full range (min-max))	(to)	(to)		

Notes:

[2] - As there were only 3 responders, DOR was not analyzed.

[3] - As there were only 3 responders, DOR was not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Time To Progression (TTP)

End point title	Time To Progression (TTP)
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End point description:

TTP is defined as the time in days from the date of first study drug administration to the date of first documentation of PD. PD is defined as 20% increase in the sum of the longest diameter of target lesions. Enrollment was closed after 31 participants were enrolled based on interim analysis results, which did not show the level of response needed to justify further investigation.

End point type	Secondary
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End point timeframe:

Every 2 cycles up to 12 months until PD; Participants who discontinue study drug before PD: FU - every 12 weeks up to 12 months until PD/other cancer therapy; CA 125 Day 1 of cycle, End of Treatment and FU (Up to 22 Months)

End point values	Alisertib 50 mg (Platinum- Refractory)	Alisertib 50 mg (Platinum- Resistant)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[4]	0 ^[5]		
Units: days				
median (full range (min-max))	(to)	(to)		

Notes:

[4] - Enrollment was closed after 31 participants. TTP was not analyzed.

[5] - Enrollment was closed after 31 participants. TTP was not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate

End point title	Clinical Benefit Rate
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End point description:

Clinical benefit rate is defined as the percentage of participants with response and stable disease (SD), where in order for SD to qualify as having clinical benefit, there must be no progression of neoplastic disease for at least 4 treatment cycles. Response-evaluable population is defined as all participants who have measurable neoplastic disease according to the RECIST criteria OR participants with a CA 125 level > 40 units/mL and clinical evidence of neoplastic disease and receive at least 1 dose of alisertib and have at least 1 post-baseline response assessment.

End point type	Secondary
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End point timeframe:

Every 2 cycles up to 12 months until PD; Participants who discontinue study drug before PD: FU - every 12 weeks up to 12 months until PD/other cancer therapy; CA 125 Day 1 of cycle, End of Treatment and FU (Up to 22 Months)

End point values	Alisertib 50 mg (Platinum- Refractory)	Alisertib 50 mg (Platinum- Resistant)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	25		
Units: percentage of participants	0	32		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment-Emergent Adverse Events and Serious Adverse Events

End point title	Number of Participants with Treatment-Emergent Adverse Events and Serious Adverse Events
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End point description:

An Adverse Event (AE) is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. A Serious Adverse Event (SAE) A serious is any experience that suggests a significant hazard, contraindication, side effect or precaution that: results in death, is life-threatening, required in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect or is medically significant. A treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset that occurs after receiving study drug. Safety Population is defined as all participants who received any amount of alisertib.

End point type	Secondary
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End point timeframe:

First dose to 30 days past last dose (Up to 18.9 Months)

End point values	Alisertib 50 mg (Platinum- Refractory)	Alisertib 50 mg (Platinum- Resistant)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	25		
Units: participants				
AE	6	24		
SAE	4	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Abnormal Vital Signs reported as Treatment-Emergent Adverse Events

End point title	Number of Participants with Abnormal Vital Signs reported as Treatment-Emergent Adverse Events
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End point description:

Vital signs included blood pressure, pulse rate, and oral temperature collected throughout the study. A treatment-emergent adverse event is defined as an adverse event with an onset that occurs after receiving study drug. Safety Population is defined as all participants who received any amount of alisertib.

End point type	Secondary
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End point timeframe:

Baseline, Cycle 1 Days 8 and 15, then Day 1 of every cycle (21 days), End of Treatment, End of Study/FU every 12 weeks for up to 12 months (Up to 22 Months)

End point values	Alisertib 50 mg (Platinum- Refractory)	Alisertib 50 mg (Platinum- Resistant)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	25		
Units: participants				
Pyrexia	2	6		
Dyspnoea	0	4		
Weight decreased	0	3		
Tachycardia	0	2		
Hypertension	0	2		
Dyspnoea exertional	0	1		
Bradycardia	0	1		
Shock	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Abnormal Laboratory Values reported as Treatment-Emergent Adverse Events

End point title	Number of Participants with Abnormal Laboratory Values reported as Treatment-Emergent Adverse Events
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End point description:

Laboratory tests included Hematology and Chemistry. Abnormal laboratory value were assessed as an AE if the value leads to discontinuation or delay in treatment, dose modification, therapeutic intervention, or is considered by the investigator to be a clinically significant change from baseline. A treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset that occurs after receiving study drug. Safety Population is defined as all participants who received any amount of alisertib.

