Clinical trial results:
A Phase 2 Study Evaluating the Efficacy and Safety of Selinexor (KPT-330) in Subjects with Recurrent Gliomas

Summary

EudraCT number	2013-003668-30
Trial protocol	DK NL
Global end of trial date	23 January 2020

Results information

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

Trial information

Trial identification

Sponsor protocol code	KCP-330-004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01986348
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 Trials Information, Karyopharm Therapeutic Inc., +1 617658 0600, clinicaltrials@karyopharm.com
Scientific contact	Clinical Trials Information, Karyopharm Therapeutic Inc., +1 617658 0600, 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	23 January 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 January 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy of selinexor in adults with recurrent glioblastoma (GBM) as determined by the 6-months progression-free survival 6mPFS rate (Arms B, C, and D).

Protection of trial subjects:

The study was conducted in accordance with the ethical principles originating in the Declaration of Helsinki in place at the time of study conduct. The study was conducted in compliance with the International Council for Harmonisation (ICH) E6 Guideline for Good Clinical Practice (GCP) (Committee for Proprietary Medicinal Products [CPMP] guideline CPMP/ICH/135/95), United States Code of Federal Code of Regulations, and all applicable local regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 March 2014
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	Netherlands: 12
Country: Number of subjects enrolled	Denmark: 19
Country: Number of subjects enrolled	United States: 45
Worldwide total number of subjects	76
EEA total number of subjects	31

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)	63

From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 6 sites across the United States of America, Denmark and Netherland between 03 March 2014 and 23 January 2020.

Pre-assignment

Screening details:

A total of 76 subjects were enrolled, randomized and treated in this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: Selinexor 60mg and Surgery

Arm description:

Subjects who required surgery received up to 3 doses of selinexor oral tablets 60 milligrams (mg) twice weekly (BIW) on Day1, Day 3 and between 2 and 48 hours prior to surgery, subsequently underwent surgery for resection of their tumor and resumed selinexor oral tablets 60 mg BIW after recovery, during Week 1 to 4 of each 4-week cycle, until progression of disease (PD) or development of unacceptable toxicities.

Arm type	Experimental
Investigational medicinal product name	Selinexor
Investigational medicinal product code	KPT-330
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects who required surgery received up to 3 doses of oral selinexor tablets 60 mg twice weekly (BIW).

Arm title	Arm B: Selinexor 50mg/m^2

Arm description:

Subjects who were not eligible for surgery received selinexor oral tablets 50 mg per square meter (mg/m^2) BIW during Week 1 to 4 of each 4-week cycle until PD or development of unacceptable toxicities.

Arm type	Experimental
Investigational medicinal product name	Selinexor
Investigational medicinal product code	KPT-330
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects who were not eligible for surgery received selinexor oral tablets 50 mg/m^2 BIW.

Arm title	Arm C: Selinexor 60 mg

Arm description:

Subjects who were not eligible for surgery received selinexor oral tablets 60 mg BIW during Week 1 to 4 of each 4-week cycle until PD or development of unacceptable toxicities.

Arm type	Experimental

Investigational medicinal product name	Selinexor
Investigational medicinal product code	KPT-330
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects who were not eligible for surgery received selinexor oral tablets 60mg.

Arm title	Arm D: Selinexor 80 mg

Arm description:

Subjects who were not eligible for surgery received selinexor oral tablets 80 mg once weekly (QW) during Week 1 to 4 of each 4-week cycle until PD or development of unacceptable toxicities.

Arm type	Experimental
Investigational medicinal product name	Selinexor
Investigational medicinal product code	KPT-330
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects who were not eligible for surgery received selinexor oral tablets 80 mg.

Number of subjects in period 1	Arm A: Selinexor 60mg and Surgery	Arm B: Selinexor 50mg/m^2	Arm C: Selinexor 60 mg
Started	8	24	14
Completed	0	0	0
Not completed	8	24	14
Consent withdrawn by subject	-	1	2
Physician decision	-	-	-
Death	8	22	10
Study terminated by sponsor	-	-	-
Unspecified	-	1	-
Progressive disease	-	-	2
Lost to follow-up	-	-	-

Number of subjects in period 1	Arm D: Selinexor 80 mg
Started	30
Completed	0
Not completed	30
Consent withdrawn by subject	1
Physician decision	1
Death	21
Study terminated by sponsor	3
Unspecified	2
Progressive disease	-
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	Arm A: Selinexor 60mg and Surgery
Reporting group description:	
Subjects who required surgery received up to 3 doses of selinexor oral tablets 60 milligrams (mg) twice weekly (BIW) on Day1, Day 3 and between 2 and 48 hours prior to surgery, subsequently underwent surgery for resection of their tumor and resumed selinexor oral tablets 60 mg BIW after recovery, during Week 1 to 4 of each 4-week cycle, until progression of disease (PD) or development of unacceptable toxicities.	
Reporting group title	Arm B: Selinexor 50mg/m^2
Reporting group description:	
Subjects who were not eligible for surgery received selinexor oral tablets 50 mg per square meter (mg/m^2) BIW during Week 1 to 4 of each 4-week cycle until PD or development of unacceptable toxicities.	
Reporting group title	Arm C: Selinexor 60 mg
Reporting group description:	
Subjects who were not eligible for surgery received selinexor oral tablets 60 mg BIW during Week 1 to 4 of each 4-week cycle until PD or development of unacceptable toxicities.	
Reporting group title	Arm D: Selinexor 80 mg
Reporting group description:	
Subjects who were not eligible for surgery received selinexor oral tablets 80 mg once weekly (QW) during Week 1 to 4 of each 4-week cycle until PD or development of unacceptable toxicities.	

Reporting group values	Arm A: Selinexor 60mg and Surgery	Arm B: Selinexor 50mg/m^2	Arm C: Selinexor 60 mg
Number of subjects	8	24	14
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	56.6	51.1	49.5
standard deviation	± 6.70	± 13.04	± 12.36
Gender categorical Units: Subjects			
Female	1	5	5
Male	7	19	9
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	8	20	8
Unknown or Not Reported	0	4	6
Race Units: Subjects			
Asian	0	0	0
White	8	24	8
Unknown/Not Provided	0	0	6

Reporting group values	Arm D: Selinexor 80 mg	Total	
Number of subjects	30	76	

Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	54.3		
standard deviation	± 11.98	-	
Gender categorical Units: Subjects			
Female	11	22	
Male	19	54	
Ethnicity Units: Subjects			
Hispanic or Latino	3	3	
Not Hispanic or Latino	24	60	
Unknown or Not Reported	3	13	
Race Units: Subjects			
Asian	1	1	
White	25	65	
Unknown/Not Provided	4	10	

End points

End points reporting groups

Reporting group title	Arm A: Selinexor 60mg and Surgery

Reporting group description:

Subjects who required surgery received up to 3 doses of selinexor oral tablets 60 milligrams (mg) twice weekly (BIW) on Day1, Day 3 and between 2 and 48 hours prior to surgery, subsequently underwent surgery for resection of their tumor and resumed selinexor oral tablets 60 mg BIW after recovery, during Week 1 to 4 of each 4-week cycle, until progression of disease (PD) or development of unacceptable toxicities.

Reporting group title	Arm B: Selinexor 50mg/m^2

Reporting group description:

Subjects who were not eligible for surgery received selinexor oral tablets 50 mg per square meter (mg/m^2) BIW during Week 1 to 4 of each 4-week cycle until PD or development of unacceptable toxicities.

Reporting group title	Arm C: Selinexor 60 mg

Reporting group description:

Subjects who were not eligible for surgery received selinexor oral tablets 60 mg BIW during Week 1 to 4 of each 4-week cycle until PD or development of unacceptable toxicities.

Reporting group title	Arm D: Selinexor 80 mg

Reporting group description:

Subjects who were not eligible for surgery received selinexor oral tablets 80 mg once weekly (QW) during Week 1 to 4 of each 4-week cycle until PD or development of unacceptable toxicities.

Primary: Percentage of Subjects With 6-Month Progression-Free Survival

End point title	Percentage of Subjects With 6-Month Progression-Free

End point description:

Analysis of 6mPFS was performed by calculating estimated survival probability of having PFS ≥ 6 months based on Kaplan-Meier method, where PFS was defined as time from the start of study treatment until first documented progression based on Response Assessment in Neuro-Oncology (RANO) criteria, or death from any cause. Progressive disease occurs when either of the criteria was present: ≥ 25% increase in T1 gadolinium enhancing disease, increase in T2/ Fluid-attenuated inversion recovery (FLAIR), detection of new lesions, or decreased clinical status. Modified intent-to-treat (mITT) population consisted of all enrolled subjects in Arms B, C and D who had received at least 1 dose of study medication and have at least 1 post-baseline efficacy follow-up assessment, unless the subject discontinued treatment prior to the first post baseline assessment due to death, toxicity, or PD. Data for this endpoint was not planned to be collected and analysed for Arm A: Selinexor 60 mg and Surgery.

End point type	Primary

End point timeframe:

From start of study treatment up to disease progression or death, whichever occurred first (assessed up to Month 6)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, only descriptive analyses was planned for this endpoint.

[2] - 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: Data for this endpoint was not planned to be collected and analyzed for Arm A: Selinexor 60 mg and Surgery.

End point values	Arm B: Selinexor 50mg/m^2	Arm C: Selinexor 60 mg	Arm D: Selinexor 80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	13	30	
Units: Percentage of subjects				
number (confidence interval 95%)	9.72 (2.67 to 35.39)	7.69 (1.17 to 50.57)	17.24 (7.77 to 38.27)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)[3]

End point description:

The ORR was determined as percentage of subjects who had either complete response (CR) or partial response (PR) using the RANO criteria. CR: No T1 gadolinium enhancing disease, stable or decreasing T2/FLAIR, no new lesions, no corticosteroid use and stable, or increasing clinical status. PR: ≥50% decrease in T1 gadolinium enhancing disease, stable or decreasing T2/FLAIR, no new lesions, stable or decreased use of corticosteroids, and stable or increased clinical status. mITT population consisted of all enrolled subjects in Arms B, C and D who had received at least 1 dose of study medication and have at least 1 post-baseline efficacy follow-up assessment, unless the subject discontinued treatment prior to the first post baseline assessment due to death, toxicity, or disease progression. Data for this outcome measure was not planned to be collected and analyzed for Arm A: Selinexor 60 mg and Surgery.

End point type	Secondary

End point timeframe:

Up to 71 months

Notes:

[3] - 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: Data for this endpoint was not planned to be collected and analyzed for Arm A: Selinexor 60 mg and Surgery.

End point values	Arm B: Selinexor 50mg/m^2	Arm C: Selinexor 60 mg	Arm D: Selinexor 80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	13	30	
Units: Percentage of subject				
number (confidence interval 95%)	8.3 (1.0 to 27.0)	7.7 (0.2 to 36.0)	10.0 (2.1 to 26.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)[4]

End point description:

The OS was calculated from the date of start of study treatment to the date of death. Subjects who were still alive prior to the data cut-off for final efficacy analysis, or who dropout prior to study end,

were censored on the day they were last known to be alive. The OS was estimated using Kaplan-Meier method. mITT population consisted of all enrolled Subjects in Arms B, C and D who had received at least 1 dose of study medication and have at least 1 post-baseline efficacy follow-up assessment, unless the subject discontinued treatment prior to the first post baseline assessment due to death, toxicity, or disease progression. Data for this outcome measure was not planned to be collected and analyzed for Arm A: Selinexor 60 mg and Surgery. Here, "99999" represent data could not be estimated due to higher number (>50%) of censored subjects.

End point type	Secondary

End point timeframe:

From date of study treatment up to date of death (assessed up to 71 months)

Notes:

[4] - 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: Data for this endpoint was not planned to be collected and analyzed for Arm A: Selinexor 60 mg and Surgery.

End point values	Arm B: Selinexor 50mg/m^2	Arm C: Selinexor 60 mg	Arm D: Selinexor 80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	13	30	
Units: Months				
median (confidence interval 95%)	10.51 (4.93 to 16.95)	8.48 (7.29 to 99999)	10.15 (7.03 to 15.38)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS)

End point title	Progression-free Survival (PFS)[5]

End point description:

The PFS was calculated from the date of start of study treatment to the date of disease progression based on RANO criteria, or date of death should progression not have occurred. Progressive disease occurs when either of the criteria was present: ≥25% increase in T1 gadolinium enhancing disease, increased T2/FLAIR, detection of new lesions, or decreased clinical status. mITT population consisted of all enrolled subjects in Arms B, C and D who had received at least 1 dose of study medication and have at least 1 post-baseline efficacy follow-up assessment, unless the subject discontinued treatment prior to the first post baseline assessment due to death, toxicity, or disease progression. Data for this outcome measure was not planned to be collected and analyzed for Arm A: Selinexor 60 mg and Surgery.

End point type	Secondary

End point timeframe:

From start of study treatment up to disease progression (assessed up to 71 months)

Notes:

[5] - 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: Data for this endpoint was not planned to be collected and analyzed for Arm A: Selinexor 60 mg and Surgery.

End point values	Arm B: Selinexor 50mg/m^2	Arm C: Selinexor 60 mg	Arm D: Selinexor 80 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	13	30	
Units: Months				
median (confidence interval 95%)	1.64 (1.18 to 3.15)	1.87 (1.84 to 14.88)	1.87 (1.81 to 3.02)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. A serious adverse event (SAE) was defined as an AE that was fatal; life threatening (places the subject at immediate risk of death); requires in-patient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; was a congenital anomaly/birth defect; and other important medical events. TEAE was defined as any AE with onset or worsening of a pre-existing condition on or after the first administration of study medication through 30 days following last dose or any event considered drug-related by the Investigator through the end of the study. TEAEs included both serious and non-serious TEAEs. Safety population consisted of all subjects who had received any amount of study treatment.

End point type	Secondary

End point timeframe:

From start of study treatment administration up to 71 months

End point values	Arm A: Selinexor 60mg and Surgery	Arm B: Selinexor 50mg/m^2	Arm C: Selinexor 60 mg	Arm D: Selinexor 80 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	24	14	30
Units: Subjects				
Subjects with TEAEs	8	24	14	30
Subjects with TESAEs	5	7	7	7

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study treatment administration up to 71 months

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Arm A: Selinexor 60 mg and Surgery

Reporting group description:

Subjects who required surgery received up to 3 doses of selinexor oral tablets 60 mg BIW on Day 1, Day 3 and between 2 and 48 hours prior to surgery, subsequently underwent surgery for resection of their tumor and resumed selinexor oral tablets 60 mg BIW after recovery, during Week 1 to 4 of each 4-week cycle, until PD or development of unacceptable toxicities.

Reporting group title	Arm B: Selinexor 50 mg/m^2

Reporting group description:

Subjects who were not eligible for surgery received selinexor oral tablets 50 mg/m^2 BIW during Week 1 to 4 of each 4-week cycle until PD or development of unacceptable toxicities.

Reporting group title	Arm C: Selinexor 60 mg

Reporting group description:

Subjects who were not eligible for surgery received selinexor oral tablets 60 mg BIW during Week 1 to 4 of each 4-week cycle until PD or development of unacceptable toxicities.

Reporting group title	Arm D: Selinexor 80 mg

Reporting group description:

Subjects who were not eligible for surgery received selinexor oral tablets 80 mg QW during Week 1 to 4 of each 4-week cycle until PD or development of unacceptable toxicities.

Serious adverse events	Arm A: Selinexor 60 mg and Surgery	Arm B: Selinexor 50 mg/m^2	Arm C: Selinexor 60 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 8 (62.50%)	7 / 24 (29.17%)	7 / 14 (50.00%)
number of deaths (all causes)	8	22	10
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial tumour haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	1 / 24 (4.17%)	0 / 14 (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

Injury, poisoning and procedural complications			
Acetabulum fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shunt malfunction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
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			
Embolism			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 14 (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
Hypertension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Brain oedema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrospinal fluid leakage			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 14 (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
Cerebrovascular accident			

subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 14 (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
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	1 / 24 (4.17%)	0 / 14 (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
Headache			
subjects affected / exposed	0 / 8 (0.00%)	1 / 24 (4.17%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocephalus			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 14 (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
Seizure			
subjects affected / exposed	0 / 8 (0.00%)	1 / 24 (4.17%)	3 / 14 (21.43%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			

subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 14 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 14 (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 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Meningitis bacterial			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 14 (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			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			

subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 14 (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
Urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 14 (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
Hyperglycaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 24 (4.17%)	0 / 14 (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
Hyperlipasaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 24 (4.17%)	0 / 14 (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
Hypophosphataemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 24 (4.17%)	0 / 14 (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

Serious adverse events	Arm D: Selinexor 80 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 30 (23.33%)		
number of deaths (all causes)	21		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			

subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intracranial tumour haemorrhage				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Acetabulum fracture				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Concussion				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Shunt malfunction				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Embolism				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Brain oedema				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Cerebrospinal fluid leakage				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumocephalus				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	2 / 30 (6.67%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	3 / 30 (10.00%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Asthenia				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Fatigue			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Meningitis bacterial			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			

subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperlipasaemia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypophosphataemia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Arm A: Selinexor 60 mg and Surgery	Arm B: Selinexor 50 mg/m^2	Arm C: Selinexor 60 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	24 / 24 (100.00%)	14 / 14 (100.00%)
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Flushing			
subjects affected / exposed	1 / 8 (12.50%)	1 / 24 (4.17%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Embolism			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 8 (62.50%)	19 / 24 (79.17%)	11 / 14 (78.57%)
occurrences (all)	5	19	11
Gait disturbance			
subjects affected / exposed	5 / 8 (62.50%)	5 / 24 (20.83%)	3 / 14 (21.43%)
occurrences (all)	5	5	3
Oedema peripheral			
subjects affected / exposed	3 / 8 (37.50%)	1 / 24 (4.17%)	2 / 14 (14.29%)
occurrences (all)	3	1	2
Malaise			
subjects affected / exposed	1 / 8 (12.50%)	1 / 24 (4.17%)	3 / 14 (21.43%)
occurrences (all)	1	1	3
Face oedema			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	2 / 14 (14.29%)
occurrences (all)	0	2	2
Non-cardiac chest pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Pyrexia			

subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 8 (12.50%)	3 / 24 (12.50%)	1 / 14 (7.14%)
occurrences (all)	1	3	1
Dyspnoea			
subjects affected / exposed	1 / 8 (12.50%)	1 / 24 (4.17%)	4 / 14 (28.57%)
occurrences (all)	1	1	4
Oropharyngeal pain			
subjects affected / exposed	2 / 8 (25.00%)	1 / 24 (4.17%)	0 / 14 (0.00%)
occurrences (all)	2	1	0
Epistaxis			
subjects affected / exposed	0 / 8 (0.00%)	3 / 24 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	3	0
Nasal congestion			
subjects affected / exposed	1 / 8 (12.50%)	2 / 24 (8.33%)	0 / 14 (0.00%)
occurrences (all)	1	2	0
Rhinitis allergic			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Apnoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Pulmonary embolism			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Psychiatric disorders			
Confusional state			
subjects affected / exposed	2 / 8 (25.00%)	4 / 24 (16.67%)	1 / 14 (7.14%)
occurrences (all)	2	4	1
Depression			

subjects affected / exposed	1 / 8 (12.50%)	1 / 24 (4.17%)	2 / 14 (14.29%)
occurrences (all)	1	1	2
Insomnia			
subjects affected / exposed	0 / 8 (0.00%)	4 / 24 (16.67%)	1 / 14 (7.14%)
occurrences (all)	0	4	1
Anxiety			
subjects affected / exposed	1 / 8 (12.50%)	1 / 24 (4.17%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Abnormal behaviour			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	2 / 14 (14.29%)
occurrences (all)	0	0	2
Mood altered			
subjects affected / exposed	0 / 8 (0.00%)	1 / 24 (4.17%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Personality change			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Investigations			
Weight decreased			
subjects affected / exposed	1 / 8 (12.50%)	5 / 24 (20.83%)	6 / 14 (42.86%)
occurrences (all)	1	5	6
Alanine aminotransferase increased			
subjects affected / exposed	2 / 8 (25.00%)	1 / 24 (4.17%)	0 / 14 (0.00%)
occurrences (all)	2	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 8 (12.50%)	1 / 24 (4.17%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 8 (12.50%)	1 / 24 (4.17%)	1 / 14 (7.14%)
occurrences (all)	1	1	1
Contusion			

subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Incision site pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Spinal compression fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Wound dehiscence			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	1 / 8 (12.50%)	10 / 24 (41.67%)	6 / 14 (42.86%)
occurrences (all)	1	10	6
Headache			
subjects affected / exposed	4 / 8 (50.00%)	5 / 24 (20.83%)	6 / 14 (42.86%)
occurrences (all)	4	5	6
Dizziness			
subjects affected / exposed	3 / 8 (37.50%)	6 / 24 (25.00%)	4 / 14 (28.57%)
occurrences (all)	3	6	4
Memory impairment			
subjects affected / exposed	1 / 8 (12.50%)	2 / 24 (8.33%)	2 / 14 (14.29%)
occurrences (all)	1	2	2
Aphasia			
subjects affected / exposed	1 / 8 (12.50%)	2 / 24 (8.33%)	0 / 14 (0.00%)
occurrences (all)	1	2	0
Balance disorder			
subjects affected / exposed	1 / 8 (12.50%)	1 / 24 (4.17%)	2 / 14 (14.29%)
occurrences (all)	1	1	2
Dysarthria			

subjects affected / exposed	0 / 8 (0.00%)	4 / 24 (16.67%)	0 / 14 (0.00%)
occurrences (all)	0	4	0
Seizure			
subjects affected / exposed	2 / 8 (25.00%)	1 / 24 (4.17%)	0 / 14 (0.00%)
occurrences (all)	2	1	0
Haemorrhage intracranial			
subjects affected / exposed	2 / 8 (25.00%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Hemiparesis			
subjects affected / exposed	1 / 8 (12.50%)	2 / 24 (8.33%)	0 / 14 (0.00%)
occurrences (all)	1	2	0
Neuropathy peripheral			
subjects affected / exposed	1 / 8 (12.50%)	3 / 24 (12.50%)	0 / 14 (0.00%)
occurrences (all)	1	3	0
Tremor			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Coordination abnormal			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Depressed level of consciousness			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Disturbance in attention			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Hemianopia homonymous			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
IIIrd nerve disorder			
subjects affected / exposed	1 / 8 (12.50%)	1 / 24 (4.17%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Lethargy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Motor dysfunction			

subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Paraesthesia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Taste disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Visual field defect			
subjects affected / exposed	0 / 8 (0.00%)	1 / 24 (4.17%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Ataxia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Cerebrospinal fluid leakage			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Intracranial pressure increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Upper motor neurone lesion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	6 / 8 (75.00%)	16 / 24 (66.67%)	6 / 14 (42.86%)
occurrences (all)	6	16	6
Leukopenia			
subjects affected / exposed	0 / 8 (0.00%)	7 / 24 (29.17%)	1 / 14 (7.14%)
occurrences (all)	0	7	1

Neutropenia			
subjects affected / exposed	1 / 8 (12.50%)	7 / 24 (29.17%)	2 / 14 (14.29%)
occurrences (all)	1	7	2
Anaemia			
subjects affected / exposed	2 / 8 (25.00%)	5 / 24 (20.83%)	1 / 14 (7.14%)
occurrences (all)	2	5	1
Lymphopenia			
subjects affected / exposed	2 / 8 (25.00%)	2 / 24 (8.33%)	0 / 14 (0.00%)
occurrences (all)	2	2	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Hypoacusis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 8 (0.00%)	6 / 24 (25.00%)	1 / 14 (7.14%)
occurrences (all)	0	6	1
Dry eye			
subjects affected / exposed	1 / 8 (12.50%)	1 / 24 (4.17%)	1 / 14 (7.14%)
occurrences (all)	1	1	1
Cataract			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Periorbital oedema			
subjects affected / exposed	1 / 8 (12.50%)	1 / 24 (4.17%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Visual acuity reduced			
subjects affected / exposed	0 / 8 (0.00%)	3 / 24 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	3	0
Gastrointestinal disorders			

Nausea			
subjects affected / exposed	6 / 8 (75.00%)	12 / 24 (50.00%)	9 / 14 (64.29%)
occurrences (all)	6	12	9
Vomiting			
subjects affected / exposed	1 / 8 (12.50%)	9 / 24 (37.50%)	5 / 14 (35.71%)
occurrences (all)	1	9	5
Constipation			
subjects affected / exposed	3 / 8 (37.50%)	8 / 24 (33.33%)	7 / 14 (50.00%)
occurrences (all)	3	8	7
Diarrhoea			
subjects affected / exposed	2 / 8 (25.00%)	3 / 24 (12.50%)	3 / 14 (21.43%)
occurrences (all)	2	3	3
Dry mouth			
subjects affected / exposed	1 / 8 (12.50%)	3 / 24 (12.50%)	2 / 14 (14.29%)
occurrences (all)	1	3	2
Dyspepsia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	1 / 14 (7.14%)
occurrences (all)	0	2	1
Abdominal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	1 / 14 (7.14%)
occurrences (all)	0	2	1
Toothache			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Pruritus			
subjects affected / exposed	2 / 8 (25.00%)	1 / 24 (4.17%)	0 / 14 (0.00%)
occurrences (all)	2	1	0
Dry skin			

subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Rash maculo-papular			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	1 / 8 (12.50%)	1 / 24 (4.17%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Purpura			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Night Sweats			
subjects affected / exposed	0 / 8 (0.00%)	1 / 24 (4.17%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	1 / 8 (12.50%)	3 / 24 (12.50%)	2 / 14 (14.29%)
occurrences (all)	1	3	2
Pollakiuria			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	1 / 14 (7.14%)
occurrences (all)	0	2	1
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 8 (0.00%)	4 / 24 (16.67%)	0 / 14 (0.00%)
occurrences (all)	0	4	0
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 8 (12.50%)	3 / 24 (12.50%)	4 / 14 (28.57%)
occurrences (all)	1	3	4
Back pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	2 / 14 (14.29%)
occurrences (all)	1	0	2
Myalgia			

subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Osteoporosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	2 / 24 (8.33%)	1 / 14 (7.14%)
occurrences (all)	0	2	1
Urinary tract infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 8 (12.50%)	1 / 24 (4.17%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Bronchitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 8 (37.50%)	12 / 24 (50.00%)	10 / 14 (71.43%)
occurrences (all)	3	12	10
Hyponatraemia			

subjects affected / exposed	4 / 8 (50.00%)	11 / 24 (45.83%)	3 / 14 (21.43%)
occurrences (all)	4	11	3
Hypophosphataemia			
subjects affected / exposed	3 / 8 (37.50%)	5 / 24 (20.83%)	0 / 14 (0.00%)
occurrences (all)	3	5	0
Hyperglycaemia			
subjects affected / exposed	0 / 8 (0.00%)	4 / 24 (16.67%)	1 / 14 (7.14%)
occurrences (all)	0	4	1
Dehydration			
subjects affected / exposed	1 / 8 (12.50%)	3 / 24 (12.50%)	0 / 14 (0.00%)
occurrences (all)	1	3	0
Hypokalaemia			
subjects affected / exposed	1 / 8 (12.50%)	2 / 24 (8.33%)	2 / 14 (14.29%)
occurrences (all)	1	2	2
Hyperkalaemia			
subjects affected / exposed	0 / 8 (0.00%)	3 / 24 (12.50%)	0 / 14 (0.00%)
occurrences (all)	0	3	0
Hyperlipasaemia			
subjects affected / exposed	2 / 8 (25.00%)	1 / 24 (4.17%)	0 / 14 (0.00%)
occurrences (all)	2	1	0
Hypercreatininaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Hyperamylasaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 24 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Arm D: Selinexor 80 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 30 (100.00%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	6 / 30 (20.00%)		
occurrences (all)	6		
Flushing			

subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Embolism			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	16 / 30 (53.33%)		
occurrences (all)	16		
Gait disturbance			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Oedema peripheral			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Malaise			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Face oedema			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Non-cardiac chest pain			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	4 / 30 (13.33%)		
occurrences (all)	4		
Dyspnoea			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Oropharyngeal pain			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Epistaxis			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Rhinitis allergic			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Apnoea			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Pulmonary embolism			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	5 / 30 (16.67%)		
occurrences (all)	5		
Depression			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Anxiety			

subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Abnormal behaviour			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Mood altered			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Personality change			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Investigations			
Weight decreased			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Alanine aminotransferase increased			
subjects affected / exposed	5 / 30 (16.67%)		
occurrences (all)	5		
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	5 / 30 (16.67%)		
occurrences (all)	5		
Contusion			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Incision site pain			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Spinal compression fracture			

subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Wound dehiscence			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	4 / 30 (13.33%)		
occurrences (all)	4		
Headache			
subjects affected / exposed	5 / 30 (16.67%)		
occurrences (all)	5		
Dizziness			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Memory impairment			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Aphasia			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Balance disorder			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Dysarthria			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Seizure			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Haemorrhage intracranial			

subjects affected / exposed	2 / 30 (6.67%)			
occurrences (all)	2			
Hemiparesis				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences (all)	1			
Neuropathy peripheral				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences (all)	0			
Tremor				
subjects affected / exposed	2 / 30 (6.67%)			
occurrences (all)	2			
Coordination abnormal				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences (all)	0			
Depressed level of consciousness				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences (all)	1			
Disturbance in attention				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences (all)	0			
Hemianopia homonymous				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences (all)	1			
IIIrd nerve disorder				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences (all)	0			
Lethargy				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences (all)	1			
Motor dysfunction				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences (all)	0			
Paraesthesia				
subjects affected / exposed	2 / 30 (6.67%)			
occurrences (all)	2			
Syncope				

subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Taste disorder			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Visual field defect			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Ataxia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Cerebrospinal fluid leakage			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Intracranial pressure increased			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Upper motor neurone lesion			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	11 / 30 (36.67%)		
occurrences (all)	11		
Leukopenia			
subjects affected / exposed	14 / 30 (46.67%)		
occurrences (all)	14		
Neutropenia			
subjects affected / exposed	10 / 30 (33.33%)		
occurrences (all)	10		
Anaemia			
subjects affected / exposed	6 / 30 (20.00%)		
occurrences (all)	6		

Lymphopenia subjects affected / exposed occurrences (all)	8 / 30 (26.67%) 8		
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all) Hypoacusis subjects affected / exposed occurrences (all)	 1 / 30 (3.33%) 1 2 / 30 (6.67%) 2		
Eye disorders Vision blurred subjects affected / exposed occurrences (all) Dry eye subjects affected / exposed occurrences (all) Cataract subjects affected / exposed occurrences (all) Eye pain subjects affected / exposed occurrences (all) Periorbital oedema subjects affected / exposed occurrences (all) Visual acuity reduced subjects affected / exposed occurrences (all)	 4 / 30 (13.33%) 4 1 / 30 (3.33%) 1 3 / 30 (10.00%) 3 2 / 30 (6.67%) 2 1 / 30 (3.33%) 1 0 / 30 (0.00%) 0		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Constipation	 21 / 30 (70.00%) 21 13 / 30 (43.33%) 13 		

subjects affected / exposed	7 / 30 (23.33%)		
occurrences (all)	7		
Diarrhoea			
subjects affected / exposed	6 / 30 (20.00%)		
occurrences (all)	6		
Dry mouth			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Abdominal pain			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Stomatitis			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	4 / 30 (13.33%)		
occurrences (all)	4		
Pruritus			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Dry skin			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Rash maculo-papular			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		

Purpura subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
Night Sweats subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
Renal and urinary disorders Urinary incontinence subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 3		
Pollakiuria subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Endocrine disorders Cushingoid subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
Inappropriate antidiuretic hormone secretion subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
Musculoskeletal and connective tissue disorders Muscular weakness subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2		
Back pain subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2		
Myalgia subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Neck pain subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Osteoporosis subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		

Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Urinary tract infection			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Cystitis			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	8 / 30 (26.67%)		
occurrences (all)	8		
Hyponatraemia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Hypophosphataemia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Dehydration			

subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Hyperkalaemia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Hyperlipasaemia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Hypercreatininaemia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Hyperamylasaemia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 November 2013	Protocol Amendment 2: - Description of the use of new dosing and the tablet formulation planned for use in this study was added. Identified the initial starting dose for all subjects at 50 mg/m2 (35 mg/m2 as per original protocol) based on clinical experience. - Revised the dose modification criteria for thrombocytopenia (to hold the drug for ≥Grade 3 thrombocytopenia until resolved to ≤ Grade 1 and then resume at a lower dose; specified when to further dose reduce and when to discontinue for recurrent toxicity) and for renal toxicity based on NCI-CTCAE (Version 4.03) criteria for serum creatinine levels. - Expanded the inclusion criteria to allow enrollment of subjects with AST levels less than twice the upper limit of normal (< 2 x ULN). - Clarified that the 7 surgical subjects planned to be enrolled in Arm A will receive 3 doses instead of 2 to 3 doses prior to surgery. - Revised the selinexor administration time after brain surgery for subjects in Arm A based on data regarding previously observed thrombocytopenia in Phase I human experience. The initial protocol stated that selinexor would be administered post-operatively 1 to 5 weeks from the date of surgery.
16 July 2014	Protocol Amendment 3: - Expanded the number of subjects in Arm A from 7 to 20 subjects based on initial PK data from 5 subjects dosed 2 hours prior to surgery suggest that selinexor consistently reaches therapeutic concentrations (50-300 nM) within brain tumor lesions. Thus, further exploration was warranted. Enrollment method was updated as sequential enrollment into Groups 1-4 with 5 subjects per group. Following enrollment completion of Group 1 selinexor tumor exposure was to be evaluated and enrollment of each subsequent group to be initiated if selinexor tumor levels exceeds 25 nM levels. Subjects were to receive 3 doses of selinexor (BIW on Day 1 and 3, and between 2 and 48 hours prior to surgery on Day 8-10). - Expanded the overall number of subjects enrolled in the study from approximately 37 to approximately 50 subjects due to increase in number of subjects in Arm A. - Updated information related to the MTD to specify that escalating beyond 70 mg/m2 BIW was prohibited in any study.

23 March 2015	Protocol Amendment 4: - Changed to flat dosing: 60 mg BIW during Weeks 1-3 of each 4-week cycle (Arms A, B, C, E, and F) and 80 mg QIW (Arm D) based on the analysis of prolonged dosing results in KCP-330-002: a dose of 35 mg/m2 (~60 mg) BIW had acceptable efficacy and improved long-term tolerability and a dose of 50 mg/m2 (~85 mg) BIW was tolerated and cleared DLT evaluation. - Added Arms C and D (1:1 randomization) to compare the efficacy, tolerability and safety of selinexor (60 mg) administered BIW during Weeks 1-3 of each 4 week cycle (Arm C) with selinexor (80 mg) administered QIW (Arm D). - Added Arm E for subjects with malignant gliomas other than GBM and Arm F for subjects with GBM or anaplastic gliomas (AG) with bevacizumab-refractory recurrent disease with approximately 10 subjects in each new arm to evaluate preliminary evidence of efficacy of selinexor in these exploratory populations. - Updated the planned number of subjects from 50 to 115. - Revised inclusion criteria to include diagnoses for the new exploratory arms (Arms E and F): Arm E "Pathologically confirmed malignant gliomas other than GBM (WHO Grade 3 anaplastic astrocytomas, oligodendrogliomas, or oligo-astrocytomas), with radiographic evidence of recurrent disease after treatment with temozolomide and radiotherapy", Arm F "Pathologically confirmed GBM (including all histologic variants) or AG with bevacizumab-refractory disease (defined as recurrence or progression of disease per RANO criteria during prior therapy with bevacizumab or other direct VEGF/VEGFR inhibitors) with radiographic evidence of recurrent disease after treatment with temozolomide and radiotherapy". - Revised the dose adjustment guidelines for selinexor-related toxicities to include supportive treatment based on the event and the severity of the event. - Deleted PK blood draws for Arm B because enrollment in Arm B had been stopped and additional PK data were not needed.
01 July 2015	Protocol Amendment 5: - Expanded Arm E by 10 subjects (for a total of 20 subjects) due to the limited availability of treatment options for this subject population and updated total sample size from 115 to 125. - Revised the end of study definition to clarify that the study will continue after collection of data for the primary analysis (6mPFS). - Revised the mITT population (primary efficacy population) to include subjects who discontinued treatment prior to the first post-baseline assessment due to death, toxicity, or disease progression, to adopt a more conservative approach by including subjects who do not have at least 1 post-dosing efficacy evaluation due to death, toxicity, or disease progression. -Changed dosing frequency of selinexor from BIW during Weeks 1-3 of each 4-week cycle to BIW during Weeks 1-4 of each cycle for arms with BIW dosing. This was based on discussions with Investigators who indicated that some subjects could benefit from dosing during Week 4, especially if they were tolerating the drug well and did not require a dosing break to mitigate side effects.
13 November 2015	Protocol Amendment 6: - To eliminate Arms E and F (which were introduced in the last protocol amendment but did not yet contain enrolled subjects) as these arms are not going forward due to budgetary limitations. - To add an exclusion criterion requiring subjects not to have undergone major surgery within 4 weeks prior to Cycle 1 Day 1. - Revised the end of study definition (text in bold was added and strikethrough was deleted): The study will continue until the last subject in the study has died, has been off study treatment for 12 months has been lost to follow-up, or has withdrawn consent, whichever occurs first.

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.

Study was terminated due to Sponsor decision (all except 1 subject were off-treatment and 2 subjects were in survival follow-up).

Notes: