



Clinical trial results:

A Phase 1b/2 study to assess the safety, tolerability and efficacy of BGB-290 in combination with radiation therapy and/or temozolomide in subjects with first-line or recurrent/refractory glioblastoma

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2017-001554-33 |
| Trial protocol | NL |
| Global end of trial date | 17 March 2021 |

Results information

| | |
|--------------------------------|--|
| Result version number | v2 (current) |
| This version publication date | 22 June 2022 |
| First version publication date | 19 March 2022 |
| Version creation reason | • Correction of full data set Time frame needed to be changed |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | BGB-290-104 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03150862 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | BeiGene, Ltd |
| Sponsor organisation address | 2955 Campus Drive, Suite 200, San Mateo, CA , United States, 94403 |
| Public contact | Clinical Trial Information Email, BeiGene USA, Inc., +1 877-828-5568 , clinicaltrials@beigene.com |
| Scientific contact | Clinical Trial Information Email, BeiGene USA, Inc., +1 877-828-5568 , clinicaltrials@beigene.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 | 13 April 2021 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 17 March 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

PHASE 1:

1) Arm A:

- To assess safety and tolerability of BGB-290 combined with RT
- To identify dose-limiting toxicity (DLT) and determine the maximum tolerated dose (MTD) or maximum administered dose (MAD) for BGB-290 combined with RT
- To select the recommended Phase 2 schedule for full-dose BGB 290 combined with RT

2) Arm B:

- To assess safety and tolerability of BGB-290 combined with RT and TMZ
- To identify DLTs and determine the MTD or MAD for TMZ combined with RT and the MTD/MAD for BGB-290 of Arm A
- To select the RP2D for TMZ combined with RT and the MTD/MAD for BGB-290 of Arm A

3) Arm C:

- To assess safety and tolerability of BGB-290 combined with TMZ
- To identify DLTs and determine the MTD or MAD for TMZ combined with full-dose BGB-290
- To select the RP2D for TMZ combined with full-dose BGB 290

PHASE 2:

To assess the efficacy of BGB-290 combined with:

1) RT (Arm A)

2) RT and TMZ (Arm B)

3) TMZ (Arm C)

Protection of trial subjects:

This study was conducted in accordance with Sponsor procedures, which comply with the principles of Good Clinical Practice, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guidelines, the Declaration of Helsinki, and local regulatory requirements.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 24 July 2017 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Netherlands: 4 |
| Country: Number of subjects enrolled | Switzerland: 1 |
| Country: Number of subjects enrolled | United States: 111 |

| | |
|------------------------------------|-----|
| Worldwide total number of subjects | 116 |
| EEA total number of subjects | 4 |

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) | 84 |
| From 65 to 84 years | 31 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details:

This study was conducted in 20 centers and 116 participants were treated.

Pre-assignment

Screening details:

This study consisted of a dose escalation phase and a dose expansion phase. A total of 116 participants were recruited in Netherlands, Switzerland and United States.

Period 1

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

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Arm A: Dose Escalation (DE) - Pamiparib 2Wks + RT 6 Wks |

Arm description:

Participants with newly diagnosed unmethylated glioblastoma (GBM) received 60 milligrams (mg) pamiparib orally twice daily (BID) for 2 weeks in combination with up to 60 Gy radiation for 6 weeks

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Pamiparib |
| Investigational medicinal product code | BGB-290 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

60 mg pamiparib BID for 2 weeks in combination with up to 60 Gy radiation for 6 weeks

| | |
|------------------|--------------------------------------|
| Arm title | Arm A: DE-Pamiparib 4 Wks + RT 6 Wks |
|------------------|--------------------------------------|

Arm description:

Participants with newly diagnosed unmethylated GBM received 60 mg pamiparib orally for 4 weeks in combination with up to 60 Gy radiation for 6 weeks

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Pamiparib |
| Investigational medicinal product code | BGB-290 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

60 mg pamiparib BID for 4 weeks in combination with up to 60 Gy radiation for 6 weeks

| | |
|------------------|--------------------------------------|
| Arm title | Arm A: DE- Pamiparib 6Wks + RT 6 Wks |
|------------------|--------------------------------------|

Arm description:

Participants with newly diagnosed unmethylated GBM received 60 mg pamiparib orally for 6 weeks in combination with up to 60 Gy radiation for 6 weeks

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|---|--|
| Investigational medicinal product name | Pamiparib |
| Investigational medicinal product code | BGB-290 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 60 mg pamiparib BID for 6 weeks in combination with up to 60 Gy radiation for 6 weeks | |
| Arm title | Arm A: Dose Expansion (E) - Pamiparib 6 Wks + RT 6 Wks |
| Arm description: | |
| Participants with newly diagnosed unmethylated GBM received 60 mg pamiparib orally for 6 weeks in combination with up to 60 Gy radiation for 6 weeks | |
| Arm type | Experimental |
| Investigational medicinal product name | Pamiparib |
| Investigational medicinal product code | BGB-290 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 60 mg pamiparib BID for 6 weeks in combination with up to 60 Gy radiation for 6 weeks | |
| Arm title | Arm B: DE-Pamiparib 6 Wks + RT 6 Wks + + Temozolomide |
| Arm description: | |
| Participants with newly diagnosed unmethylated GBM received 60 mg pamiparib orally for 6 weeks in combination with up to 60 Gy radiation for 6 weeks and 60 mg temozolomide Wks 1 and 5 | |
| Arm type | Experimental |
| Investigational medicinal product name | Pamiparib |
| Investigational medicinal product code | BGB-290 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 60 mg pamiparib BID for 6 weeks in combination with up to 60 Gy radiation for 6 weeks | |
| Investigational medicinal product name | Temozolomide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 60 mg temozolomide wks 1 and 5 | |
| Arm title | Arm C: DE – Pamiparib + Temozolomide 20 mg |
| Arm description: | |
| Participants with both methylated and unmethylated recurrent/refractory GBM received 60 mg pamiparib BID and 20 mg temozolomide once daily orally from Day 1 to Day 21 | |
| Arm type | Experimental |
| Investigational medicinal product name | Pamiparib |
| Investigational medicinal product code | BGB-290 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 60 mg pamiparib BID for 6weeks in combination with up to 60 Gy radiation for 6 weeks | |

| | |
|--|--------------|
| Investigational medicinal product name | Temozolomide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

temozolomide 40 mg once daily from Day 1 to day 21

| | |
|------------------|--|
| Arm title | Arm C: DE – Pamiparib + Temozolomide 40 mg |
|------------------|--|

Arm description:

Participants with both methylated and unmethylated recurrent/refractory GBM received 60 mg pamiparib BID and 40 mg temozolomide once daily orally from Day 1 to Day 21

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

Dosage and administration details:

temozolomide 40 mg once daily from Day 1 to day 21

| | |
|------------------|--|
| Arm title | Arm C: E- Pamiparib + Temozolomide 60 mg |
|------------------|--|

Arm description:

Participants with both methylated and unmethylated recurrent/refractory GBM received 60 mg pamiparib BID and 60 mg temozolomide once daily orally from Day 1 to Day 7

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

Dosage and administration details:

temozolomide 60 mg once daily from Day 1 to day 21

| Number of subjects in period 1 | Arm A: Dose Escalation (DE) - Pamiparib 2Wks + RT 6 Wks | Arm A: DE- Pamiparib 4 Wks + RT 6 Wks | Arm A: DE- Pamiparib 6Wks + RT 6 Wks |
|---------------------------------------|---|---------------------------------------|--------------------------------------|
| Started | 3 | 8 | 9 |
| Completed | 0 | 0 | 0 |
| Not completed | 3 | 8 | 9 |
| Consent withdrawn by subject | 1 | 1 | - |
| Sponsor's Decision | - | - | - |
| Roll-Over to Long term | - | - | - |
| Death | 2 | 7 | 8 |
| Progressive Disease | - | - | - |
| Lost to follow-up | - | - | 1 |
| Change in Methylation status | - | - | - |

| Number of subjects in period 1 | Arm A: Dose Expansion (E) - Pamiparib 6 Wks + RT 6 Wks | Arm B: DE- Pamiparib 6 Wks + RT 6 Wks + + Temozolomide | Arm C: DE – Pamiparib + Temozolomide 20 mg |
|---------------------------------------|--|--|--|
| Started | 40 | 9 | 9 |
| Completed | 0 | 0 | 0 |
| Not completed | 40 | 9 | 9 |
| Consent withdrawn by subject | 3 | 1 | 1 |
| Sponsor's Decision | 10 | 3 | - |
| Roll-Over to Long term | - | - | - |
| Death | 27 | 4 | 8 |
| Progressive Disease | - | - | - |
| Lost to follow-up | - | - | - |
| Change in Methylation status | - | 1 | - |

| Number of subjects in period 1 | Arm C: DE – Pamiparib + Temozolomide 40 mg | Arm C: E- Pamiparib + Temozolomide 60 mg |
|---------------------------------------|--|--|
| Started | 8 | 30 |
| Completed | 0 | 0 |
| Not completed | 8 | 30 |
| Consent withdrawn by subject | 1 | 3 |
| Sponsor's Decision | 1 | 1 |
| Roll-Over to Long term | - | 1 |
| Death | 6 | 21 |
| Progressive Disease | - | 2 |
| Lost to follow-up | - | 2 |
| Change in Methylation status | - | - |

Baseline characteristics

Reporting groups

| | |
|--|---|
| Reporting group title | Arm A: Dose Escalation (DE) - Pamiparib 2Wks + RT 6 Wks |
| Reporting group description: | |
| Participants with newly diagnosed unmethylated glioblastoma (GBM) received 60 milligrams (mg) pamiparib orally twice daily (BID) for 2 weeks in combination with up to 60 Gy radiation for 6 weeks | |
| Reporting group title | Arm A: DE-Pamiparib 4 Wks + RT 6 Wks |
| Reporting group description: | |
| Participants with newly diagnosed unmethylated GBM received 60 mg pamiparib orally for 4 weeks in combination with up to 60 Gy radiation for 6 weeks | |
| Reporting group title | Arm A: DE- Pamiparib 6Wks + RT 6 Wks |
| Reporting group description: | |
| Participants with newly diagnosed unmethylated GBM received 60 mg pamiparib orally for 6 weeks in combination with up to 60 Gy radiation for 6 weeks | |
| Reporting group title | Arm A: Dose Expansion (E) - Pamiparib 6 Wks + RT 6 Wks |
| Reporting group description: | |
| Participants with newly diagnosed unmethylated GBM received 60 mg pamiparib orally for 6 weeks in combination with up to 60 Gy radiation for 6 weeks | |
| Reporting group title | Arm B: DE-Pamiparib 6 Wks + RT 6 Wks + + Temozolomide |
| Reporting group description: | |
| Participants with newly diagnosed unmethylated GBM received 60 mg pamiparib orally for 6 weeks in combination with up to 60 Gy radiation for 6 weeks and 60 mg temozolomide Wks 1 and 5 | |
| Reporting group title | Arm C: DE – Pamiparib + Temozolomide 20 mg |
| Reporting group description: | |
| Participants with both methylated and unmethylated recurrent/refractory GBM received 60 mg pamiparib BID and 20 mg temozolomide once daily orally from Day 1 to Day 21 | |
| Reporting group title | Arm C: DE – Pamiparib + Temozolomide 40 mg |
| Reporting group description: | |
| Participants with both methylated and unmethylated recurrent/refractory GBM received 60 mg pamiparib BID and 40 mg temozolomide once daily orally from Day 1 to Day 21 | |
| Reporting group title | Arm C: E- Pamiparib + Temozolomide 60 mg |
| Reporting group description: | |
| Participants with both methylated and unmethylated recurrent/refractory GBM received 60 mg pamiparib BID and 60 mg temozolomide once daily orally from Day 1 to Day 7 | |

| Reporting group values | Arm A: Dose Escalation (DE) - Pamiparib 2Wks + RT 6 Wks | Arm A: DE- Pamiparib 4 Wks + RT 6 Wks | Arm A: DE- Pamiparib 6Wks + RT 6 Wks |
|---|---|---------------------------------------|--------------------------------------|
| Number of subjects | 3 | 8 | 9 |
| Age categorical Units: Subjects | | | |
| Age continuous Units: years arithmetic mean standard deviation | 59.7 ± 8.39 | 63.4 ± 8.80 | 58.8 ± 7.66 |
| Gender categorical Units: Subjects | | | |
| Female | 0 | 1 | 2 |
| Male | 3 | 7 | 7 |

| | | | |
|---|---|---|---|
| Race/Ethnicity, Customized Units: Subjects | | | |
| Asian | 0 | 0 | 1 |
| Black or African American | 0 | 1 | 1 |
| White | 3 | 7 | 7 |
| Unknown/Not Reported | 0 | 0 | 0 |

| | | | |
|------------------------------------|--|--|--|
| Reporting group values | Arm A: Dose Expansion (E) - Pamiparib 6 Wks + RT 6 Wks | Arm B: DE- Pamiparib 6 Wks + RT 6 Wks + + Temozolomide | Arm C: DE - Pamiparib + Temozolomide 20 mg |
| Number of subjects | 40 | 9 | 9 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|---------|--------|---------|
| Age continuous Units: years | | | |
| arithmetic mean | 56.7 | 60.9 | 49.2 |
| standard deviation | ± 13.48 | ± 9.94 | ± 12.63 |
| Gender categorical Units: Subjects | | | |
| Female | 17 | 4 | 1 |
| Male | 23 | 5 | 8 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Asian | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 1 |
| White | 38 | 9 | 7 |
| Unknown/Not Reported | 2 | 0 | 1 |

| | | | |
|------------------------------------|--|--|-------|
| Reporting group values | Arm C: DE - Pamiparib + Temozolomide 40 mg | Arm C: E- Pamiparib + Temozolomide 60 mg | Total |
| Number of subjects | 8 | 30 | 116 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|---------|---------|-----|
| Age continuous Units: years | | | |
| arithmetic mean | 49.1 | 58.6 | |
| standard deviation | ± 15.51 | ± 10.54 | - |
| Gender categorical Units: Subjects | | | |
| Female | 4 | 10 | 39 |
| Male | 4 | 20 | 77 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Asian | 0 | 1 | 2 |
| Black or African American | 0 | 0 | 3 |
| White | 8 | 27 | 106 |
| Unknown/Not Reported | 0 | 2 | 5 |

End points

End points reporting groups

| | |
|--|---|
| Reporting group title | Arm A: Dose Escalation (DE) - Pamiparib 2Wks + RT 6 Wks |
| Reporting group description: Participants with newly diagnosed unmethylated glioblastoma (GBM) received 60 milligrams (mg) pamiparib orally twice daily (BID) for 2 weeks in combination with up to 60 Gy radiation for 6 weeks | |
| Reporting group title | Arm A: DE-Pamiparib 4 Wks + RT 6 Wks |
| Reporting group description: Participants with newly diagnosed unmethylated GBM received 60 mg pamiparib orally for 4 weeks in combination with up to 60 Gy radiation for 6 weeks | |
| Reporting group title | Arm A: DE- Pamiparib 6Wks + RT 6 Wks |
| Reporting group description: Participants with newly diagnosed unmethylated GBM received 60 mg pamiparib orally for 6 weeks in combination with up to 60 Gy radiation for 6 weeks | |
| Reporting group title | Arm A: Dose Expansion (E) - Pamiparib 6 Wks + RT 6 Wks |
| Reporting group description: Participants with newly diagnosed unmethylated GBM received 60 mg pamiparib orally for 6 weeks in combination with up to 60 Gy radiation for 6 weeks | |
| Reporting group title | Arm B: DE-Pamiparib 6 Wks + RT 6 Wks + + Temozolomide |
| Reporting group description: Participants with newly diagnosed unmethylated GBM received 60 mg pamiparib orally for 6 weeks in combination with up to 60 Gy radiation for 6 weeks and 60 mg temozolomide Wks 1 and 5 | |
| Reporting group title | Arm C: DE – Pamiparib + Temozolomide 20 mg |
| Reporting group description: Participants with both methylated and unmethylated recurrent/refractory GBM received 60 mg pamiparib BID and 20 mg temozolomide once daily orally from Day 1 to Day 21 | |
| Reporting group title | Arm C: DE – Pamiparib + Temozolomide 40 mg |
| Reporting group description: Participants with both methylated and unmethylated recurrent/refractory GBM received 60 mg pamiparib BID and 40 mg temozolomide once daily orally from Day 1 to Day 21 | |
| Reporting group title | Arm C: E- Pamiparib + Temozolomide 60 mg |
| Reporting group description: Participants with both methylated and unmethylated recurrent/refractory GBM received 60 mg pamiparib BID and 60 mg temozolomide once daily orally from Day 1 to Day 7 | |

Primary: Phase 1b Escalation Phase: Number of Participants with Dose-Limiting Toxicities (DLTs) as assessed by CTCAE

| | |
|---|---|
| End point title | Phase 1b Escalation Phase: Number of Participants with Dose-Limiting Toxicities (DLTs) as assessed by CTCAE ^{[1][2]} |
| End point description: A DLT is defined as one of the following toxicities occurring during the DLT assessment window: Grade ≥3 non-hematologic, non-hepatic major organ adverse event (AE) Grade 4 neutropenia lasting >7 days Grade ≥3 febrile neutropenia Grade 3 thrombocytopenia with clinically significant bleeding Grade 4 thrombocytopenia lasting > 3 days and requiring transfusion, or any decreased platelet count <15,000/mm ³ / <15.0 x 10 ⁹ /L Grade ≥4 anemia Grade ≥3 total bilirubin or hepatic transaminases (ALT [SGPT] or AST [SGOT]) | |
| End point type | Primary |
| End point timeframe: Arm A: Day 1 Pamiparib dose until 4 weeks after the last RT; Arm B: Day 1 of Pamiparib and Temozolomide until 4 | |

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: Endpoint is descriptive and no statistical analyses were performed per protocol

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: DLTs were collected only for escalation phase per protocol

| End point values | Arm A: Dose Escalation (DE) - Pamiparib 2Wks + RT 6 Wks | Arm A: DE-Pamiparib 4 Wks + RT 6 Wks | Arm A: DE-Pamiparib 6Wks + RT 6 Wks | Arm B: DE-Pamiparib 6 Wks + RT 6 Wks + + Temozolomide |
|-------------------------------|---|--------------------------------------|-------------------------------------|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 8 | 9 | 9 |
| Units: Number of participants | 0 | 0 | 2 | 1 |

| End point values | Arm C: DE - Pamiparib + Temozolomide 20 mg | Arm C: DE - Pamiparib + Temozolomide 40 mg | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 8 | | |
| Units: Number of participants | 0 | 3 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1b Escalation Phase: Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs) as Assessed by CTCAE

| | |
|-----------------|---|
| End point title | Phase 1b Escalation Phase: Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs) as Assessed by CTCAE ^[3] ^[4] |
|-----------------|---|

End point description:

Safety analysis Set;

A treatment-emergent adverse event (TEAE) is defined as an AE that had an onset date on or after first dose of study treatment or was worsening in severity from baseline (pretreatment) up to 30 days following permanent study treatment discontinuation or initiation of new anti-cancer therapy, whichever occurs first.

An SAE is any untoward medical occurrence that, at any dose meets at least one of the following criteria: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect, is considered a significant medical AE based on medical judgment. SAEs were collected from the day the participant signs the Informed Consent Form (ICF). SAEs were collected from the day the participant signs the Informed Consent Form (ICF).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From initiation of study treatment (for TEAE) or from the date informed consent has been signed (for SAE), until 30 days after last study treatment or initiation of new anticancer therapy, whichever occurs first

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Endpoint is descriptive and no statistical analyses were performed per protocol

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Phase 1b data are reported per protocol

| End point values | Arm A: Dose Escalation (DE) - Pamiparib 2Wks + RT 6 Wks | Arm A: DE-Pamiparib 4 Wks + RT 6 Wks | Arm A: DE-Pamiparib 6Wks + RT 6 Wks | Arm B: DE-Pamiparib 6 Wks + RT 6 Wks + + Temozolomide |
|-----------------------------------|---|--------------------------------------|-------------------------------------|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 8 | 9 | 9 |
| Units: Number of participants | | | | |
| Participants with At Least 1 TEAE | 3 | 8 | 9 | 9 |
| TEAE with Grade 3 or Higher | 1 | 3 | 4 | 4 |
| Treatment Emergent SAEs | 0 | 2 | 2 | 2 |
| TEAE Leading to Death | 0 | 0 | 0 | 0 |

| End point values | Arm C: DE - Pamiparib + Temozolomide 20 mg | Arm C: DE - Pamiparib + Temozolomide 40 mg | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 8 | | |
| Units: Number of participants | | | | |
| Participants with At Least 1 TEAE | 9 | 8 | | |
| TEAE with Grade 3 or Higher | 5 | 7 | | |
| Treatment Emergent SAEs | 4 | 3 | | |
| TEAE Leading to Death | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1b Escalation Phase Arm C: Number of Participants with Clinically Relevant Changes in Vital signs and Clinical Laboratory Measurements

| | |
|-----------------|--|
| End point title | Phase 1b Escalation Phase Arm C: Number of Participants with Clinically Relevant Changes in Vital signs and Clinical Laboratory Measurements ^{[5][6]} |
|-----------------|--|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From the date of first dose up to end of study (EOS) visit (up to 3 years and 7.5 months)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Endpoint is descriptive and no statistical analyses were performed per protocol

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Arms C data are reported per protocol.

| End point values | Arm C: DE – Pamiparib + Temozolomide 20 mg | Arm C: DE – Pamiparib + Temozolomide 40 mg | | |
|-------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 8 | | |
| Units: Number of Participants | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2 Arm A Expansion Phase: Modified Disease Control Rate as Assessed by Response Assessment in Neuro-Oncology (RANO) Criteria

| | |
|-----------------|---|
| End point title | Phase 2 Arm A Expansion Phase: Modified Disease Control Rate as Assessed by Response Assessment in Neuro-Oncology (RANO) Criteria ^{[7][8]} |
|-----------------|---|

End point description:

Modified DCR is defined as the percentage of participants with complete response (CR), partial response (PR) or stable disease (SD) per RANO criteria as the response assessment at the end-of-treatment (EOT) visit. The Efficacy Analysis Set includes participants in the Safety Analysis Set who had a tumor assessment at baseline and at End of Treatment unless discontinued treatment or study early due to disease progression or death prior to tumor assessment.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From the date of first dose up to EOS visit (3 years and 7.5 months)

Notes:

[7] - 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: Endpoint is descriptive and no statistical analyses were performed per protocol

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Arm A data are reported per protocol.

| End point values | Arm A: Dose Expansion (E) – Pamiparib 6 Wks + RT 6 Wks | | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 32 | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 65.6 (46.8 to 81.4) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2 Arm C: Objective Response Rate (ORR) as Assessed Using RANO Criteria

| | |
|-----------------|---|
| End point title | Phase 2 Arm C: Objective Response Rate (ORR) as Assessed Using RANO Criteria ^{[9][10]} |
|-----------------|---|

End point description:

ORR (objective response rate) is defined as percentage of participants with best overall response of CR or PR per RANO criteria (confirmed by a subsequent tumor assessment at least four weeks apart). The Efficacy Analysis Set includes participants in the Safety Analysis Set who had measurable disease at baseline and at least one postbaseline tumor assessment unless discontinued treatment or study early due to disease progression or death prior to tumor assessment.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From the date of first dose up to first documentation of disease progression while participant is alive (3 years and 7.5 months)

Notes:

[9] - 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: Endpoint is descriptive and no statistical analyses were performed per protocol

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Arms C data are reported per protocol.

| | | | | |
|-----------------------------------|---|--|--|--|
| End point values | Arm C: E-Pamiparib + Temozolomide 60 mg | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 28 | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 3 (2.3 to 28.2) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1b Arm C: Number of Cycles of Treatment Received by Participants

| | |
|-----------------|--|
| End point title | Phase 1b Arm C: Number of Cycles of Treatment Received by Participants ^{[11][12]} |
|-----------------|--|

End point description:

Data shows the percentage of participants who received treatment for the given number of cycles.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From the date of first dose up to EOS visit (up to 3 years and 7.5 months)

Notes:

[11] - 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: Endpoint is descriptive and no statistical analyses were performed per protocol

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Arm C data are reported per protocol.

| End point values | Arm C: DE – Pamiparib + Temozolomide 20 mg | Arm C: DE – Pamiparib + Temozolomide 40 mg | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 8 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| <1 cycle | 22.2 | 37.5 | | |
| 1 cycle | 44.4 | 0 | | |
| 2 cycles | 11.1 | 25.0 | | |
| 3 cycles | 0 | 12.5 | | |
| 4 cycles | 11.1 | 0 | | |
| 5 cycles | 11.1 | 0 | | |
| 6 cycles | 0 | 0 | | |
| 7 cycles | 0 | 0 | | |
| >7 cycles | 0 | 25.0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1b Arm C: Average Dose Intensity of Pamiparib And TMZ Received per Participant

| | |
|-----------------|--|
| End point title | Phase 1b Arm C: Average Dose Intensity of Pamiparib And TMZ Received per Participant ^{[13][14]} |
|-----------------|--|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From the date of first dose until EOS visit (up to 3 years and 7.5 months)

Notes:

[13] - 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: Endpoint is descriptive and no statistical analyses were performed per protocol

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Arm C data are reported per protocol.

| End point values | Arm C: DE – Pamiparib + Temozolomide 20 mg | Arm C: DE – Pamiparib + Temozolomide 40 mg | | |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 8 | | |
| Units: Milligrams/Day | | | | |
| arithmetic mean (standard deviation) | | | | |
| Pamiparib | 97.5 (± 25.41) | 107.6 (± 14.65) | | |
| TMZ | 13.6 (± 1.88) | 28.2 (± 10.80) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1B and Phase 2:Pharmacokinetics: Ctrough of Pamiparib

| | |
|------------------------|---|
| End point title | Phase 1B and Phase 2:Pharmacokinetics: Ctrough of Pamiparib |
| End point description: | The Pharmacokinetic Analysis Set includes all participants for whom valid pamiparib PK parameters can be estimated. Participants with available data were included in the analysis. |
| End point type | Secondary |
| End point timeframe: | Pre-dose, 2 hours post dose on Days 1 and 15 of radiation Therapy |

| End point values | Arm A: Dose Escalation (DE) - Pamiparib 2Wks + RT 6 Wks | Arm A: DE- Pamiparib 4 Wks + RT 6 Wks | Arm A: DE- Pamiparib 6Wks + RT 6 Wks | Arm A: Dose Expansion (E) - Pamiparib 6 Wks + RT 6 Wks |
|--------------------------------------|---|---------------------------------------|--------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 5 | 6 | 35 |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | 891.3 (± 444.51) | 1817.0 (± 1226.53) | 1848.3 (± 784.38) | 2239.9 (± 1011.07) |

| End point values | Arm B: DE- Pamiparib 6 Wks + RT 6 Wks + + Temozolomide | Arm C: DE – Pamiparib + Temozolomide 20 mg | Arm C: DE – Pamiparib + Temozolomide 40 mg | Arm C: E- Pamiparib + Temozolomide 60 mg |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 | 6 | 6 | 25 |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | 2134.3 (± 953.06) | 1893.3 (± 718.46) | 1550.8 (± 1422.55) | 1500.2 (± 943.35) |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b Arm A and Arm B Escalation Phase: Modified Disease Control Rate as Assessed by RANO Criteria

| | |
|-----------------|---|
| End point title | Phase 1b Arm A and Arm B Escalation Phase: Modified Disease Control Rate as Assessed by RANO Criteria ^[15] |
|-----------------|---|

End point description:

Modified DCR is defined as the percentage of participants with complete response (CR), partial response (PR) or stable disease (SD) per RANO criteria as the response assessment at the end-of-treatment (EOT) visit. Efficacy Analysis Set

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the date of first dose up to first documentation of disease progression while participant is alive (3 years and 7.5 months)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Arms a and B data are reported per protocol.

| End point values | Arm A: Dose Escalation (DE) - Pamiparib 2Wks + RT 6 Wks | Arm A: DE-Pamiparib 4 Wks + RT 6 Wks | Arm A: DE-Pamiparib 6Wks + RT 6 Wks | Arm B: DE-Pamiparib 6 Wks + RT 6 Wks + + Temozolomide |
|-----------------------------------|---|--------------------------------------|-------------------------------------|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 7 | 5 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 66.7 (9.4 to 99.2) | 100.0 (54.1 to 100.0) | 42.9 (9.9 to 81.6) | 80.0 (28.4 to 99.5) |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b Escalation Phase Arm C: Disease Control Rate as Assessed by RANO Criteria

| | |
|-----------------|--|
| End point title | Phase 1b Escalation Phase Arm C: Disease Control Rate as Assessed by RANO Criteria ^[16] |
|-----------------|--|

End point description:

DCR is defined as the percentage of participants with best overall response of CR, PR or SD per RANO criteria. CR or PR will be confirmed by a subsequent tumor assessment at least four weeks apart. Efficacy Analysis Set

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the date of first dose up to first documentation of disease progression while participant is alive (3 years and 7.5 months)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Arm C data are reported per protocol.

| End point values | Arm C: DE – Pamiparib + Temozolomide 20 mg | Arm C: DE – Pamiparib + Temozolomide 40 mg | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 7 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 55.6 (21.2 to 86.3) | 71.4 (29.0 to 96.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b and Phase 2 Arms A and B: ORR as Assessed Using RANO Criteria

| | |
|-----------------|--|
| End point title | Phase 1b and Phase 2 Arms A and B: ORR as Assessed Using RANO Criteria ^[17] |
|-----------------|--|

End point description:

ORR is defined as percentage of participants with best overall response of CR or PR per RANO criteria (confirmed by a subsequent tumor assessment at least four weeks apart). Efficacy Analysis Set

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the date of first dose up to first documentation of disease progression while participant is alive (3 years and 7.5 months)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Arms a and B data are reported per protocol.

| End point values | Arm A: Dose Escalation (DE) - Pamiparib 2Wks + RT 6 Wks | Arm A: DE- Pamiparib 4 Wks + RT 6 Wks | Arm A: DE- Pamiparib 6Wks + RT 6 Wks | Arm A: Dose Expansion (E) - Pamiparib 6 Wks + RT 6 Wks |
|-----------------------------------|---|---------------------------------------|--------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 7 | 32 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 0 (0.0 to 70.8) | 16.7 (0.4 to 64.1) | 0 (0.0 to 41.0) | 3.1 (0.1 to 16.2) |

| End point values | Arm B: DE- | | | |
|------------------|------------|--|--|--|
|------------------|------------|--|--|--|

| | | | | |
|-----------------------------------|--|--|--|--|
| | Pamiparib 6 Wks + RT 6 Wks + + Temozolomide | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 5 | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 0 (0.0 to 52.2) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b and Phase2 Arms A, B and C: Clinical Benefit Rate as Assessed Using RANO Criteria

| | |
|--|--|
| End point title | Phase 1b and Phase2 Arms A, B and C: Clinical Benefit Rate as Assessed Using RANO Criteria |
| End point description: | |
| Clinical benefit rate (CBR) is defined as the percentage of participants with best overall response of CR, PR or SD ≥ 24 weeks per RANO criteria (confirmed by a subsequent tumor assessment at least four weeks apart). Efficacy Analysis Set | |
| End point type | Secondary |
| End point timeframe: | |
| From the date of first dose up to first documentation of disease progression while participant is alive (3 years and 7.5 months) | |

| End point values | Arm A: Dose Escalation (DE) - Pamiparib 2Wks + RT 6 Wks | Arm A: DE- Pamiparib 4 Wks + RT 6 Wks | Arm A: DE- Pamiparib 6Wks + RT 6 Wks | Arm A: Dose Expansion (E) - Pamiparib 6 Wks + RT 6 Wks |
|-----------------------------------|---|---------------------------------------|--------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 7 | 32 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 0 (0.0 to 70.8) | 33.3 (4.3 to 77.7) | 0 (0.0 to 41.0) | 37.6 (21.1 to 56.34) |

| End point values | Arm B: DE- Pamiparib 6 Wks + RT 6 Wks + + Temozolomide | Arm C: DE - Pamiparib + Temozolomide 20 mg | Arm C: DE - Pamiparib + Temozolomide 40 mg | Arm C: E- Pamiparib + Temozolomide 60 mg |
|-----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 5 | 9 | 7 | 28 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 40.0 (5.3 to 85.3) | 0 (0.0 to 33.6) | 28.6 (3.7 to 71.0) | 17.9 (6.1 to 36.9) |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b and Phase 2 Arms A, B and C: Duration of Response (DOR) as Assessed Using RANO Criteria

| | |
|-----------------|--|
| End point title | Phase 1b and Phase 2 Arms A, B and C: Duration of Response (DOR) as Assessed Using RANO Criteria |
|-----------------|--|

End point description:

DOR is defined as the time from the date of the earliest documented response to disease progression or death for any cause whichever occurs earlier. Efficacy Analysis Set; 9999 = Not estimable due to insufficient number of events

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first documentation of CR or PR to first documentation of disease progression or death (up to 3 years and 7.5 months)

| End point values | Arm A: Dose Escalation (DE) - Pamiparib 2Wks + RT 6 Wks | Arm A: DE- Pamiparib 4 Wks + RT 6 Wks | Arm A: DE- Pamiparib 6Wks + RT 6 Wks | Arm A: Dose Expansion (E) - Pamiparib 6 Wks + RT 6 Wks |
|----------------------------------|---|---------------------------------------|--------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[18] | 1 | 0 ^[19] | 1 ^[20] |
| Units: Months | | | | |
| median (confidence interval 95%) | (to) | 6.44 (-9999 to 9999) | (to) | 10.32 (-9999 to 9999) |

Notes:

[18] - Only the participants with objective responses were included in DOR analysis.

[19] - Only the participants with objective responses were included in DOR analysis.

[20] - Only the participants with objective responses were included in DOR analysis.

| End point values | Arm B: DE- Pamiparib 6 Wks + RT 6 Wks + + Temozolomide | Arm C: DE - Pamiparib + Temozolomide 20 mg | Arm C: DE - Pamiparib + Temozolomide 40 mg | Arm C: E- Pamiparib + Temozolomide 60 mg |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[21] | 0 ^[22] | 1 | 3 |
| Units: Months | | | | |
| median (confidence interval 95%) | (to) | (to) | 11.7 (-9999 to 9999) | 9999 (12.68 to 9999) |

Notes:

[21] - Only the participants with objective responses were included in DOR analysis.

[22] - Only the participants with objective responses were included in DOR analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b and Phase2 Arms A, B and C: Progression free survival (PFS) as Assessed Using RANO Criteria

| | |
|-----------------|--|
| End point title | Phase 1b and Phase2 Arms A, B and C: Progression free survival (PFS) as Assessed Using RANO Criteria |
|-----------------|--|

End point description:

PFS is defined as the time from the first dose date to disease progression per RANO criteria or death, whichever occurs first.

9999 = Not estimable due to insufficient number of events

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the date of first dose up to first documentation of disease progression or death (up to 3 years and 7.5 months)

| End point values | Arm A: Dose Escalation (DE) - Pamiparib 2Wks + RT 6 Wks | Arm A: DE- Pamiparib 4 Wks + RT 6 Wks | Arm A: DE- Pamiparib 6Wks + RT 6 Wks | Arm A: Dose Expansion (E) - Pamiparib 6 Wks + RT 6 Wks |
|----------------------------------|---|---------------------------------------|--------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 8 | 9 | 40 |
| Units: Months | | | | |
| median (confidence interval 95%) | 3.12 (2.79 to 3.29) | 8.94 (3.78 to 11.56) | 2.56 (2.14 to 9999) | 4.44 (3.29 to 6.24) |

| End point values | Arm B: DE- Pamiparib 6 Wks + RT 6 Wks + + Temozolomide | Arm C: DE - Pamiparib + Temozolomide 20 mg | Arm C: DE - Pamiparib + Temozolomide 40 mg | Arm C: E- Pamiparib + Temozolomide 60 mg |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 9 | 8 | 30 |
| Units: Months | | | | |
| median (confidence interval 95%) | 5.75 (2.37 to 6.47) | 1.81 (0.82 to 3.48) | 2.66 (0.66 to 7.39) | 1.87 (1.48 to 1.91) |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b and Phase2 Arms A, B and C: Overall survival (OS)

| | |
|-----------------|--|
| End point title | Phase 1b and Phase2 Arms A, B and C: Overall survival (OS) |
|-----------------|--|

End point description:

OS is defined as the time from the first dose date to date of death for any cause. 9999 = Not estimable due to insufficient number of events.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From the date of first dose up to EOS visit (3 years and 7.5 months) | |

| End point values | Arm A: Dose Escalation (DE) - Pamiparib 2Wks + RT 6 Wks | Arm A: DE- Pamiparib 4 Wks + RT 6 Wks | Arm A: DE- Pamiparib 6Wks + RT 6 Wks | Arm A: Dose Expansion (E) - Pamiparib 6 Wks + RT 6 Wks |
|----------------------------------|---|---------------------------------------|--------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 8 | 9 | 40 |
| Units: Months | | | | |
| median (confidence interval 95%) | 14.46 (13.93 to 14.98) | 13.44 (4.14 to 20.24) | 10.25 (4.44 to 19.84) | 12.71 (9.79 to 14.46) |

| End point values | Arm B: DE- Pamiparib 6 Wks + RT 6 Wks + + Temozolomide | Arm C: DE - Pamiparib + Temozolomide 20 mg | Arm C: DE - Pamiparib + Temozolomide 40 mg | Arm C: E- Pamiparib + Temozolomide 60 mg |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 9 | 8 | 30 |
| Units: Months | | | | |
| median (confidence interval 95%) | 14.23 (7.98 to 9999) | 6.00 (2.60 to 9.79) | 8.62 (2.96 to 9999) | 7.79 (6.21 to 10.68) |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2 Arms A and C Expansion Phase: Number of Participants with Treatment Emergent adverse events (TEAEs) and Serious adverse events (SAEs)

| | |
|-----------------|---|
| End point title | Phase 2 Arms A and C Expansion Phase: Number of Participants with Treatment Emergent adverse events (TEAEs) and Serious adverse events (SAEs) ^[23] |
|-----------------|---|

End point description:

A treatment-emergent adverse event (TEAE) is defined as an AE that had an onset date on or after first dose of study treatment or was worsening in severity from baseline (pretreatment) up to 30 days following permanent study treatment discontinuation or initiation of new anti-cancer therapy, whichever occurs first.

An SAE is any untoward medical occurrence that, at any dose meets at least one of the following criteria: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect, is considered a significant medical AE based on medical judgment. SAEs were collected from the day the participant signs the Informed Consent Form (ICF).

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From initiation of study treatment (for TEAE) or from the date informed consent has been signed (for SAE), until 30 days after last study treatment or initiation of new anticancer therapy, whichever occurs first | |

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Arms A and C data are reported per protocol.

| End point values | Arm A: Dose Expansion (E) - Pamiparib 6 Wks + RT 6 Wks | Arm C: E- Pamiparib + Temozolomide 60 mg | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 30 | | |
| Units: Number of participants | | | | |
| Participants with at Least 1 TEAE | 40 | 29 | | |
| TEAE with Grade 3 or Higher | 25 | 19 | | |
| Treatment Emergent SAEs | 18 | 11 | | |
| TEAE Leading to Death | 3 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2 Expansion Phase Arm A and C: Number of Participants with Clinically Relevant Changes in Vital signs and Clinical Laboratory Measurements

| | |
|-----------------|--|
| End point title | Phase 2 Expansion Phase Arm A and C: Number of Participants with Clinically Relevant Changes in Vital signs and Clinical Laboratory Measurements ^[24] |
|-----------------|--|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the date of first dose up to EOS visit (3 years and 7.5 months)

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Arms A and C data are reported per protocol

| End point values | Arm A: Dose Expansion (E) - Pamiparib 6 Wks + RT 6 Wks | Arm C: E- Pamiparib + Temozolomide 60 mg | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 30 | | |
| Units: Number of participants | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2 Arms A and C Expansion Phase: Number of Cycles of Treatment Received by Participants

| | |
|-----------------|--|
| End point title | Phase 2 Arms A and C Expansion Phase: Number of Cycles of Treatment Received by Participants ^[25] |
|-----------------|--|

End point description:

Data shows the percentage of participants who received treatment for the given number of cycles.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From date of first dose up to EOS Visit (up to 3 years and 7.5 months)

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Arms A and C data are reported per protocol

| End point values | Arm A: Dose Expansion (E) - Pamiparib 6 Wks + RT 6 Wks | Arm C: E- Pamiparib + Temozolomide 60 mg | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 30 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| <1 cycle | 10.3 | 26.7 | | |
| 1 cycle | 31.0 | 26.7 | | |
| 3 cycles | 6.9 | 3.3 | | |
| 2 cycles | 6.9 | 23.3 | | |
| 4 cycles | 10.3 | 3.3 | | |
| 5 cycles | 10.3 | 0.0 | | |
| 6 cycles | 10.3 | 0.0 | | |
| 7 cycles | 0.0 | 0.0 | | |
| >7 cycles | 13.8 | 16.7 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2 Arms A and C Expansion Phase: Average Dose Intensity of Pamiparib and TMZ Received per Participant

| | |
|-----------------|--|
| End point title | Phase 2 Arms A and C Expansion Phase: Average Dose Intensity of Pamiparib and TMZ Received per Participant ^[26] |
|-----------------|--|

End point description:

9999 = Not applicable since no TMZ was administered in this arm

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From date of first dose up to EOS Visit (up to 3 years and 7.5 months)

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Arms A and C data are reported per protocol.

| End point values | Arm A: Dose Expansion (E) - Pamiparib 6 Wks + RT 6 Wks | Arm C: E- Pamiparib + Temozolomide 60 mg | | |
|--------------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 30 | | |
| Units: Milligrams/Day | | | | |
| arithmetic mean (standard deviation) | | | | |
| Pamiparib | 109.0 (± 22.07) | 109.5 (± 15.22) | | |
| TMZ | 9999 (± 9999) | 19.6 (± 11.60) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From initiation of study treatment (for TEAE) or from the date informed consent has been signed (for SAE), until
30 days after last study treatment or initiation of new anticancer therapy, whichever occurs first

Adverse event reporting additional description:

A treatment-emergent adverse event (TEAE) is defined as an AE that had an onset date on or after first dose of study treatment or was worsening in severity from baseline (pretreatment) up to 30 days following permanent study treatment discontinuation or initiation of new anti-cancer therapy, whichever occurs first.

An SAE is any untoward medical o

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 23.0 |

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Arm 1Arm A: DE - Pamiparib 2 Wks + Radiation Therapy (RT) 6 Wk |
|-----------------------|--|

Reporting group description:

Participants with newly diagnosed unmethylated glioblastoma (GBM) received 60 mg pamiparib orally BID for 2 weeks in combination with up to 60 Gy radiation for 6 weeks

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Arm A: DE-Pamiparib 4 Wks + RT 6 Wks |
|-----------------------|--------------------------------------|

Reporting group description:

Participants with newly diagnosed unmethylated GBM received 60 mg pamiparib orally for 4 weeks in combination with up to 60 Gy radiation for 6 weeks

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Arm A: DE- Pamiparib 6Wks + RT 6 Wks |
|-----------------------|--------------------------------------|

Reporting group description:

Participants with newly diagnosed unmethylated GBM received 60 mg pamiparib orally for 6 weeks in combination with up to 60 Gy radiation for 6 weeks

| | |
|-----------------------|--|
| Reporting group title | Arm A: Dose Expansion (E) - Pamiparib 6 Wks + RT 6 Wks |
|-----------------------|--|

Reporting group description:

Participants with newly diagnosed unmethylated GBM received 60 mg pamiparib orally for 6 weeks in combination with up to 60 Gy radiation for 6 weeks

| | |
|-----------------------|---|
| Reporting group title | Arm B: DE-Pamiparib 6 Wks + RT 6 Wks + Temozolomide |
|-----------------------|---|

Reporting group description:

Participants with newly diagnosed unmethylated GBM received 60 mg pamiparib orally for 6 weeks in combination with up to 60 Gy radiation for 6 weeks and 60 mg temozolomide Wks 1 and 5

| | |
|-----------------------|--|
| Reporting group title | Arm C: DE – Pamiparib + Temozolomide 20 mg |
|-----------------------|--|

Reporting group description:

Participants with both methylated and unmethylated recurrent/refractory GBM received 60 mg pamiparib BID and 20 mg temozolomide once daily orally from Day 1 to Day 21

| | |
|-----------------------|--|
| Reporting group title | Arm C: DE – Pamiparib + Temozolomide 40 mg |
|-----------------------|--|

Reporting group description:

Participants with both methylated and unmethylated recurrent/refractory GBM received 60 mg pamiparib BID and 40 mg temozolomide once daily orally from Day 1 to Day 21

| | |
|-----------------------|--|
| Reporting group title | Arm C: E- Pamiparib + Temozolomide 60 mg |
|-----------------------|--|

Reporting group description:

Participants with both methylated and unmethylated recurrent/refractory GBM received 60 mg pamiparib BID and 60 mg temozolomide once daily orally from Day 1 to Day 7

| Serious adverse events | Arm 1Arm A: DE - Pamiparib 2 Wks + Radiation Therapy (RT) 6 Wk | Arm A: DE- Pamiparib 4 Wks + RT 6 Wks | Arm A: DE- Pamiparib 6Wks + RT 6 Wks |
|---|--|---------------------------------------|--------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 8 (25.00%) | 2 / 9 (22.22%) |
| number of deaths (all causes) | 2 | 7 | 8 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Malignant melanoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour flare | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolism | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |

| | | | |
|---|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Impaired healing | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Laryngeal haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |

| | | | |
|---|---------------|---------------|---------------|
| Agitation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subarachnoid haematoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Aphasia | | | |

| | | | |
|---|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Apraxia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Brain oedema | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral cyst | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depressed level of consciousness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysaesthesia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysarthria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemiparesis | | | |

| | | | |
|---|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemiplegia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydrocephalus | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Partial seizures | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychogenic seizure | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vasogenic cerebral oedema | | | |

| | | | |
|---|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (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 | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile neutropenia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Anal incontinence | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (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 |

| | | | |
|---|---------------|---------------|----------------|
| Nausea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |

| | | | |
|---|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Arm A: Dose Expansion (E) - Pamiparib 6 Wks + RT 6 Wks | Arm B: DE- Pamiparib 6 Wks + RT 6 Wks + Temozolomide | Arm C: DE - Pamiparib + Temozolomide 20 mg |
|---|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 18 / 40 (45.00%) | 2 / 9 (22.22%) | 4 / 9 (44.44%) |
| number of deaths (all causes) | 27 | 4 | 8 |
| number of deaths resulting from adverse events | 3 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Malignant melanoma | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour flare | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (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 |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolism | | | |

| | | | |
|--|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematoma | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fatigue | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gait disturbance | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (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 |
| Impaired healing | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |

| | | | |
|---|----------------|---------------|---------------|
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Laryngeal haemorrhage | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 3 / 40 (7.50%) | 0 / 9 (0.00%) | 0 / 9 (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 |
| Psychiatric disorders | | | |
| Agitation | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (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 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mental status changes | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (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 |
| Suicide attempt | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (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 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subarachnoid haematoma | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Aphasia | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Apraxia | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Brain oedema | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (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 |
| Cerebral cyst | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depressed level of consciousness | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (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 |
| Dysaesthesia | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysarthria | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (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 |
| Hemiparesis | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemiplegia | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (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 |
| Hydrocephalus | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorder | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (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 |
| Partial seizures | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (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 |
| Psychogenic seizure | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 1 / 9 (11.11%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (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 | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (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 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile neutropenia | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (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 |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |

| | | | |
|---|----------------|---------------|---------------|
| Anal incontinence | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (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 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (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 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (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 | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neck pain | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (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 | | | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (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 |
| Wound infection | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (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 |

| Serious adverse events | Arm C: DE – Pamiparib + Temozolomide 40 mg | Arm C: E- Pamiparib + Temozolomide 60 mg | |
|---|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | 11 / 30 (36.67%) | |
| number of deaths (all causes) | 6 | 21 | |
| number of deaths resulting from adverse events | 0 | 1 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Malignant melanoma | | | |

| | | | |
|--|----------------|----------------|--|
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tumour flare | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Embolism | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 30 (6.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematoma | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chills | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Fatigue | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Impaired healing | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Laryngeal haemorrhage | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Agitation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 30 (3.33%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---------------|----------------|--|
| Mental status changes | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subarachnoid haematoma | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Aphasia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Apraxia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Brain oedema | | | |

| | | | |
|---|---------------|----------------|--|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral cyst | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depressed level of consciousness | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysaesthesia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysarthria | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hemiparesis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hemiplegia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hydrocephalus | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorder | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Partial seizures | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychogenic seizure | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Seizure | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vasogenic cerebral oedema | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Anal incontinence | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|---------------|----------------|--|
| Rash | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 30 (6.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neck pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound infection | | | |

| | | | |
|---|---------------|----------------|--|
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 3 %

| Non-serious adverse events | Arm 1Arm A: DE - Pamiparib 2 Wks + Radiation Therapy (RT) 6 Wk | Arm A: DE- Pamiparib 4 Wks + RT 6 Wks | Arm A: DE- Pamiparib 6Wks + RT 6 Wks |
|---|--|---------------------------------------|--------------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 3 (100.00%) | 8 / 8 (100.00%) | 9 / 9 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Renal hamartoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pallor | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chills | | | |

| | | | |
|---------------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Early satiety | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Fatigue | | | |
| subjects affected / exposed | 3 / 3 (100.00%) | 2 / 8 (25.00%) | 6 / 9 (66.67%) |
| occurrences (all) | 3 | 2 | 7 |
| Feeling cold | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Swelling face | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Vessel puncture site pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal | | | |

| | | | |
|---------------------------------------|---------------|----------------|----------------|
| disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dysphonia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 8 (25.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Hiccups | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laryngeal inflammation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 1 | 1 |
| Nasal polyps | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Productive cough | | | |

| | | | |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus congestion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Psychiatric disorders | | | |
| Agitation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Alcohol abuse | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 8 (25.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 2 | 1 |
| Decreased interest | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|---------------|---------------|---------------|
| Insomnia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Irritability | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Persistent depressive disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood bilirubin unconjugated increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cortisol decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphocyte count decreased | | | |

| | | | |
|--|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye contusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fall | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pseudomeningocele | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Radiation injury | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Radiation skin injury | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Skin laceration subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Subdural haematoma subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 8 (12.50%) 1 | 0 / 9 (0.00%) 0 |
| Traumatic haematoma subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Cardiac disorders | | | |
| Angina pectoris subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Bradycardia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 8 (12.50%) 1 | 0 / 9 (0.00%) 0 |
| Sinus tachycardia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Tachycardia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 8 (12.50%) 1 | 0 / 9 (0.00%) 0 |
| Ventricular extrasystoles subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Nervous system disorders | | | |
| Ageusia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Amnesia subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 1 / 8 (12.50%) 1 | 0 / 9 (0.00%) 0 |
| Aphasia | | | |

| | | | |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 3 / 9 (33.33%) |
| occurrences (all) | 0 | 1 | 3 |
| Ataxia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Balance disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all) | 0 | 0 | 2 |
| Brain oedema | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Carpal tunnel syndrome | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cerebrospinal fluid leakage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cognitive disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Disturbance in attention | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Drizzling | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysaesthesia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysarthria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysgeusia | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyslexia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Encephalopathy | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Facial paralysis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Facial paresis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 8 (12.50%) | 4 / 9 (44.44%) |
| occurrences (all) | 1 | 1 | 4 |
| Hemianopia homonymous | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Hemiparesis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypersomnia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Memory impairment | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Muscle spasticity | | | |

| | | | |
|--------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myoclonus | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 1 | 1 |
| Partial seizures | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 1 | 1 |
| Peripheral motor neuropathy | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Taste disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Tremor | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 2 |
| Visual field defect | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|--|--------------------|---------------------|---------------------|
| Increased tendency to bruise subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Leukopenia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Lymphopenia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Neutropenia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Ear and labyrinth disorders | | | |
| Ear congestion subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 8 (12.50%) 1 | 0 / 9 (0.00%) 0 |
| Ear discomfort subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 8 (12.50%) 1 | 0 / 9 (0.00%) 0 |
| Ear pain subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Hypoacusis subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Tinnitus subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Vertigo subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 1 / 9 (11.11%) 2 |
| Eye disorders | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| Dry eye | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Erythema of eyelid | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lacrimation increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 1 | 1 |
| Photophobia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Visual impairment | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 8 (12.50%) | 1 / 9 (11.11%) |
| occurrences (all) | 1 | 1 | 1 |
| Breath odour | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Colitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |

| | | | |
|----------------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 3 / 9 (33.33%) |
| occurrences (all) | 0 | 1 | 3 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 8 (25.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 1 | 1 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eructation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Femoral hernia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperaesthesia teeth | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Melaena | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nausea | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 3 / 8 (37.50%) | 5 / 9 (55.56%) |
| occurrences (all) | 1 | 3 | 5 |
| Oral dysaesthesia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Retching | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth discolouration | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Umbilical hernia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 8 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all) | 1 | 0 | 2 |
| Vomiting projectile | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Hepatic lesion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Alopecia | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 2 / 3 (66.67%) | 2 / 8 (25.00%) | 2 / 9 (22.22%) |
| occurrences (all) | 2 | 2 | 2 |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 1 | 1 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pain of skin | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 8 (25.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Petechiae | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Purpura | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin atrophy | | | |

| | | | |
|--|--------------------|--------------------|--------------------|
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Polyuria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Back pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flank pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Groin pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |

| | | | |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 1 | 1 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in jaw | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tenosynovitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|------------------------------------|---------------|----------------|---------------|
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Osteomyelitis chronic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Wound infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 8 (12.50%) | 3 / 9 (33.33%) |
| occurrences (all) | 1 | 1 | 3 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 1 | 0 | 1 |
| Hypernatraemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | Arm A: Dose Expansion (E) - Pamiparib 6 Wks + RT 6 Wks | Arm B: DE- Pamiparib 6 Wks + RT 6 Wks + Temozolomide | Arm C: DE - Pamiparib + Temozolomide 20 mg |
|---|--|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 40 / 40 (100.00%) | 9 / 9 (100.00%) | 9 / 9 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Renal hamartoma | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |

| | | | |
|--|------------------|----------------|----------------|
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 2 / 9 (22.22%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 9 (11.11%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 1 | 1 |
| Pallor | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Early satiety | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 29 / 40 (72.50%) | 6 / 9 (66.67%) | 1 / 9 (11.11%) |
| occurrences (all) | 34 | 7 | 1 |
| Feeling cold | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gait disturbance | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 2 / 9 (22.22%) | 1 / 9 (11.11%) |
| occurrences (all) | 2 | 2 | 1 |
| Influenza like illness | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Malaise | | | |
| subjects affected / exposed | 3 / 40 (7.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 1 | 0 | 1 |
| Oedema peripheral | | | |
| subjects affected / exposed | 4 / 40 (10.00%) | 2 / 9 (22.22%) | 1 / 9 (11.11%) |
| occurrences (all) | 4 | 2 | 1 |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 1 | 0 | 1 |
| Swelling face | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vessel puncture site pain | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 4 / 40 (10.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 5 | 0 | 1 |
| Dysphonia | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Dyspnoea exertional | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hiccups | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 2 |
| Laryngeal inflammation | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 3 / 40 (7.50%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Nasal polyps | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinus congestion | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wheezing | | | |

| | | | |
|--|---------------------|--------------------|--------------------|
| subjects affected / exposed occurrences (all) | 0 / 40 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Psychiatric disorders | | | |
| Agitation | | | |
| subjects affected / exposed | 4 / 40 (10.00%) | 1 / 9 (11.11%) | 1 / 9 (11.11%) |
| occurrences (all) | 4 | 1 | 1 |
| Alcohol abuse | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 6 / 40 (15.00%) | 2 / 9 (22.22%) | 0 / 9 (0.00%) |
| occurrences (all) | 6 | 2 | 0 |
| Confusional state | | | |
| subjects affected / exposed | 4 / 40 (10.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Decreased interest | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Depression | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 6 / 40 (15.00%) | 2 / 9 (22.22%) | 0 / 9 (0.00%) |
| occurrences (all) | 6 | 2 | 0 |
| Irritability | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Persistent depressive disorder | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 3 / 40 (7.50%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 3 | 0 | 1 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 3 / 40 (7.50%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 3 | 0 | 1 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 1 / 9 (11.11%) | 2 / 9 (22.22%) |
| occurrences (all) | 4 | 1 | 2 |
| Blood bilirubin unconjugated increased | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 4 / 40 (10.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Cortisol decreased | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 3 / 40 (7.50%) | 2 / 9 (22.22%) | 3 / 9 (33.33%) |
| occurrences (all) | 3 | 2 | 3 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 6 / 40 (15.00%) | 3 / 9 (33.33%) | 2 / 9 (22.22%) |
| occurrences (all) | 9 | 3 | 2 |
| Platelet count decreased | | | |
| subjects affected / exposed | 7 / 40 (17.50%) | 1 / 9 (11.11%) | 3 / 9 (33.33%) |
| occurrences (all) | 8 | 2 | 3 |
| Weight decreased | | | |
| subjects affected / exposed | 9 / 40 (22.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 10 | 0 | 0 |
| White blood cell count decreased | | | |

| | | | |
|--|----------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 6 / 40 (15.00%) 8 | 4 / 9 (44.44%) 7 | 2 / 9 (22.22%) 2 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Eye contusion | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fall | | | |
| subjects affected / exposed | 5 / 40 (12.50%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 6 | 1 | 0 |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pseudomeningocele | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Radiation injury | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Radiation skin injury | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Traumatic haematoma | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Ventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Ageusia | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Amnesia | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aphasia | | | |
| subjects affected / exposed | 6 / 40 (15.00%) | 1 / 9 (11.11%) | 1 / 9 (11.11%) |
| occurrences (all) | 7 | 2 | 1 |
| Ataxia | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Balance disorder | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Brain oedema | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Carpal tunnel syndrome | | | |

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| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cerebrospinal fluid leakage | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cognitive disorder | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 0 / 9 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all) | 2 | 0 | 2 |
| Disturbance in attention | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 1 | 0 | 1 |
| Dizziness | | | |
| subjects affected / exposed | 11 / 40 (27.50%) | 2 / 9 (22.22%) | 1 / 9 (11.11%) |
| occurrences (all) | 12 | 2 | 1 |
| Drizzling | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysaesthesia | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Dysarthria | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 10 / 40 (25.00%) | 2 / 9 (22.22%) | 1 / 9 (11.11%) |
| occurrences (all) | 11 | 2 | 1 |
| Dyslexia | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Encephalopathy | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Facial paralysis | | | |

| | | | |
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| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Facial paresis | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Headache | | | |
| subjects affected / exposed | 18 / 40 (45.00%) | 2 / 9 (22.22%) | 1 / 9 (11.11%) |
| occurrences (all) | 24 | 3 | 1 |
| Hemianopia homonymous | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hemiparesis | | | |
| subjects affected / exposed | 8 / 40 (20.00%) | 3 / 9 (33.33%) | 3 / 9 (33.33%) |
| occurrences (all) | 9 | 3 | 3 |
| Hypersomnia | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Memory impairment | | | |
| subjects affected / exposed | 6 / 40 (15.00%) | 1 / 9 (11.11%) | 1 / 9 (11.11%) |
| occurrences (all) | 6 | 1 | 1 |
| Muscle spasticity | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myoclonus | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 1 / 9 (11.11%) | 1 / 9 (11.11%) |
| occurrences (all) | 1 | 1 | 1 |
| Partial seizures | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Peripheral motor neuropathy | | | |

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| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 2 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Seizure | | | |
| subjects affected / exposed | 6 / 40 (15.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 9 | 0 | 1 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Taste disorder | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tremor | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Visual field defect | | | |
| subjects affected / exposed | 3 / 40 (7.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 13 / 40 (32.50%) | 4 / 9 (44.44%) | 3 / 9 (33.33%) |
| occurrences (all) | 19 | 7 | 3 |
| Increased tendency to bruise | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lymphopenia | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |

| | | | |
|---|----------------------|---------------------|---------------------|
| Thrombocytopenia subjects affected / exposed occurrences (all) | 4 / 40 (10.00%) 5 | 1 / 9 (11.11%) 1 | 0 / 9 (0.00%) 0 |
| Ear and labyrinth disorders | | | |
| Ear congestion subjects affected / exposed occurrences (all) | 0 / 40 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Ear discomfort subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 1 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Ear pain subjects affected / exposed occurrences (all) | 2 / 40 (5.00%) 2 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Hypoacusis subjects affected / exposed occurrences (all) | 2 / 40 (5.00%) 2 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Tinnitus subjects affected / exposed occurrences (all) | 3 / 40 (7.50%) 3 | 1 / 9 (11.11%) 1 | 0 / 9 (0.00%) 0 |
| Vertigo subjects affected / exposed occurrences (all) | 0 / 40 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Eye disorders | | | |
| Dry eye subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 1 | 0 / 9 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Erythema of eyelid subjects affected / exposed occurrences (all) | 0 / 40 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Lacrimation increased subjects affected / exposed occurrences (all) | 0 / 40 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Photophobia subjects affected / exposed occurrences (all) | 0 / 40 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Vision blurred | | | |

| | | | |
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| subjects affected / exposed | 3 / 40 (7.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Visual impairment | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 5 / 40 (12.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 8 | 0 | 0 |
| Breath odour | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Colitis | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 14 / 40 (35.00%) | 3 / 9 (33.33%) | 2 / 9 (22.22%) |
| occurrences (all) | 16 | 3 | 2 |
| Diarrhoea | | | |
| subjects affected / exposed | 12 / 40 (30.00%) | 2 / 9 (22.22%) | 2 / 9 (22.22%) |
| occurrences (all) | 17 | 2 | 2 |
| Dry mouth | | | |
| subjects affected / exposed | 4 / 40 (10.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |

| | | | |
|----------------------------------|------------------|----------------|----------------|
| Eructation | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Femoral hernia | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperaesthesia teeth | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Melaena | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 29 / 40 (72.50%) | 7 / 9 (77.78%) | 4 / 9 (44.44%) |
| occurrences (all) | 42 | 8 | 4 |
| Oral dysaesthesia | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Retching | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |

| | | | |
|--|------------------------|---------------------|---------------------|
| Tooth discolouration subjects affected / exposed occurrences (all) | 0 / 40 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Umbilical hernia subjects affected / exposed occurrences (all) | 0 / 40 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Vomiting subjects affected / exposed occurrences (all) | 13 / 40 (32.50%) 20 | 2 / 9 (22.22%) 2 | 1 / 9 (11.11%) 1 |
| Vomiting projectile subjects affected / exposed occurrences (all) | 0 / 40 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Hepatobiliary disorders Hepatic lesion subjects affected / exposed occurrences (all) | 0 / 40 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all) | 0 / 40 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Alopecia subjects affected / exposed occurrences (all) | 14 / 40 (35.00%) 16 | 4 / 9 (44.44%) 4 | 0 / 9 (0.00%) 0 |
| Dermatitis subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 1 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Dermatitis acneiform subjects affected / exposed occurrences (all) | 2 / 40 (5.00%) 2 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Dermatitis contact subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 1 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Dry skin subjects affected / exposed occurrences (all) | 0 / 40 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Erythema | | | |

| | | | |
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| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pain of skin | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Petechiae | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Purpura | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 3 / 9 (33.33%) | 2 / 9 (22.22%) |
| occurrences (all) | 1 | 3 | 2 |
| Skin atrophy | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematuria | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|-----------------|----------------|----------------|
| Polyuria | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Urinary incontinence | | | |
| subjects affected / exposed | 6 / 40 (15.00%) | 2 / 9 (22.22%) | 1 / 9 (11.11%) |
| occurrences (all) | 6 | 2 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 2 / 9 (22.22%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Back pain | | | |
| subjects affected / exposed | 3 / 40 (7.50%) | 1 / 9 (11.11%) | 1 / 9 (11.11%) |
| occurrences (all) | 3 | 1 | 1 |
| Flank pain | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Groin pain | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 1 / 9 (11.11%) | 1 / 9 (11.11%) |
| occurrences (all) | 1 | 1 | 1 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pain in extremity | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pain in jaw | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tenosynovitis | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye infection | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 2 / 9 (22.22%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 40 (2.50%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Osteomyelitis chronic | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|------------------------|---------------------|---------------------|
| Postoperative wound infection subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 1 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Sinusitis subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 1 | 1 / 9 (11.11%) 1 | 0 / 9 (0.00%) 0 |
| Tooth infection subjects affected / exposed occurrences (all) | 0 / 40 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 2 / 40 (5.00%) 3 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 2 | 1 / 9 (11.11%) 1 | 0 / 9 (0.00%) 0 |
| Wound infection subjects affected / exposed occurrences (all) | 0 / 40 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite subjects affected / exposed occurrences (all) | 14 / 40 (35.00%) 15 | 4 / 9 (44.44%) 4 | 2 / 9 (22.22%) 2 |
| Dehydration subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 2 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 2 / 40 (5.00%) 3 | 1 / 9 (11.11%) 1 | 2 / 9 (22.22%) 2 |
| Hypernatraemia subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 1 | 1 / 9 (11.11%) 1 | 1 / 9 (11.11%) 1 |
| Hypoalbuminaemia subjects affected / exposed occurrences (all) | 1 / 40 (2.50%) 1 | 0 / 9 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Hypocalcaemia | | | |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 40 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypokalaemia | | | |
| subjects affected / exposed | 2 / 40 (5.00%) | 2 / 9 (22.22%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 4 / 40 (10.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 7 | 0 | 0 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 3 / 40 (7.50%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 4 | 0 | 1 |

| Non-serious adverse events | Arm C: DE – Pamiparib + Temozolomide 40 mg | Arm C: E- Pamiparib + Temozolomide 60 mg | |
|--|---|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 7 / 8 (87.50%) | 29 / 30 (96.67%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Renal hamartoma | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Pallor | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| General disorders and administration site conditions | | | |

| | | |
|-----------------------------|----------------|------------------|
| Asthenia | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 2 |
| Chest pain | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Chills | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Early satiety | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Fatigue | | |
| subjects affected / exposed | 4 / 8 (50.00%) | 17 / 30 (56.67%) |
| occurrences (all) | 4 | 20 |
| Feeling cold | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Gait disturbance | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 2 / 30 (6.67%) |
| occurrences (all) | 1 | 2 |
| Influenza like illness | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Malaise | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 2 |
| Non-cardiac chest pain | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Oedema peripheral | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 3 / 30 (10.00%) |
| occurrences (all) | 0 | 4 |
| Pyrexia | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 3 / 30 (10.00%) |
| occurrences (all) | 0 | 3 |

| | | | |
|---|---------------|-----------------|--|
| Swelling face | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Vessel puncture site pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Cough | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 30 (6.67%) | |
| occurrences (all) | 0 | 3 | |
| Dysphonia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 4 / 30 (13.33%) | |
| occurrences (all) | 0 | 5 | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hiccups | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Laryngeal inflammation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Nasal congestion | | | |

| | | | |
|-----------------------------|----------------|-----------------|--|
| subjects affected / exposed | 1 / 8 (12.50%) | 3 / 30 (10.00%) | |
| occurrences (all) | 1 | 3 | |
| Nasal polyps | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Productive cough | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Sinus congestion | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Wheezing | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Psychiatric disorders | | | |
| Agitation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Alcohol abuse | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Confusional state | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 3 / 30 (10.00%) | |
| occurrences (all) | 0 | 3 | |

| | | | |
|--|---------------------|----------------------|--|
| Decreased interest subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 30 (0.00%) 0 | |
| Depression subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 3 / 30 (10.00%) 3 | |
| Insomnia subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 4 / 30 (13.33%) 4 | |
| Irritability subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 30 (0.00%) 0 | |
| Persistent depressive disorder subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 1 / 30 (3.33%) 1 | |
| Suicidal ideation subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 1 / 30 (3.33%) 1 | |
| Investigations | | | |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 1 / 30 (3.33%) 1 | |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 30 (0.00%) 0 | |
| Blood bilirubin increased subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 1 / 30 (3.33%) 1 | |
| Blood bilirubin unconjugated increased subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 30 (0.00%) 0 | |
| Blood creatinine increased subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 2 / 30 (6.67%) 3 | |
| Cortisol decreased | | | |

| | | | |
|--|----------------|-----------------|--|
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 4 / 30 (13.33%) | |
| occurrences (all) | 1 | 5 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 5 / 30 (16.67%) | |
| occurrences (all) | 2 | 10 | |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 8 / 30 (26.67%) | |
| occurrences (all) | 1 | 18 | |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 3 / 30 (10.00%) | |
| occurrences (all) | 1 | 3 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 6 / 30 (20.00%) | |
| occurrences (all) | 1 | 10 | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 3 / 30 (10.00%) | |
| occurrences (all) | 0 | 3 | |
| Eye contusion | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Fall | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | 5 / 30 (16.67%) | |
| occurrences (all) | 3 | 8 | |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Pseudomeningocele | | | |

| | | | |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 30 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Radiation injury | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Radiation skin injury | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 30 (6.67%) | |
| occurrences (all) | 0 | 3 | |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Traumatic haematoma | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Ventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Nervous system disorders | | | |
| Ageusia | | | |

| | | |
|-----------------------------|----------------|-----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Amnesia | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 0 | 2 |
| Aphasia | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 3 / 30 (10.00%) |
| occurrences (all) | 0 | 3 |
| Ataxia | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Balance disorder | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Brain oedema | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 0 |
| Carpal tunnel syndrome | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Cerebrospinal fluid leakage | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Cognitive disorder | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Disturbance in attention | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Dizziness | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 8 / 30 (26.67%) |
| occurrences (all) | 1 | 8 |
| Drizzling | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Dysaesthesia | | |

| | | |
|-----------------------------|----------------|-----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Dysarthria | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Dysgeusia | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 0 | 3 |
| Dyslexia | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Encephalopathy | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Epilepsy | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 3 |
| Facial paralysis | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Facial paresis | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Headache | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 8 / 30 (26.67%) |
| occurrences (all) | 0 | 11 |
| Hemianopia homonymous | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Hemiparesis | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 4 / 30 (13.33%) |
| occurrences (all) | 1 | 4 |
| Hypersomnia | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 0 | 2 |
| Hypoaesthesia | | |

| | | |
|-------------------------------|---------------|-----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Memory impairment | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Muscle spasticity | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 2 |
| Myoclonus | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Paraesthesia | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 0 | 2 |
| Partial seizures | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Peripheral motor neuropathy | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Peripheral sensory neuropathy | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Seizure | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 4 / 30 (13.33%) |
| occurrences (all) | 0 | 4 |
| Somnolence | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Taste disorder | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Tremor | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Visual field defect | | |

| | | | |
|--|--------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 2 / 30 (6.67%) 2 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | 6 / 30 (20.00%) | |
| occurrences (all) | 6 | 15 | |
| Increased tendency to bruise | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 30 (6.67%) | |
| occurrences (all) | 0 | 2 | |
| Lymphopenia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 4 / 30 (13.33%) | |
| occurrences (all) | 0 | 4 | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 3 / 30 (10.00%) | |
| occurrences (all) | 1 | 3 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 3 / 30 (10.00%) | |
| occurrences (all) | 2 | 3 | |
| Ear and labyrinth disorders | | | |
| Ear congestion | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Ear discomfort | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Ear pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hypoacusis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Tinnitus | | | |

| | | | |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 30 (3.33%) | |
| occurrences (all) | 1 | 1 | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Erythema of eyelid | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Lacrimation increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Photophobia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Visual impairment | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Breath odour | | | |

| | | |
|----------------------------------|----------------|------------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Colitis | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Constipation | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 12 / 30 (40.00%) |
| occurrences (all) | 2 | 17 |
| Diarrhoea | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 4 / 30 (13.33%) |
| occurrences (all) | 1 | 5 |
| Dry mouth | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Dyspepsia | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 0 | 2 |
| Dysphagia | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Eructation | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Femoral hernia | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Flatulence | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Gastrooesophageal reflux disease | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 30 (3.33%) |
| occurrences (all) | 1 | 1 |
| Haematemesis | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Hyperaesthesia teeth | | |

| | | | |
|-----------------------------|----------------|------------------|--|
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 2 | |
| Melaena | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Nausea | | | |
| subjects affected / exposed | 4 / 8 (50.00%) | 13 / 30 (43.33%) | |
| occurrences (all) | 5 | 18 | |
| Oral dysaesthesia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Retching | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Tooth discolouration | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Umbilical hernia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Vomiting | | | |
| subjects affected / exposed | 4 / 8 (50.00%) | 7 / 30 (23.33%) | |
| occurrences (all) | 5 | 15 | |
| Vomiting projectile | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Hepatobiliary disorders | | | |
| Hepatic lesion | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 2 | |

| | | | |
|--|---------------|----------------|--|
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Dry skin | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Erythema | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Night sweats | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pain of skin | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Petechiae | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pruritus | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Purpura | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 30 (6.67%) | |
| occurrences (all) | 0 | 2 | |
| Skin atrophy | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pollakiuria | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 30 (3.33%) | |
| occurrences (all) | 1 | 1 | |
| Polyuria | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 30 (6.67%) | |
| occurrences (all) | 0 | 2 | |
| Back pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Flank pain | | | |

| | | | |
|-----------------------------|----------------|-----------------|--|
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Groin pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 3 / 30 (10.00%) | |
| occurrences (all) | 1 | 3 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 30 (6.67%) | |
| occurrences (all) | 0 | 3 | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 3 / 30 (10.00%) | |
| occurrences (all) | 0 | 3 | |
| Neck pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Pain in jaw | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Tenosynovitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |
| Eye infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) | |
| occurrences (all) | 0 | 1 | |

| | | |
|-----------------------------------|---------------|----------------|
| Hordeolum | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Influenza | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Oral candidiasis | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 2 |
| Oral herpes | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 0 | 3 |
| Osteomyelitis chronic | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Otitis media | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Pneumonia | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Postoperative wound infection | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Sinusitis | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 |
| Tooth infection | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Upper respiratory tract infection | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |
| Urinary tract infection | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 |

| | | | |
|--|---------------------|----------------------|--|
| Wound infection subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 2 / 30 (6.67%) 2 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 7 / 30 (23.33%) 8 | |
| Dehydration subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 0 / 30 (0.00%) 0 | |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 1 / 30 (3.33%) 1 | |
| Hypernatraemia subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 30 (0.00%) 0 | |
| Hypoalbuminaemia subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 30 (0.00%) 0 | |
| Hypocalcaemia subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 30 (0.00%) 0 | |
| Hypokalaemia subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 1 / 30 (3.33%) 1 | |
| Hyponatraemia subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 1 / 30 (3.33%) 1 | |
| Hypophosphataemia subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 0 / 30 (0.00%) 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|---|
| 23 July 2018 | <p>Overall Inclusion/Exclusion Criteria: Integrated comments received from MHRA regarding contraception language for both males and females and to align this protocol with other pamiparib studies and ensure consistency of language used in describing the process for management of safety.</p> <p>MGMT Analysis: Clarified that the provision of archival tumor tissue for central confirmation of MGMT status is mandatory in the expansion phase of the study because central testing of MGMT promoter status will be done.</p> <p>Criteria Specific to Arm C: To update the criterion for enrollment in Arm C of the study with more precise guidance as to what prior treatments are allowed or excluded and to define the timing of the first progression required for study entry.</p> <p>Overall Study Design: To update that after completion of RT, patients in Arm A (both dose escalation and expansion) and Arm B dose escalation have the option to continue receiving pamiparib in combination with TMZ (maintenance treatment); to note that for Arm B expansion, maintenance treatment of pamiparib in combination with TMZ will be mandatory; and lastly, overall, to make editorial and formatting changes throughout to enhance clarity and readability.</p> <p>Safety: Update the DLT criteria to reflect management of cytopenias in a GBM population and to align this protocol with other pamiparib studies and ensure consistency of language used in describing the process for management of safety.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported