Clinical trial results:
A Randomized, Double-Blind, Phase 2, Dose-Ranging Study to Evaluate the Safety and Efficacy of Veliparib and Whole Brain Radiation Therapy Versus Placebo and Whole Brain Radiation Therapy in Subjects with Brain Metastases from Non-Small Cell Lung Cancer

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2011-003618-18
Trial protocol	NO BE CZ FI ES HU
Global end of trial date	22 January 2015

Results information

Result version number	v1
This version publication date	18 May 2016
First version publication date	18 May 2016

Trial information

Trial identification

Sponsor protocol code	M10-897

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01657799
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	Abbott House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4XE
Public contact	Global Medical Information, AbbVie, 001 800-633-9110,
Scientific contact	Vincent Giranda, MD, AbbVie, Vincent.Giranda@abbvie.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	22 January 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 January 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess whether the addition of Veliparib when given during whole brain radiation therapy (WBRT) improves Overall Survival (OS) for subjects with brain metastases from Non-small Cell Lung Cancer (NSCLC).

Protection of trial subjects:

Subject, subject's caregiver and/or or subject's representative (if applicable) read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 October 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	48 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 3
Country: Number of subjects enrolled	Australia: 31
Country: Number of subjects enrolled	Canada: 28
Country: Number of subjects enrolled	Chile: 10
Country: Number of subjects enrolled	Egypt: 5
Country: Number of subjects enrolled	Korea, Republic of: 33
Country: Number of subjects enrolled	Russian Federation: 36
Country: Number of subjects enrolled	Taiwan: 30
Country: Number of subjects enrolled	Ukraine: 15
Country: Number of subjects enrolled	United States: 36
Country: Number of subjects enrolled	Norway: 8
Country: Number of subjects enrolled	Spain: 27
Country: Number of subjects enrolled	Belgium: 17
Country: Number of subjects enrolled	Czech Republic: 14
Country: Number of subjects enrolled	Finland: 5
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Hungary: 4

Worldwide total number of subjects	307
EEA total number of subjects	80

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)	205
From 65 to 84 years	100
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 307 subjects were randomized; 1 subject did not receive study drug and was excluded from the safety analysis.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo BID plus WBRT

Arm description:

Placebo for veliparib twice daily (BID) during whole brain radiation therapy (WBRT). Treatment with WBRT began on Day 1. All subjects received a total of 30.0 Gy of WBRT given in 10 daily fractions of 3.0 Gy, excluding weekends and holidays. WBRT could be interrupted for up to a total of 7 days; however, no more than 4 consecutive days of interruption was permitted.

Arm type	Placebo
Investigational medicinal product name	placebo for veliparib capsule
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

All subjects self-administered placebo for veliparib BID continuously throughout the entire course of WBRT, starting on Day 1 and including weekends or holidays when WBRT was not given, plus an additional day of dosing with placebo for veliparib BID the day following the last day of treatment with WBRT.

Arm title	Veliparib 50 mg BID plus WBRT

Arm description:

Veliparib 50 mg twice daily (BID) during whole brain radiation therapy (WBRT). Treatment with WBRT began on Day 1. All subjects received a total of 30.0 Gy of WBRT given in 10 daily fractions of 3.0 Gy, excluding weekends and holidays. WBRT could be interrupted for up to a total of 7 days; however, no more than 4 consecutive days of interruption was permitted.

Arm type	Experimental
Investigational medicinal product name	veliparib 50 mg capsule
Investigational medicinal product code	
Other name	ABT-888
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

All subjects self-administered veliparib 50 mg BID continuously throughout the entire course of WBRT, starting on Day 1 and including weekends or holidays when WBRT was not given, plus an additional day of dosing with veliparib 50 mg BID the day following the last day of treatment with WBRT.

Arm title	Veliparib 200 mg BID plus WBRT

Arm description:

Veliparib 200 mg twice daily (BID) during whole brain radiation therapy (WBRT). Treatment with WBRT

began on Day 1. All subjects received a total of 30.0 Gy of WBRT given in 10 daily fractions of 3.0 Gy, excluding weekends and holidays. WBRT could be interrupted for up to a total of 7 days; however, no more than 4 consecutive days of interruption was permitted.

Arm type	Experimental
Investigational medicinal product name	veliparib 100 mg capsule
Investigational medicinal product code	
Other name	ABT-888
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

All subjects self-administered veliparib 200 mg BID continuously throughout the entire course of WBRT, starting on Day 1 and including weekends or holidays when WBRT was not given, plus an additional day of dosing with veliparib 200 mg BID the day following the last day of treatment with WBRT.

Number of subjects in period 1	Placebo BID plus WBRT	Veliparib 50 mg BID plus WBRT	Veliparib 200 mg BID plus WBRT
Started	102	103	102
Completed	0	0	0
Not completed	102	103	102
Disease progression	2	4	4
Radiographic and clinical brain metastases	16	11	15
Adverse event related to progression	6	8	12
Not specified	52	62	49
Progressive disease clinical	7	4	7
Withdrew consent	13	10	10
Lost to follow-up	1	-	1
Adverse event not related to progression	5	4	4

Baseline characteristics

Reporting groups	
Reporting group title	Placebo BID plus WBRT

Reporting group description:

Placebo for veliparib twice daily (BID) during whole brain radiation therapy (WBRT). Treatment with WBRT began on Day 1. All subjects received a total of 30.0 Gy of WBRT given in 10 daily fractions of 3.0 Gy, excluding weekends and holidays. WBRT could be interrupted for up to a total of 7 days; however, no more than 4 consecutive days of interruption was permitted.

Reporting group title	Veliparib 50 mg BID plus WBRT

Reporting group description:

Veliparib 50 mg twice daily (BID) during whole brain radiation therapy (WBRT). Treatment with WBRT began on Day 1. All subjects received a total of 30.0 Gy of WBRT given in 10 daily fractions of 3.0 Gy, excluding weekends and holidays. WBRT could be interrupted for up to a total of 7 days; however, no more than 4 consecutive days of interruption was permitted.

Reporting group title	Veliparib 200 mg BID plus WBRT

Reporting group description:

Veliparib 200 mg twice daily (BID) during whole brain radiation therapy (WBRT). Treatment with WBRT began on Day 1. All subjects received a total of 30.0 Gy of WBRT given in 10 daily fractions of 3.0 Gy, excluding weekends and holidays. WBRT could be interrupted for up to a total of 7 days; however, no more than 4 consecutive days of interruption was permitted.

Reporting group values	Placebo BID plus WBRT	Veliparib 50 mg BID plus WBRT	Veliparib 200 mg BID plus WBRT
Number of subjects	102	103	102
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	60	59.8	61.8
standard deviation	± 9.71	± 8.74	± 9.08
Gender categorical Units: Subjects			
Female	46	42	36
Male	56	61	66
Race Units: Subjects			
White	79	85	66
Black	0	2	6
Asian	22	16	28
Natiave Hawaiian or Pacific Islander	1	0	0
Multirace	0	0	2

Reporting group values	Total		
Number of subjects	307		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- 		
Gender categorical Units: Subjects			
Female	124		
Male	183		
Race Units: Subjects			
White	230		
Black	8		
Asian	66		
Natiave Hawaiian or Pacific Islander	1		
Multirace	2		

End points

End points reporting groups

Reporting group title	Placebo BID plus WBRT

Reporting group description:

Placebo for veliparib twice daily (BID) during whole brain radiation therapy (WBRT). Treatment with WBRT began on Day 1. All subjects received a total of 30.0 Gy of WBRT given in 10 daily fractions of 3.0 Gy, excluding weekends and holidays. WBRT could be interrupted for up to a total of 7 days; however, no more than 4 consecutive days of interruption was permitted.

Reporting group title	Veliparib 50 mg BID plus WBRT

Reporting group description:

Veliparib 50 mg twice daily (BID) during whole brain radiation therapy (WBRT). Treatment with WBRT began on Day 1. All subjects received a total of 30.0 Gy of WBRT given in 10 daily fractions of 3.0 Gy, excluding weekends and holidays. WBRT could be interrupted for up to a total of 7 days; however, no more than 4 consecutive days of interruption was permitted.

Reporting group title	Veliparib 200 mg BID plus WBRT

Reporting group description:

Veliparib 200 mg twice daily (BID) during whole brain radiation therapy (WBRT). Treatment with WBRT began on Day 1. All subjects received a total of 30.0 Gy of WBRT given in 10 daily fractions of 3.0 Gy, excluding weekends and holidays. WBRT could be interrupted for up to a total of 7 days; however, no more than 4 consecutive days of interruption was permitted.

Primary: Overall Survival: Percentage of Participants with an Event

End point title	Overall Survival: Percentage of Participants with an Event[1]

End point description:

Overall survival was defined as the number of days from the date of randomization to the date of the subject's death. All events of death were included, regardless of whether the event occurred while the subject was still taking study treatment or after the subject discontinued study treatment. If a subject had not died, the data were censored at the date the subject was last known to be alive.

End point type	Primary

End point timeframe:

From randomization up to 36 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive data were summarized for this end point per protocol.

End point values	Placebo BID plus WBRT	Veliparib 50 mg BID plus WBRT	Veliparib 200 mg BID plus WBRT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	102	102	
Units: percentage of subjects				
number (not applicable)	73.5	74.8	71.6	

Statistical analyses

No statistical analyses for this end point

Primary: Overall Survival: Time to Event

End point title	Overall Survival: Time to Event

End point description:

Overall survival was defined as the number of days from the date of randomization to the date of the subject's death. All events of death were included, regardless of whether the event occurred while the subject was still taking study treatment or after the subject discontinued study treatment. If a subject had not died, the data were censored at the date the subject was last known to be alive. Overall survival was estimated for each treatment group using Kaplan-Meier methodology.

End point type	Primary

End point timeframe:

From randomization up to 36 months

End point values	Placebo BID plus WBRT	Veliparib 50 mg BID plus WBRT	Veliparib 200 mg BID plus WBRT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	103	102	
Units: days				
median (confidence interval 95%)	185 (137 to 251)	209 (169 to 264)	209 (138 to 255)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The primary analysis used a Hochberg testing procedure to preserve the familywise error rate for multiple comparisons, where the larger P-value for the comparisons of veliparib 50 mg BID + WBRT with placebo BID + WBRT and veliparib 200 mg BID + WBRT with placebo BID + WBRT were compared to an $\alpha = 0.05$. If statistically significant ($P \leq 0.05$), both comparisons were considered significant. If the larger P-value was not statistically significant, the smaller P-value was compared to an $\alpha = 0.025$.

Comparison groups	Placebo BID plus WBRT v Veliparib 50 mg BID plus WBRT
Number of subjects included in analysis	205
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.933 [2]
Method	Logrank

Notes:

[2] - Log-rank test stratified by Graded Prognostic Assessment (GPA) score (≤2.5 or >2.5) at screening. Nominal P values were reported.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The primary analysis used a Hochberg testing procedure to preserve the familywise error rate for multiple comparisons, where the larger P-value for the comparisons of veliparib 50 mg BID + WBRT with placebo BID + WBRT and veliparib 200 mg BID + WBRT with placebo BID + WBRT were compared to an $\alpha = 0.05$. If statistically significant ($P \leq 0.05$), both comparisons were considered significant. If the larger P-value was not statistically significant, the smaller P-value was compared to an $\alpha = 0.025$.

Comparison groups	Placebo BID plus WBRT v Veliparib 50 mg BID plus WBRT

Number of subjects included in analysis	205
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.927 [3]
Method	Cox proportional hazard model
Parameter estimate	Cox proportional hazard
Point estimate	0.985
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.716
upper limit	1.355

Notes:

[3] - Cox proportional hazard model stratified by GPA score (≤2.5 or >2.5) at screening. Nominal P values were reported.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

The primary analysis used a Hochberg testing procedure to preserve the familywise error rate for multiple comparisons, where the larger P-value for the comparisons of veliparib 50 mg BID + WBRT with placebo BID + WBRT and veliparib 200 mg BID + WBRT with placebo BID + WBRT were compared to an α = 0.05. If statistically significant (P ≤ 0.05), both comparisons were considered significant. If the larger P-value was not statistically significant, the smaller P-value was compared to an α = 0.025.