End point type	Secondary
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End point timeframe:

Baseline, Cycle 1 Days 8 and 15, then Every cycle Days 1, 8 and 15 to End of Treatment Up to 18.0 Months

End point values	Alisertib 50 mg (Platinum- Refractory)	Alisertib 50 mg (Platinum- Resistant)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	25		
Units: participants				
Neutropenia	3	17		
Anaemia	2	14		
Leukopenia	1	11		
Thrombocytopenia	1	8		
Dehydration	1	7		
Hypokalaemia	2	4		
Alanine aminotransferase increased	0	6		
Aspartate aminotransferase increased	0	6		
Hyperglycaemia	1	4		
Hypomagnesaemia	1	4		
Blood alkaline phosphatase increased	1	4		
Febrile neutropenia	0	3		
Hyponatraemia	1	2		
Haemoglobin decreased	1	2		
Granulocytopenia	0	2		
Neutrophil count increased	0	2		
White blood cell count increased	0	2		
Hyperbilirubinaemia	1	1		
Lymphopenia	1	0		
Hyperkalaemia	0	1		
Hypernatraemia	0	1		
Hypercholesterolaemia	0	1		
Transaminases increased	1	0		
Granulocyte count decreased	0	1		
Blood calcium increased	0	1		
Blood magnesium decreased	0	1		
Platelet count decreased	1	0		
Blood albumin decreased	0	1		
Creatinine renal clearance decreased	0	1		
Hypoxia	0	1		
Bacteraemia	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First dose of study drug to 30 past last dose of study drug (Up to 18.9 Months)

Adverse event reporting additional description:

At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	8.1
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Reporting groups

Reporting group title	Alisertib 50 mg (Platinum-Refractory)
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Reporting group description:

Alisertib 50 mg, capsules, orally, twice daily for 7 days, followed by 14-day washout period in 21-day cycles until disease progression or unacceptable treatment-related toxicity (Up to 26 Cycles). Platinum-refractory disease is characterized by a lack of response, progression, or recurrence of disease during a course of platinum-based therapy.

Reporting group title	Alisertib 50 mg (Platinum-Resistant)
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Reporting group description:

Alisertib 50 mg, capsules, orally, twice daily for 7 days, followed by 14-day washout period in 21-day cycles until disease progression or unacceptable treatment-related toxicity (Up to 26 Cycles). Platinum-resistant disease is characterized by progression or recurrence of malignant disease within 6 months after completion of a platinum-based regimen.

Serious adverse events	Alisertib 50 mg (Platinum-Refractory)	Alisertib 50 mg (Platinum-Resistant)	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	7 / 25 (28.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Vascular disorders			
Shock			
subjects affected / exposed	1 / 6 (16.67%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Hypoaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Febrile neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 25 (12.00%)	
occurrences causally related to treatment / all	0 / 0	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 25 (8.00%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Stomatitis			
subjects affected / exposed	1 / 6 (16.67%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abdominal mass			
subjects affected / exposed	0 / 6 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 6 (16.67%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 6 (16.67%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 6 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Clostridium colitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalaemia			

subjects affected / exposed	1 / 6 (16.67%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Alisertib 50 mg (Platinum-Refractory)	Alisertib 50 mg (Platinum-Resistant)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	24 / 25 (96.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 6 (50.00%)	15 / 25 (60.00%)	
occurrences (all)	5	25	
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	5 / 25 (20.00%)	
occurrences (all)	1	5	
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 25 (12.00%)	
occurrences (all)	0	4	
Chills			
subjects affected / exposed	1 / 6 (16.67%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	3 / 25 (12.00%)	
occurrences (all)	0	4	
Early satiety			

subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 25 (4.00%) 1	
Reproductive system and breast disorders Vaginal haemorrhage subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 25 (8.00%) 2	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Pharyngolaryngeal pain subjects affected / exposed occurrences (all) Rhinitis allergic subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0	4 / 25 (16.00%) 4 4 / 25 (16.00%) 10 4 / 25 (16.00%) 4 2 / 25 (8.00%) 4	
Psychiatric disorders Depression subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0 1 / 6 (16.67%) 1	2 / 25 (8.00%) 2 1 / 25 (4.00%) 1	
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Aspartate aminotransferase increased subjects affected / exposed occurrences (all) Blood alkaline phosphatase increased	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0	6 / 25 (24.00%) 9 6 / 25 (24.00%) 9	

subjects affected / exposed	1 / 6 (16.67%)	4 / 25 (16.00%)	
occurrences (all)	2	24	
Haemoglobin decreased			
subjects affected / exposed	1 / 6 (16.67%)	2 / 25 (8.00%)	
occurrences (all)	1	13	
Weight decreased			
subjects affected / exposed	0 / 6 (0.00%)	3 / 25 (12.00%)	
occurrences (all)	0	4	
Neutrophil count increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	5	
White blood cell count increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	5	
Platelet count decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Transaminases increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 6 (16.67%)	5 / 25 (20.00%)	
occurrences (all)	1	12	
Somnolence			
subjects affected / exposed	0 / 6 (0.00%)	4 / 25 (16.00%)	
occurrences (all)	0	6	
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Dysgeusia			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 25 (8.00%) 2	
Depressed level of consciousness subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 25 (0.00%) 0	
Blood and lymphatic system disorders			
Neutropenia subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 5	16 / 25 (64.00%) 58	
Anaemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	13 / 25 (52.00%) 24	
Leukopenia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	11 / 25 (44.00%) 51	
Thrombocytopenia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 2	7 / 25 (28.00%) 17	
Granulocytopenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 25 (8.00%) 9	
Lymphopenia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 25 (0.00%) 0	
Eye disorders			
Vision blurred subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 25 (4.00%) 1	
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 3	14 / 25 (56.00%) 37	
Stomatitis subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2	13 / 25 (52.00%) 19	
Nausea			

subjects affected / exposed	3 / 6 (50.00%)	11 / 25 (44.00%)	
occurrences (all)	5	15	
Vomiting			
subjects affected / exposed	4 / 6 (66.67%)	8 / 25 (32.00%)	
occurrences (all)	5	11	
Abdominal pain			
subjects affected / exposed	2 / 6 (33.33%)	8 / 25 (32.00%)	
occurrences (all)	2	9	
Constipation			
subjects affected / exposed	1 / 6 (16.67%)	4 / 25 (16.00%)	
occurrences (all)	1	7	
Ascites			
subjects affected / exposed	1 / 6 (16.67%)	2 / 25 (8.00%)	
occurrences (all)	1	3	
Flatulence			
subjects affected / exposed	1 / 6 (16.67%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	4	
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	3	
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Gingival bleeding			
subjects affected / exposed	0 / 6 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Abdominal rigidity			
subjects affected / exposed	1 / 6 (16.67%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Gastritis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			

Hyperbilirubinaemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 25 (4.00%) 1	
Skin and subcutaneous tissue disorders			
Alopecia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	14 / 25 (56.00%) 18	
Dry skin subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	5 / 25 (20.00%) 5	
Pruritus subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	4 / 25 (16.00%) 4	
Rash pruritic subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	4 / 25 (16.00%) 5	
Erythema subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	2 / 25 (8.00%) 3	
Hyperhidrosis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 25 (8.00%) 4	
Palmar-plantar erythrodysaesthesia syndrome subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 25 (8.00%) 3	
Renal and urinary disorders			
Bladder spasm subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 25 (0.00%) 0	
Renal failure acute subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 25 (0.00%) 0	
Ureteric obstruction subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 25 (0.00%) 0	
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	1 / 6 (16.67%)	3 / 25 (12.00%)	
occurrences (all)	1	4	
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	6	
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Shoulder pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Musculoskeletal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal stiffness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 6 (16.67%)	3 / 25 (12.00%)	
occurrences (all)	1	4	
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	3	
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	3	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	0 / 6 (0.00%)	7 / 25 (28.00%)	
occurrences (all)	0	7	
Dehydration			

subjects affected / exposed	1 / 6 (16.67%)	6 / 25 (24.00%)	
occurrences (all)	2	15	
Hyperglycaemia			
subjects affected / exposed	1 / 6 (16.67%)	4 / 25 (16.00%)	
occurrences (all)	1	11	
Hypokalaemia			
subjects affected / exposed	1 / 6 (16.67%)	4 / 25 (16.00%)	
occurrences (all)	1	5	
Hypomagnesaemia			
subjects affected / exposed	1 / 6 (16.67%)	4 / 25 (16.00%)	
occurrences (all)	1	8	
Hyponatraemia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 25 (8.00%)	
occurrences (all)	1	2	

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