



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 | | |
| Native 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 $\alpha = 0.05$. 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 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 $\alpha = 0.05$. 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 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 |
| Gastroesophageal 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 occurrences (all) | 14 / 101 (13.86%) 17 | 5 / 103 (4.85%) 5 | 9 / 102 (8.82%) 11 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 6 / 101 (5.94%) 6 | 6 / 103 (5.83%) 6 | 2 / 102 (1.96%) 2 |
| Dyspnoea subjects affected / exposed occurrences (all) | 14 / 101 (13.86%) 19 | 7 / 103 (6.80%) 7 | 10 / 102 (9.80%) 10 |
| Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) | 19 / 101 (18.81%) 19 | 15 / 103 (14.56%) 15 | 15 / 102 (14.71%) 15 |
| Rash subjects affected / exposed occurrences (all) | 2 / 101 (1.98%) 2 | 6 / 103 (5.83%) 6 | 7 / 102 (6.86%) 7 |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 8 / 101 (7.92%) 8 | 6 / 103 (5.83%) 6 | 2 / 102 (1.96%) 2 |
| Insomnia subjects affected / exposed occurrences (all) | 11 / 101 (10.89%) 11 | 10 / 103 (9.71%) 10 | 6 / 102 (5.88%) 6 |
| Musculoskeletal and connective tissue disorders Muscular weakness subjects affected / exposed occurrences (all) | 6 / 101 (5.94%) 6 | 7 / 103 (6.80%) 7 | 4 / 102 (3.92%) 4 |
| Infections and infestations Oral candidiasis subjects affected / exposed occurrences (all) | 7 / 101 (6.93%) 7 | 3 / 103 (2.91%) 3 | 5 / 102 (4.90%) 5 |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 14 / 101 (13.86%) 16 | 11 / 103 (10.68%) 12 | 15 / 102 (14.71%) 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 if 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