Comparison groups	Placebo BID plus WBRT v Veliparib 200 mg BID plus WBRT
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.909 [4]
Method	Logrank

Notes:

[4] - Log-rank test stratified by GPA score (≤2.5 or >2.5) at screening. Nominal P values were reported.

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

The primary analysis used a Hochberg testing procedure to preserve the familywise error rate for multiple comparisons, where the larger P-value for the comparisons of veliparib 50 mg BID + WBRT with placebo BID + WBRT and veliparib 200 mg BID + WBRT with placebo BID + WBRT were compared to an α = 0.05. If statistically significant (P ≤ 0.05), both comparisons were considered significant. If the larger P-value was not statistically significant, the smaller P-value was compared to an α = 0.025.

Comparison groups	Placebo BID plus WBRT v Veliparib 200 mg BID plus WBRT
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.906 [5]
Method	Cox proportional hazard model
Parameter estimate	Cox proportional hazard
Point estimate	0.981
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.354

Notes:

[5] - Cox proportional hazard model stratified by GPA score (≤2.5 or >2.5) at screening. Nominal P values were reported.

Secondary: Best Tumor Response Rate

End point title	Best Tumor Response Rate

End point description:

The best tumor response rate was calculated as the percentage of subjects with a complete response or partial response, as determined by brain scan imaging (magnetic resonance image [MRI]/ computed tomography [CT] scan) by a central imaging vendor.

End point type	Secondary

End point timeframe:

From randomization up to 24 months

End point values	Placebo BID plus WBRT	Veliparib 50 mg BID plus WBRT	Veliparib 200 mg BID plus WBRT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	103	102	
Units: percentage of subjects				
number (confidence interval 95%)	41.2 (31.5 to 51.4)	36.9 (27.6 to 47)	42.2 (32.4 to 52.3)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The P-value was calculated based on Cochran-Mantel-Haenszel (CMH) test stratified by GPA score (≤2.5 or >2.5) at screening.

Comparison groups	Placebo BID plus WBRT v Veliparib 50 mg BID plus WBRT
Number of subjects included in analysis	205
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.535
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The P-value was calculated based on CMH test stratified by GPA score (≤2.5 or >2.5) at screening.

Comparison groups	Placebo BID plus WBRT v Veliparib 200 mg BID plus WBRT

Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.898
Method	Cochran-Mantel-Haenszel

Secondary: Intracranial Progression (Radiographic): Percentage of Participants with an Event

End point title	Intracranial Progression (Radiographic): Percentage of Participants with an Event

End point description:

Time to intracranial progression (radiographic) was defined as the number of days from the date of randomization to the date of the subject's first experience of intracranial progression, as determined by brain scan imaging (magnetic resonance image [MRI]/ computed tomography [CT] scan) by a central imaging vendor. All confirmed events of intracranial progression were included, regardless of whether the event occurred while the subject was still taking study treatment or had previously discontinued study treatment. If the subject did not have a confirmed event of intracranial progression, the subject's data were censored at the date of the subject's last available intracranial progression assessment.

End point type	Secondary

End point timeframe:

From randomization up to 24 months

End point values	Placebo BID plus WBRT	Veliparib 50 mg BID plus WBRT	Veliparib 200 mg BID plus WBRT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	103	102	
Units: percentage of subjects				
number (not applicable)	25.5	34	31.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Intracranial Progression (Radiographic): Time to Event

End point title	Intracranial Progression (Radiographic): Time to Event

End point description:

Time to intracranial progression (radiographic) was defined as the number of days from the date of randomization to the date of the subject's first experience of intracranial progression, as determined by brain scan imaging (magnetic resonance image [MRI]/ computed tomography [CT] scan) by a central imaging vendor. All confirmed events of intracranial progression were included, regardless of whether the event occurred while the subject was still taking study treatment or had previously discontinued study treatment. If the subject did not have a confirmed event of intracranial progression, the subject's data were censored at the date of the subject's last available intracranial progression assessment. Time to intracranial progression (radiographic) was estimated for each treatment group using Kaplan-Meier methodology. 9999 represents data not calculable.

End point type	Secondary

End point timeframe:

From randomization up to 24 months

End point values	Placebo BID plus WBRT	Veliparib 50 mg BID plus WBRT	Veliparib 200 mg BID plus WBRT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	103	102	
Units: days				
median (confidence interval 95%)	259 (184 to 9999)	226 (147 to 360)	224 (137 to 358)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
The P-value was calculated based on Log-rank test stratified by GPA score (≤2.5 or >2.5) at screening.	
Comparison groups	Placebo BID plus WBRT v Veliparib 50 mg BID plus WBRT
Number of subjects included in analysis	205
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.314
Method	Logrank

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
The P-value was calculated based on Cox proportional hazard model stratified by GPA score (≤2.5 or >2.5) at screening.	
Comparison groups	Placebo BID plus WBRT v Veliparib 50 mg BID plus WBRT
Number of subjects included in analysis	205
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.313
Method	Cox proportional hazard model
Parameter estimate	Cox proportional hazard
Point estimate	1.301
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	2.186

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

The P-value was calculated based on Log-rank test stratified by GPA score (≤2.5 or >2.5) at screening.

Comparison groups	Placebo BID plus WBRT v Veliparib 200 mg BID plus WBRT
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.536
Method	Logrank

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

The P-value was calculated based on Cox proportional hazard model stratified by GPA score (≤2.5 or >2.5) at screening.

Comparison groups	Placebo BID plus WBRT v Veliparib 200 mg BID plus WBRT
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.354
Method	Cox proportional hazard model
Parameter estimate	Cox proportional hazard
Point estimate	1.181
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.698
upper limit	1.999

Secondary: Clinical Brain Metastasis Progression: Percentage of Participants with an Event

End point title	Clinical Brain Metastasis Progression: Percentage of Participants with an Event

End point description:

Time to clinical brain metastases progression was defined as the number of days from randomization to the date of the subject's first experience of clinical brain metastases progression, as assessed by a team of neuro-oncology experts (Event Review Board). All events of clinical brain metastasis progression were included, regardless of whether the event occurred while the subject was still receiving study treatment or had previously discontinued study treatment. If a subject did not have an event of clinical brain metastases progression, the subject's data were censored at the date of the subject's last available clinical disease progression assessment.

End point type	Secondary

End point timeframe:

From randomization up to 24 months

End point values	Placebo BID plus WBRT	Veliparib 50 mg BID plus WBRT	Veliparib 200 mg BID plus WBRT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	103	102	
Units: percentage of subjects				
number (not applicable)	28.4	74.8	71.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Brain Metastasis Progression: Time to Event

End point title	Clinical Brain Metastasis Progression: Time to Event

End point description:

Time to clinical brain metastases progression was defined as the number of days from randomization to the date of the subject's first experience of clinical brain metastases progression, as assessed by a team of neuro-oncology experts (Event Review Board). All events of clinical brain metastasis progression were included, regardless of whether the event occurred while the subject was still receiving study treatment or had previously discontinued study treatment. If a subject did not have an event of clinical brain metastases progression, the subject's data were censored at the date of the subject's last available clinical disease progression assessment. Time to clinical brain metastasis progression was estimated for each treatment group using Kaplan-Meier methodology. 9999 represents data not calculable.

End point type	Secondary

End point timeframe:

From randomization up to 24 months

End point values	Placebo BID plus WBRT	Veliparib 50 mg BID plus WBRT	Veliparib 200 mg BID plus WBRT	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	103	102	
Units: days				
median (confidence interval 95%)	348 (216 to 9999)	286 (192 to 9999)	255 (204 to 342)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The P-value was calculated based on Log-rank test stratified by GPA score (≤2.5 or >2.5) at screening.

Comparison groups	Placebo BID plus WBRT v Veliparib 50 mg BID plus WBRT

Number of subjects included in analysis	205
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.864
Method	Logrank

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The P-value was calculated based on Cox proportional hazard model stratified by GPA score (≤2.5 or >2.5) at screening.

Comparison groups	Placebo BID plus WBRT v Veliparib 50 mg BID plus WBRT
Number of subjects included in analysis	205
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.86
Method	Cox proportional hazard model
Parameter estimate	Cox proportional hazard
Point estimate	1.047
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.626
upper limit	1.754

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

The P-value was calculated based on Log-rank test stratified by GPA score (≤2.5 or >2.5) at screening.

Comparison groups	Placebo BID plus WBRT v Veliparib 200 mg BID plus WBRT
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.301
Method	Logrank

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

The P-value was calculated based on Cox proportional hazard model stratified by GPA score (≤2.5 or >2.5) at screening.

Comparison groups	Veliparib 200 mg BID plus WBRT v Placebo BID plus WBRT

Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.289
Method	Cox proportional hazard model
Parameter estimate	Cox proportional hazard
Point estimate	1.295
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.803
upper limit	2.086

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) were collected from first dose of study drug until 30 days following last dose of study drug (up to 7 weeks).

Adverse event reporting additional description:

Serious adverse events (SAEs) were collected after informed consent was obtained and before the first dose of study drug only if they were considered by the investigator to be causally related to study-required procedures (up to 11 weeks).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Placebo BID plus WBRT

Reporting group description:

Placebo for veliparib twice daily (BID) during whole brain radiation therapy (WBRT). Treatment with WBRT began on Day 1. All subjects received a total of 30.0 Gy of WBRT given in 10 daily fractions of 3.0 Gy, excluding weekends and holidays. WBRT could be interrupted for up to a total of 7 days; however, no more than 4 consecutive days of interruption was permitted.

Reporting group title	Veliparib 50 mg BID plus WBRT

Reporting group description:

Veliparib 50 mg twice daily (BID) during whole brain radiation therapy (WBRT). Treatment with WBRT began on Day 1. All subjects received a total of 30.0 Gy of WBRT given in 10 daily fractions of 3.0 Gy, excluding weekends and holidays. WBRT could be interrupted for up to a total of 7 days; however, no more than 4 consecutive days of interruption was permitted.

Reporting group title	Veliparib 200 mg BID plus WBRT

Reporting group description:

Veliparib 200 mg twice daily (BID) during whole brain radiation therapy (WBRT). Treatment with WBRT began on Day 1. All subjects received a total of 30.0 Gy of WBRT given in 10 daily fractions of 3.0 Gy, excluding weekends and holidays. WBRT could be interrupted for up to a total of 7 days; however, no more than 4 consecutive days of interruption was permitted.

Serious adverse events	Placebo BID plus WBRT	Veliparib 50 mg BID plus WBRT	Veliparib 200 mg BID plus WBRT
Total subjects affected by serious adverse events			
subjects affected / exposed	39 / 101 (38.61%)	31 / 103 (30.10%)	36 / 102 (35.29%)
number of deaths (all causes)	76	83	76
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intracranial tumour haemorrhage			
subjects affected / exposed	0 / 101 (0.00%)	1 / 103 (0.97%)	0 / 102 (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
Malignant neoplasm progression			

subjects affected / exposed	8 / 101 (7.92%)	10 / 103 (9.71%)	16 / 102 (15.69%)
occurrences causally related to treatment / all	0 / 9	2 / 11	0 / 16
deaths causally related to treatment / all	0 / 7	2 / 9	0 / 13
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 101 (0.00%)	0 / 103 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis			
subjects affected / exposed	0 / 101 (0.00%)	1 / 103 (0.97%)	0 / 102 (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
Thrombosis			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 101 (1.98%)	0 / 103 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Mucosal inflammation			
subjects affected / exposed	0 / 101 (0.00%)	1 / 103 (0.97%)	0 / 102 (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
Pain			
subjects affected / exposed	3 / 101 (2.97%)	0 / 103 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 101 (0.00%)	0 / 103 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 101 (0.00%)	1 / 103 (0.97%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 101 (0.00%)	0 / 103 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	0 / 102 (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
Interstitial lung disease			
subjects affected / exposed	0 / 101 (0.00%)	1 / 103 (0.97%)	0 / 102 (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
Pleural effusion			
subjects affected / exposed	1 / 101 (0.99%)	1 / 103 (0.97%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 101 (0.00%)	1 / 103 (0.97%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 101 (0.00%)	1 / 103 (0.97%)	0 / 102 (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

Pulmonary artery thrombosis			
subjects affected / exposed	0 / 101 (0.00%)	0 / 103 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pulmonary embolism			
subjects affected / exposed	1 / 101 (0.99%)	3 / 103 (2.91%)	2 / 102 (1.96%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 101 (0.00%)	1 / 103 (0.97%)	0 / 102 (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
Respiratory failure			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 101 (0.00%)	0 / 103 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 101 (0.00%)	1 / 103 (0.97%)	0 / 102 (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
Lower limb fracture			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	0 / 102 (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
Cardiac disorders			
Bradycardia			

subjects affected / exposed	0 / 101 (0.00%)	1 / 103 (0.97%)	0 / 102 (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
Pericardial effusion			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	0 / 102 (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
Nervous system disorders			
Altered state of consciousness			
subjects affected / exposed	0 / 101 (0.00%)	0 / 103 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain oedema			
subjects affected / exposed	4 / 101 (3.96%)	0 / 103 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 101 (0.00%)	1 / 103 (0.97%)	0 / 102 (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
Convulsion			
subjects affected / exposed	3 / 101 (2.97%)	0 / 103 (0.00%)	2 / 102 (1.96%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dementia			
subjects affected / exposed	0 / 101 (0.00%)	1 / 103 (0.97%)	0 / 102 (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
Haemorrhagic stroke			
subjects affected / exposed	0 / 101 (0.00%)	0 / 103 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hemiplegia			

subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	0 / 102 (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
Ischaemic stroke			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	0 / 102 (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
Nerve compression			
subjects affected / exposed	0 / 101 (0.00%)	1 / 103 (0.97%)	0 / 102 (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
Status epilepticus			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	0 / 102 (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
Vasogenic cerebral oedema			
subjects affected / exposed	0 / 101 (0.00%)	1 / 103 (0.97%)	0 / 102 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	0 / 102 (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
Thrombocytopenia			
subjects affected / exposed	0 / 101 (0.00%)	0 / 103 (0.00%)	2 / 102 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			

subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	0 / 102 (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
Dyspepsia			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	0 / 102 (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
Gastric perforation			
subjects affected / exposed	0 / 101 (0.00%)	0 / 103 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	0 / 102 (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
Nausea			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	0 / 102 (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
Proctalgia			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	2 / 102 (1.96%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	0 / 102 (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			

Muscular weakness			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	0 / 102 (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
Infections and infestations			
Bacterial infection			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	0 / 102 (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
Lower respiratory tract infection			
subjects affected / exposed	0 / 101 (0.00%)	1 / 103 (0.97%)	0 / 102 (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
Lung infection			
subjects affected / exposed	2 / 101 (1.98%)	1 / 103 (0.97%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nosocomial infection			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	0 / 102 (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
Oral candidiasis			
subjects affected / exposed	0 / 101 (0.00%)	1 / 103 (0.97%)	0 / 102 (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
Oral fungal infection			
subjects affected / exposed	0 / 101 (0.00%)	1 / 103 (0.97%)	0 / 102 (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
Pneumonia			
subjects affected / exposed	8 / 101 (7.92%)	3 / 103 (2.91%)	3 / 102 (2.94%)
occurrences causally related to treatment / all	0 / 8	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 1
Pneumonia streptococcal			

subjects affected / exposed	0 / 101 (0.00%)	1 / 103 (0.97%)	0 / 102 (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
Sepsis			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 101 (0.00%)	0 / 103 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 101 (0.99%)	0 / 103 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 101 (0.00%)	0 / 103 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo BID plus WBRT	Veliparib 50 mg BID plus WBRT	Veliparib 200 mg BID plus WBRT
Total subjects affected by non-serious adverse events			
subjects affected / exposed	78 / 101 (77.23%)	76 / 103 (73.79%)	77 / 102 (75.49%)
Injury, poisoning and procedural complications			
Radiation skin injury			
subjects affected / exposed	5 / 101 (4.95%)	5 / 103 (4.85%)	6 / 102 (5.88%)
occurrences (all)	5	5	6

Nervous system disorders			
Dizziness			
subjects affected / exposed	11 / 101 (10.89%)	8 / 103 (7.77%)	10 / 102 (9.80%)
occurrences (all)	11	8	11
Dysgeusia			
subjects affected / exposed	7 / 101 (6.93%)	4 / 103 (3.88%)	2 / 102 (1.96%)
occurrences (all)	7	4	2
Headache			
subjects affected / exposed	15 / 101 (14.85%)	18 / 103 (17.48%)	21 / 102 (20.59%)
occurrences (all)	20	21	22
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	2 / 101 (1.98%)	4 / 103 (3.88%)	6 / 102 (5.88%)
occurrences (all)	2	4	8
Constipation			
subjects affected / exposed	11 / 101 (10.89%)	10 / 103 (9.71%)	11 / 102 (10.78%)
occurrences (all)	11	10	11
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	11 / 101 (10.89%)	9 / 103 (8.74%)	13 / 102 (12.75%)
occurrences (all)	13	9	16
Fatigue			
subjects affected / exposed	20 / 101 (19.80%)	27 / 103 (26.21%)	21 / 102 (20.59%)
occurrences (all)	23	30	25
Pyrexia			
subjects affected / exposed	7 / 101 (6.93%)	7 / 103 (6.80%)	4 / 102 (3.92%)
occurrences (all)	9	8	4
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	8 / 101 (7.92%)	8 / 103 (7.77%)	7 / 102 (6.86%)
occurrences (all)	9	9	7
Nausea			
subjects affected / exposed	29 / 101 (28.71%)	23 / 103 (22.33%)	32 / 102 (31.37%)
occurrences (all)	30	25	35
Vomiting			

subjects affected / exposed	14 / 101 (13.86%)	5 / 103 (4.85%)	9 / 102 (8.82%)
occurrences (all)	17	5	11
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 101 (5.94%)	6 / 103 (5.83%)	2 / 102 (1.96%)
occurrences (all)	6	6	2
Dyspnoea			
subjects affected / exposed	14 / 101 (13.86%)	7 / 103 (6.80%)	10 / 102 (9.80%)
occurrences (all)	19	7	10
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	19 / 101 (18.81%)	15 / 103 (14.56%)	15 / 102 (14.71%)
occurrences (all)	19	15	15
Rash			
subjects affected / exposed	2 / 101 (1.98%)	6 / 103 (5.83%)	7 / 102 (6.86%)
occurrences (all)	2	6	7
Psychiatric disorders			
Anxiety			
subjects affected / exposed	8 / 101 (7.92%)	6 / 103 (5.83%)	2 / 102 (1.96%)
occurrences (all)	8	6	2
Insomnia			
subjects affected / exposed	11 / 101 (10.89%)	10 / 103 (9.71%)	6 / 102 (5.88%)
occurrences (all)	11	10	6
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	6 / 101 (5.94%)	7 / 103 (6.80%)	4 / 102 (3.92%)
occurrences (all)	6	7	4
Infections and infestations			
Oral candidiasis			
subjects affected / exposed	7 / 101 (6.93%)	3 / 103 (2.91%)	5 / 102 (4.90%)
occurrences (all)	7	3	5
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	14 / 101 (13.86%)	11 / 103 (10.68%)	15 / 102 (14.71%)
occurrences (all)	16	12	16

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 March 2013	The primary purpose of this amendment was to allow for broader eligibility while maintaining subject characteristics consistent with the trial intent (e.g., subjects with diagnosed brain metastases from NSCLC who were eligible for WBRT). The changes included inclusion (CT scan of brain with or without contrast could be obtained is subject was medically ineligible for MRI) and exclusion criteria (subjects could begin treatment within 28 days instead of 21 days; removed requirement for GPA score ≤1 since the subject population was > 60 years, had multiple brain metastases, and had presence of NSCLC outside the brain); clarified procedures and timing; and increased the number of sites from 100 to 120.
08 October 2014	The study was terminated by AbbVie prior to any sites executing the study under Amendment No. 2. The primary purpose of this amendment was to include additional neurological assessments beyond the Month 24 Visit (up to Month 48) at the request of the European Medicines Agency in order to analyze if veliparib may have any long-term effect on a subject's neurological function.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported