Clinical trial results:
A Phase 2 Study of the Safety and Anti-tumor Activity of the Oral Selective Inhibitor of Nuclear Export Selinexor (KPT-330) in Patients with Initial or Refractory/Relapsed Richter's Transformation

Summary

EudraCT number	2014-001240-38
Trial protocol	ES DE GB
Global end of trial date	31 August 2016

Results information

Result version number	v1 (current)
This version publication date	20 June 2021
First version publication date	20 June 2021

Trial information

Trial identification

Sponsor protocol code	KCP-330-010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02138786
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Karyopharm Therapeutics, Inc.
Sponsor organisation address	85 Wells Avenue, Newton, MA, United States, 02459
Public contact	Clinical Trial Information Desk, Karyopharm Therapeutics, Inc., clinicaltrials@karyopharm.com
Scientific contact	Clinical Trial Information Desk, Karyopharm Therapeutics, Inc., clinicaltrials@karyopharm.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 August 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 August 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine the overall response rate (ORR), including partial response (PR) and complete response (CR), as well as the duration of response (DOR).

Protection of trial subjects:

This study was monitored in accordance with the Sponsor’s procedures, which meet the ICH Harmonised Tripartite Guidelines for GCP, with applicable local regulations, and with the ethical principles outlined in the Declaration of Helsinki.

Background therapy:

Palliative radiation therapy to non-target lesions was permitted.

Evidence for comparator:

No comparator used

Actual start date of recruitment	14 November 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	United States: 10
Worldwide total number of subjects	26
EEA total number of subjects	16

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)	6
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 15 sites in the United States and Europe between November 2014 and July 2016.

Pre-assignment

Screening details:

A total of 27 subjects were enrolled out of which 1 subjects discontinued the study before the start of the treatment. Out of which 26 subjects started the study treatment.

Period 1

Period 1 title	Baseline (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	Selinexor 60 mg/m^2 (8 Doses/Cycle)

Arm description:

Subjects received a dose of 60 milligrams/square meter (mg/m^2) of selinexor oral tablets twice weekly (Days 1 and 3) for weeks 1-4 (8 doses/cycle).

Arm type	Experimental
Investigational medicinal product name	Selinexor
Investigational medicinal product code	KPT-330
Other name	XPOVIO, NEXPOVIO
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 mg and 50 mg coated, immediate-release tablets taken orally.

Arm title	Selinexor 60 mg (6 doses/cycle)

Arm description:

Subjects received a dose of 60 milligrams (mg) of selinexor oral tablets twice weekly (Days 1 and 3) for weeks 1-3 (6 doses/cycle).

Arm type	Experimental
Investigational medicinal product name	Selinexor
Investigational medicinal product code	KPT-330
Other name	XPOVIO, NEXPOVIO
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 mg and 50 mg coated, immediate-release tablets taken orally.

Arm title	Selinexor 60 mg (8 doses/cycle)

Arm description:

Subjects received a fixed dose of 60 mg of selinexor oral tablets twice weekly (Days 1 and 3) for weeks 1-4 (8 doses/cycle).

Arm type	Experimental

Investigational medicinal product name	Selinexor
Investigational medicinal product code	KPT-330
Other name	XPOVIO, NEXPOVIO
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 mg and 50 mg coated, immediate-release tablets taken orally.

Number of subjects in period 1	Selinexor 60 mg/m^2 (8 Doses/Cycle)	Selinexor 60 mg (6 doses/cycle)	Selinexor 60 mg (8 doses/cycle)
Started	3	15	8
Completed	0	0	0
Not completed	3	15	8
Consent withdrawn by subject	1	2	-
Disease progression	1	1	3
Adverse event, non-fatal	-	2	1
Patient's wish	-	2	-
Death	1	7	2
Sponsor termination of study	-	1	1
Noncompliance	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Selinexor 60 mg/m^2 (8 Doses/Cycle)
Reporting group description:	
Subjects received a dose of 60 milligrams/square meter (mg/m^2) of selinexor oral tablets twice weekly (Days 1 and 3) for weeks 1-4 (8 doses/cycle).	
Reporting group title	Selinexor 60 mg (6 doses/cycle)
Reporting group description:	
Subjects received a dose of 60 milligrams (mg) of selinexor oral tablets twice weekly (Days 1 and 3) for weeks 1-3 (6 doses/cycle).	
Reporting group title	Selinexor 60 mg (8 doses/cycle)
Reporting group description:	
Subjects received a fixed dose of 60 mg of selinexor oral tablets twice weekly (Days 1 and 3) for weeks 1-4 (8 doses/cycle).	

Reporting group values	Selinexor 60 mg/m^2 (8 Doses/Cycle)	Selinexor 60 mg (6 doses/cycle)	Selinexor 60 mg (8 doses/cycle)
Number of subjects	3	15	8
Age categorical Units: Subjects			
Age continuous Units: years			
median	68	68	69
full range (min-max)	66 to 74	41 to 77	65 to 79
Gender categorical Units: Subjects			
Female	2	3	4
Male	1	12	4
Ethnicity Units: Subjects			
Hispanic or Latino	1	1	0
Not Hispanic or Latino	1	14	8
Unknown or Not Reported	1	0	0
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	3	15	8
More than one race	0	0	0
Unknown or Not Reported	0	0	0
ECOG score			
Performance Status as measured by Eastern Cooperative Oncology Group (ECOG) Status Scale: Score=0: Normal activity. Fully active, able to carry on all pre-disease performance without restriction; Score=1: Symptoms, but ambulatory. Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature (e.g., light housework, office work); Score=2: In bed < 50% of the time. Ambulatory and capable of all self-care, but unable to carry out any work			

activities. Up and about more than 50% of waking hours.			
Units: Subjects			
Score=0	0	5	2
Score=1	3	6	4
Score=2	0	4	1
Missing	0	0	1
Weight			
Units: Kilograms			
median	56.5	76.5	73.05
full range (min-max)	52.3 to 96.0	51.9 to 115.5	46.4 to 88.1

Reporting group values	Total		
Number of subjects	26		
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
median			
full range (min-max)	-		
Gender categorical			
Units: Subjects			
Female	9		
Male	17		
Ethnicity			
Units: Subjects			
Hispanic or Latino	2		
Not Hispanic or Latino	23		
Unknown or Not Reported	1		
Race			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	26		
More than one race	0		
Unknown or Not Reported	0		
ECOG score			
Performance Status as measured by Eastern Cooperative Oncology Group (ECOG) Status Scale: Score=0: Normal activity. Fully active, able to carry on all pre-disease performance without restriction; Score=1: Symptoms, but ambulatory. Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature (e.g., light housework, office work); Score=2: In bed < 50% of the time. Ambulatory and capable of all self-care, but unable to carry out any work activities. Up and about more than 50% of waking hours.			
Units: Subjects			
Score=0	7		
Score=1	13		
Score=2	5		
Missing	1		

Weight Units: Kilograms median full range (min-max)	- 		

End points

End points reporting groups

Reporting group title	Selinexor 60 mg/m^2 (8 Doses/Cycle)
Reporting group description:	
Subjects received a dose of 60 milligrams/square meter (mg/m^2) of selinexor oral tablets twice weekly (Days 1 and 3) for weeks 1-4 (8 doses/cycle).	
Reporting group title	Selinexor 60 mg (6 doses/cycle)
Reporting group description:	
Subjects received a dose of 60 milligrams (mg) of selinexor oral tablets twice weekly (Days 1 and 3) for weeks 1-3 (6 doses/cycle).	
Reporting group title	Selinexor 60 mg (8 doses/cycle)
Reporting group description:	
Subjects received a fixed dose of 60 mg of selinexor oral tablets twice weekly (Days 1 and 3) for weeks 1-4 (8 doses/cycle).	
Subject analysis set title	Selinexor
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All subjects who received at least 1 dose of study medication and had post-baseline efficacy follow-up information.	

Primary: Percentage of Subjects With Overall Response Rate (ORR)

End point title	Percentage of Subjects With Overall Response Rate (ORR)[1]
End point description:	
ORR was defined as the point estimate of the percentage of subjects who have complete response (CR) or partial response (PR). Disease response was assessed using the International Working Group (IWG) Response Criteria for non-Hodgkin's lymphoma (Cheson 2007), including assessment of lymph node, spleen and liver lesions by PET (positron emission tomography) scan and assessment of bone marrow biopsies by morphologic, immunohistochemistry, and flow cytometry tests. CR was defined as disappearance of all evidence of disease, and PR was defined as ≥ 50% regression of measurable disease and no new sites. Modified Intent to Treat (mITT) population, consisting of all subjects who received at least one dose of selinexor and had at least one post-baseline efficacy evaluation. Subjects without post-baseline efficacy follow-up information who discontinued the study due to toxicity, disease progression, or death were included in this population.	
End point type	Primary
End point timeframe:	
Assessments were performed at Screening or Cycle 1/Day 1 prior to dosing and on Cycle 3/Day 1 and alternate cycles thereafter until disease progression, study drug intolerability had been reached, study withdrawal, or death.	
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 testing was performed for the primary end point.	

End point values	Selinexor			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: Percentage of subjects				
number (confidence interval 95%)	4 (0.1 to 20.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Complete Response (CR)

End point title	Number of Subjects With Complete Response (CR)[2]

End point description:

Number of Subjects who achieved CR (complete disappearance of all detectable evidence of disease). Disease response was assessed using the IWG Response Criteria for non-Hodgkin's lymphoma (Cheson 2007), including assessment of lymph node, spleen and liver lesions by PET (positron emission tomography) scan and assessment of bone marrow biopsies by morphologic, immunohistochemistry, and flow cytometry tests. mITT population, consisting of all subjects who received at least one dose of selinexor and had at least one post-baseline efficacy evaluation. Subjects without post-baseline efficacy follow-up information who discontinued the study due to toxicity, disease progression, or death were included in this population.

End point type	Primary

End point timeframe:

Assessments were performed at Screening or Cycle 1/Day 1 prior to dosing and on Cycle 3/Day 1 and alternate cycles thereafter until disease progression, study drug intolerability had been reached, study withdrawal, or death.

Notes:

[2] - 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 testing was performed for the primary end point.

End point values	Selinexor			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Partial Response (PR)

End point title	Number of Subjects With Partial Response (PR)[3]

End point description:

Number of subjects whose best overall response to study treatment was PR (≥ 50% regression of measurable disease and no new sites). Disease response was assessed using the IWG Response Criteria for non-Hodgkin's lymphoma (Cheson 2007), including assessment of lymph node, spleen and liver lesions by PET (positron emission tomography) scan and assessment of bone marrow biopsies by morphologic, immunohistochemistry, and flow cytometry tests. mITT population, consisting of all subjects who received at least one dose of selinexor and had at least one post-baseline efficacy evaluation. Subjects without post-baseline efficacy follow-up information who discontinued the study due to toxicity, disease progression, or death were included in this population.

End point type	Primary

End point timeframe:

Assessments were performed at Screening or Cycle 1/Day 1 prior to dosing and on Cycle 3/Day 1 and alternate cycles thereafter until disease progression, study drug intolerability had been reached, study withdrawal, or death.

Notes:

[3] - 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 testing was performed for the primary end point.

End point values	Selinexor			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: Subjects	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Stable Disease (SD)

End point title	Number of Subjects With Stable Disease (SD)[4]

End point description:

Number of subjects whose best overall response to study treatment was SD (failure to attain criteria for CR or PR, or to meet criteria for PD). Disease response was assessed using the IWG Response Criteria for non-Hodgkin's lymphoma (Cheson 2007), including assessment of lymph node, spleen and liver lesions by PET (positron emission tomography) scan and assessment of bone marrow biopsies by morphologic, immunohistochemistry, and flow cytometry tests. mITT population, consisting of all subjects who received at least one dose of selinexor and had at least one post-baseline efficacy evaluation. Subjects without post-baseline efficacy follow-up information who discontinued the study due to toxicity, disease progression, or death were included in this population.

End point type	Primary

End point timeframe:

Assessments were performed at Screening or Cycle 1/Day 1 prior to dosing and on Cycle 3/Day 1 and alternate cycles thereafter until disease progression, study drug intolerability had been reached, study withdrawal, or death.

Notes:

[4] - 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 testing was performed for the primary end point.

End point values	Selinexor			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: Subjects	6			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Progressive Disease (PD)

End point title	Number of Subjects With Progressive Disease (PD)[5]

End point description:

Number of subjects whose best overall response to study treatment was PD (any new lesion or increase by ≥ 50% of previously involved sites from nadir). Disease response was assessed using the IWG Response Criteria for non-Hodgkin's lymphoma (Cheson 2007), including assessment of lymph node, spleen and liver lesions by PET (positron emission tomography) scan and assessment of bone marrow biopsies by morphologic, immunohistochemistry, and flow cytometry tests. mITT population, consisting of all subjects who received at least one dose of selinexor and had at least one post-baseline efficacy evaluation. Subjects without post-baseline efficacy follow-up information who discontinued the study due to toxicity, disease progression, or death were included in this population.

End point type	Primary

End point timeframe:

Assessments were performed at Screening or Cycle 1/Day 1 prior to dosing and on Cycle 3/Day 1 and alternate cycles thereafter until disease progression, study drug intolerability had been reached, study withdrawal, or death.

Notes:

[5] - 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 testing was performed for the primary end point.

End point values	Selinexor			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: Subjects	7			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Not Evaluable (NE) Response

End point title	Number of Subjects With Not Evaluable (NE) Response[6]

End point description:

Number of subjects who could not be assessed quantitatively for disease response for any reason. mITT population, consisting of all subjects who received at least one dose of selinexor and had at least one post-baseline efficacy evaluation. Subjects without post-baseline efficacy follow-up information who discontinued the study due to toxicity, disease progression, or death were included in this population.

End point type	Primary

End point timeframe:

Assessments were performed at Screening or Cycle 1/Day 1 prior to dosing and on Cycle 3/Day 1 and alternate cycles thereafter until disease progression, study drug intolerability had been reached, study withdrawal, or death.

Notes:

[6] - 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 testing was performed for the primary end point.

End point values	Selinexor			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: Subjects	11			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Disease Control Rate (DCR)

End point title	Percentage of Subjects With Disease Control Rate (DCR)

End point description:

DCR was defined as the percentage of subjects who achieved CR, PR, or SD lasting for at least 8 weeks. CR was defined as disappearance of all evidence of disease. PR was defined as ≥ 50% regression of

measurable disease and no new sites. SD was defined as failure to attain criteria for CR or PR, or to meet criteria for PD. Disease response was assessed using the IWG Response Criteria for non-Hodgkin's lymphoma (Cheson 2007), including assessment of lymph node, spleen and liver lesions by PET (positron emission tomography) scan and assessment of bone marrow biopsies by morphologic, immunohistochemistry, and flow cytometry tests. mITT population, consisting of all subjects who received at least one dose of selinexor and had at least one post-baseline efficacy evaluation. Subjects without post-baseline efficacy follow-up information who discontinued the study due to toxicity, disease progression, or death were included in this population.

End point type	Secondary

End point timeframe:

Assessments were performed at Screening or Cycle 1/Day 1 prior to dosing and on Cycle 3/Day 1 and alternate cycles thereafter until disease progression, study drug intolerability had been reached, study withdrawal, or death.

End point values	Selinexor			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: Percentage of subjects				
number (confidence interval 95%)	28.0 (12.1 to 49.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Progression Free Survival (PFS)

End point title	Duration of Progression Free Survival (PFS)

End point description:

Number of days calculated from date of start of study therapy to date of progression based on IWG criteria, or date of death if progression did not occur. Subjects who dropped out prior to study end without evidence of disease progression were censored at the day they were last known to be alive. Subjects without documented disease progression or recurrence were censored at the date of last disease assessment. Disease response was assessed using the IWG Response Criteria for non-Hodgkin's lymphoma (Cheson 2007), including assessment of lymph node, spleen and liver lesions by PET (positron emission tomography) scan and assessment of bone marrow biopsies by morphologic, immunohistochemistry, and flow cytometry tests. Analysis was performed by mITT population.

End point type	Secondary

End point timeframe:

Assessments were performed at Screening or Cycle 1/Day 1 prior to dosing and on Cycle 3/Day 1 and alternate cycles thereafter until disease progression, study drug intolerability had been reached, study withdrawal, or death.

End point values	Selinexor			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: Days				
median (confidence interval 95%)	38.0 (22.0 to 86.0)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Treatment-emergent AEs were collected from the first day of dosing (Cycle 1 Day 1) through the 30-day follow-up.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	Selinexor 60 mg/m^2 (8 Doses/Cycle)
Reporting group description:	
Subjects received a dose of 60 mg/m^2 of selinexor oral tablets twice weekly (Days 1 and 3) for weeks 1-4 (8 doses/cycle).	
Reporting group title	Selinexor 60 mg (6 doses/cycle)
Reporting group description:	
Subjects received a dose of 60 mg of selinexor oral tablets twice weekly (Days 1 and 3) for weeks 1-3 (6 doses/cycle).	
Reporting group title	Selinexor 60 mg (8 doses/cycle)
Reporting group description:	
Subjects received a fixed dose of 60 mg of selinexor oral tablets twice weekly (Days 1 and 3) for weeks 1-4 (8 doses/cycle).	

Serious adverse events	Selinexor 60 mg/m^2 (8 Doses/Cycle)	Selinexor 60 mg (6 doses/cycle)	Selinexor 60 mg (8 doses/cycle)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	9 / 15 (60.00%)	5 / 8 (62.50%)
number of deaths (all causes)	1	8	2
number of deaths resulting from adverse events	0	4	0
Investigations			
Clostridium test			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			

Deep vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Embolism arterial			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (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
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (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
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (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
Haemorrhage intracranial			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (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
Neuropathy peripheral			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 15 (0.00%)	0 / 8 (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
Fatigue			

subjects affected / exposed	1 / 3 (33.33%)	0 / 15 (0.00%)	0 / 8 (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
General physical health deterioration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Mucosal inflammation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 15 (0.00%)	0 / 8 (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
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (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 and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (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
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (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			
Dyspnoea			
subjects affected / exposed	1 / 3 (33.33%)	1 / 15 (6.67%)	0 / 8 (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
Respiratory failure			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (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

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 3 (33.33%)	0 / 15 (0.00%)	0 / 8 (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			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (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
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	2 / 8 (25.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Staphylococcal infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (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
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (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
Dehydration			
subjects affected / exposed	1 / 3 (33.33%)	0 / 15 (0.00%)	0 / 8 (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
Food intolerance			

subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (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
Hypercalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (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

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Selinexor 60 mg/m^2 (8 Doses/Cycle)	Selinexor 60 mg (6 doses/cycle)	Selinexor 60 mg (8 doses/cycle)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	15 / 15 (100.00%)	7 / 8 (87.50%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Tumour Associated Fever			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypotension			
subjects affected / exposed	2 / 3 (66.67%)	0 / 15 (0.00%)	2 / 8 (25.00%)
occurrences (all)	3	0	2
Haematoma			
subjects affected / exposed	1 / 3 (33.33%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Deep Vein Thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Embolism			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Haemorrhage			

subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hot Flush			
subjects affected / exposed	1 / 3 (33.33%)	0 / 15 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Pallor			
subjects affected / exposed	1 / 3 (33.33%)	0 / 15 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Phlebitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Post Procedural Contusion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	6 / 15 (40.00%)	2 / 8 (25.00%)
occurrences (all)	1	7	2
Fatigue			
subjects affected / exposed	2 / 3 (66.67%)	4 / 15 (26.67%)	2 / 8 (25.00%)
occurrences (all)	2	5	7
Asthenia			
subjects affected / exposed	1 / 3 (33.33%)	4 / 15 (26.67%)	2 / 8 (25.00%)
occurrences (all)	1	5	2
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	5 / 15 (33.33%)	1 / 8 (12.50%)
occurrences (all)	0	7	1
General physical health deterioration			
subjects affected / exposed	1 / 3 (33.33%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Mucosal inflammation			

subjects affected / exposed	1 / 3 (33.33%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Early Satiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Facial Pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Oedema Genital			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Pelvic Pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 3 (33.33%)	1 / 15 (6.67%)	3 / 8 (37.50%)
occurrences (all)	1	1	3
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	2 / 15 (13.33%)	1 / 8 (12.50%)
occurrences (all)	0	2	1
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Nasal Congestion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal Pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Pleural Effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Pulmonary Embolism			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Confusional State			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 3 (33.33%)	2 / 15 (13.33%)	1 / 8 (12.50%)
occurrences (all)	1	2	1
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	3 / 8 (37.50%)
occurrences (all)	0	0	4
C-reactive protein increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 15 (13.33%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 15 (13.33%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 15 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Blood Creatinine Phophokinase Decreased			

subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Blood Creatinine Phosphokinase Increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 15 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Hypophonesis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
International Normalised Ratio Increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Protein Total Decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Post Procedural Haematoma			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Skain Abrasion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 15 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	4 / 8 (50.00%)
occurrences (all)	0	1	4
Headache			
subjects affected / exposed	0 / 3 (0.00%)	3 / 15 (20.00%)	0 / 8 (0.00%)
occurrences (all)	0	4	0

Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	1 / 8 (12.50%)
occurrences (all)	0	1	3
Aphasia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Ataxia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Horner's Syndrome			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hypokinesia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Lethargy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Migraine With Aura			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Nervous System Disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Visual Field Defect			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 3 (33.33%)	8 / 15 (53.33%)	5 / 8 (62.50%)
occurrences (all)	1	16	13
Anaemia			

subjects affected / exposed	1 / 3 (33.33%)	5 / 15 (33.33%)	1 / 8 (12.50%)
occurrences (all)	1	7	1
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 15 (20.00%)	3 / 8 (37.50%)
occurrences (all)	0	5	13
Leukopenia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 15 (13.33%)	2 / 8 (25.00%)
occurrences (all)	1	3	4
Leukocytosis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 15 (13.33%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Pancytopenia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Febrile Neutropenia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 15 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Vertigo			
subjects affected / exposed	1 / 3 (33.33%)	0 / 15 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Eye Irritation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Ocular Toxicity			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Photophobia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Vision Blurred			

subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 3 (66.67%)	8 / 15 (53.33%)	3 / 8 (37.50%)
occurrences (all)	2	11	3
Diarrhoea			
subjects affected / exposed	1 / 3 (33.33%)	5 / 15 (33.33%)	3 / 8 (37.50%)
occurrences (all)	1	7	3
Vomiting			
subjects affected / exposed	1 / 3 (33.33%)	7 / 15 (46.67%)	1 / 8 (12.50%)
occurrences (all)	1	11	1
Constipation			
subjects affected / exposed	1 / 3 (33.33%)	2 / 15 (13.33%)	2 / 8 (25.00%)
occurrences (all)	1	2	2
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 15 (13.33%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Anal incontinence			
subjects affected / exposed	0 / 3 (0.00%)	2 / 15 (13.33%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Dry mouth			
subjects affected / exposed	0 / 3 (0.00%)	2 / 15 (13.33%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Abdominal Pain Lower			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Abdominal Pain Upper			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Melaena			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0

Rectal Haemorrhage			
subjects affected / exposed	1 / 3 (33.33%)	0 / 15 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Tongue Coated			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 15 (13.33%)	0 / 8 (0.00%)
occurrences (all)	0	5	0
Jaundice			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	1 / 3 (33.33%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Skin Discolouration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Skin Lesion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Urinary incontinence			

subjects affected / exposed	0 / 3 (0.00%)	2 / 15 (13.33%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Incontinence			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Renal Failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 3 (33.33%)	4 / 15 (26.67%)	0 / 8 (0.00%)
occurrences (all)	1	4	0
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Hypercreatinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	2 / 15 (13.33%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Groin Pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Muscular Weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Musculoskeletal Chest Pain			

subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Myopathy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Oral candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	2 / 8 (25.00%)
occurrences (all)	0	1	2
Urinary tract infection			
subjects affected / exposed	1 / 3 (33.33%)	1 / 15 (6.67%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Oral infection			
subjects affected / exposed	0 / 3 (0.00%)	2 / 15 (13.33%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Bacteriuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Clostridium Difficile Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Device Related Infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Herpes Ophthalmic			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Oral Herpes			
subjects affected / exposed	1 / 3 (33.33%)	0 / 15 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Osteomyelitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0

Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Respiratory Tract Infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Sepsis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 15 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 3 (66.67%)	5 / 15 (33.33%)	2 / 8 (25.00%)
occurrences (all)	2	6	3
Hyponatraemia			
subjects affected / exposed	1 / 3 (33.33%)	4 / 15 (26.67%)	2 / 8 (25.00%)
occurrences (all)	1	4	2
Hypokalaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 15 (6.67%)	3 / 8 (37.50%)
occurrences (all)	1	1	4
Hypocalcaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 15 (6.67%)	2 / 8 (25.00%)
occurrences (all)	1	1	2
Hypercalcaemia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 15 (13.33%)	0 / 8 (0.00%)
occurrences (all)	1	2	0
Hyperglycaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 15 (6.67%)	1 / 8 (12.50%)
occurrences (all)	1	8	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 15 (13.33%)	1 / 8 (12.50%)
occurrences (all)	0	2	1
Hypomagnesaemia			

subjects affected / exposed	0 / 3 (0.00%)	2 / 15 (13.33%)	1 / 8 (12.50%)
occurrences (all)	0	2	1
Hypercreatininaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	1 / 8 (12.50%)
occurrences (all)	0	2	1
Cachexia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hypermagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 15 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hypochloraemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 15 (6.67%)	0 / 8 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 June 2014	Protocol Amendment 1: - Addressed comments following Health Authority review to exclude subjects with surface antigen (HBsAg) or hepatitis B PCR positivity. - Revised selinexor risk section to remove "without bleeding" from "low platelets without bleeding". - Washout period for prior ibrutinib was changed from ≥2 weeks to 1 day prior to initiation of selinexor. - Clarified that lymph node biopsy was required, but only if it was safe for the subject to undergo biopsy. - Added description of an acute cerebellar syndrome SAE to the risks/ SAE reporting sections.
04 November 2014	Protocol Amendment 2: - Treatment holiday was added (dosing on Weeks 1-3, with no treatment during Week 4).
18 December 2014	Protocol Amendment 3: - Reduced the starting dose of selinexor to a fixed 60 mg (~35 mg/square-meter) twice weekly (Days 1 and 3 of a 3-week cycle) for all subjects with body surface area ≥ 1.3 square-meter. - Increased selinexor dose to 80 mg at Cycle 3/Day 1 unless clinically contraindicated (eg, persistent severe thrombocytopenia or fatigue) (Note: previously, dosing could be up to 120 mg for subjects with a BSA ≥ 2.0 square-meter). - Excluded subjects with body surface areas < 1.3 square-meter due to potential for tolerance issues.
22 June 2015	Protocol Amendment 4: - Replaced the requirement for prior Richter's therapy with requirement for prior CLL therapy. - Specified the objective evidence of disease progression required for subject inclusion. - Allowed subjects with liver involvement of their RT who had AST and ALT ≤ 5×ULN to enroll in the study. - Increased the windows for certain Screening assessments. - Moved assessments (eg, IgVH, karyotyping, quality of life, oxygen saturation) that were not required for Screening to Cycle 1/Day 1. - Provided additional monitoring for pregnancies. - Added analysis at a central laboratory to characterize tumor histology and confirm RT. - Replaced Follow-up Visit at 30 days after the Final Visit with a telephone call 30 days after the last dose of study treatment. * Subjects receiving ongoing treatment in 3-week cycles were permitted to continue with their original treatment regimen or switch to 4-week cycles. In addition, dosing was permitted to be increased after Cycle 1 to 80 mg twice weekly for those subjects who had no contraindicated toxicity. - Aligned steroid use with study KCP-330-009. - Update ophthalmic examination language and appendix. - Update safety reporting.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The low number of formal objective responses (leading to the termination of the study following the first stage), coupled with the high number of censored observations, limited meaningful analyses and the ability to draw conclusions from the data.

Notes: